Adherence to Antiepileptic Drugs among Patients Attending the Neuro Spinal Hospital in the United Arab Emirates

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Background: Adherence to antiepileptic drugs (AEDs) is an integral component of epilepsy management. There are no previous data in the United Arab Emirates (UAE). Objectives: The aim of this study was to assess the prevalence of AED adherence among patients attending the Neuro Spinal Hospital in UAE and to identify the predictors of nonadherence. Materials and Methods: A cross-sectional study was conducted between April 2018 and May 2019, and included consecutive patients with epileptic who were receiving AEDs for at least 6 months. A validated interviewer-administered questionnaire was used. Adherence was assessed by four-item Morisky’s Medication Adherence Scale with a score between 0 and 4. Patients were considered adherent or nonadherent for a score of zero, or 1 and more, respectively. Chi-square test, binary, and multiple logistic regression analysis were used. Results: The study included 315 respondents, 70.8% (n = 223) were adherent, the rest were nonadherent. The most common factor affecting adherence was forgetfulness. Lower education level and having a seizure within the last 6 months were significant risk of nonadherence (odds ratio [OR] 95% confidence interval [CI] = 2.6 (1.2–5.8) and 2.5 (1.3–5.2), respectively), whereas levetiracetam intake reduces the risk of nonadherence (OR: 0.5 [0.2–0.9]). Conclusions: The prevalence of AED adherence was 70.8%. Education level and having a seizure in the last 6 months were significant predictors of nonadherence, whereas levetiracetam intake reduces the risk of nonadherence.

Keywords: Adherence, antiepileptic drugs, factors, prevalence

INTRODUCTION

Epilepsy is the most common neurological problem globally, affecting about 50 million individuals, of whom, approximately 70% could live without seizure if they are properly managed.[1] Adherence to antiepileptic drugs (AEDs) is an integral component of patient management, suboptimal adherence levels is correlated with increased frequency of hospital admissions and healthcare costs.[2]

The prevalence of adherence to AED varies according to different researchers. Although Faught et al.[3] from the United States reported adherence frequency of 74%, a lower percentage for adherence was reported in another study from the Kingdom of Saudi Arabia (KSA) (61.7%)[4] and even lower in a study from Nigeria, where only 32.6% of patients with epilepsy were adherent to their medications.[5]

Many factors can affect patient adherence. The World Health Organization (WHO) grouped them into socioeconomic, health system-related, condition-related, therapy-related, and patient-related factors.[6] Gurumurthy et al.[7] found that adherence was significantly related to the socioeconomic status...
and type of epilepsy. Patients’ beliefs and fear of side effects have been identified by prior studies to be significant factors affecting adherence to AED.\(^8,9\) Other researchers stated additional factors that can affect the adherence of patients with epileptic, such as forgetfulness, personal judgment to stop medication with the absence of seizure, the number of AED used in treatment regimen, and having drug side effects.\(^10-12\)

Several methods are used to assess AED adherence such as review of records, patient self-reporting, pills count, and examining biological markers for detecting levels of AEDs or their metabolites.\(^6\) Morisky’s Medication Adherence Scale-4 (MMAS-4) is a validated assessment tool that has been widely used to assess medication adherence.\(^13\)

Systematic review demonstrated a profound lack of information regarding epilepsy in Arab countries.\(^14\) WHO data confirm a lack of knowledge related to epilepsy in the Eastern Mediterranean Region.\(^15\)

There are no available data from the United Arab Emirates (UAE) related to the prevalence of adherence of patients with epileptic to their medication. Moreover, to know about the factors that determine adherence to AED is very crucial for suggesting strategies to overcome these factors. This study was aimed at assessing the prevalence of AED adherence among patients attending the Tertiary (Neuro Spinal) Hospital in the UAE and to identify predictors of nonadherence. We hypothesize that nonadherence is influenced by sociodemography and disease-related factors.

**Materials and Methods**

A cross-sectional study was conducted between April 2018 and May 2019. The inclusion criteria were patients with epileptic attending the Neuro Spinal Hospital, during the period of study, who were receiving AEDs for at least 6 months, and who accepted to participate and sign an informed consent. For respondents <18 years old, informed consent was obtained from a parent/official guardian.

Consecutive sampling technique was used, and all patients who fulfill the inclusion criteria were approached to participate in this study. The minimum sample size was determined using the following equation: \(n = \frac{z^2pq}{d^2}\), with a marginal error of 0.05 and assumed population proportion adherence of 73% based on recent systematic review.\(^16\)

**Adherence was ascertained using Morisky’s Medication Adherence Scale-4**

The questionnaire consists of four items with a scoring system of “yes” equal to “1” and “no” equal to zero.\(^16\)

In this study, patients were considered nonadherent if they had a score of 1 or more. While ranking the participants by adherence level, patients who had scored zero, “1–2,” or “3–4” were considered to have high, medium, and low adherence level, respectively. In this study, patients are considered nonadherent if they scored 1 or more.

A validated interviewer-administered questionnaire was used. Validation was done by two faculties in the College of Pharmacy, Ajman University, and one consultant neurologist. The questionnaire included information about sociodemography, lifestyle, and factors that can affect adherence.

**Ethical issue**

Ethical approval was received from the Ethics Committees in Ajman University. Signed informed consent was obtained from participants, or the parents/official guardians for <18 years old, before recruiting them in the study. Confidentiality of the information was respected. Anonymity of the participant was ensured by not including the name.

**Methods**

After obtaining official approval from the Ethics Committees in Ajman University and Neuro Spinal Hospital, patients attending the Neuro Spinal Hospital during the time of data collection who fulfilled the inclusion criteria were asked to participate in the study. Those who had accepted to participate were informed about the objectives of the study and asked to sign an informed consent. The participants were interviewed, and their responses were administered in the questionnaires by the researcher.

**Data processing and analysis**

Collected data was entered on an Excel sheet and imported to Statistical Package for the Social Sciences (SPSS) software, version 24.0. Chi-square test and Fisher’s exact test were used to test the association between adherence and independent factor, \(t\) test was used to test the significance of difference between two means, and binary and multiple logistic regression analysis were used to identify factors that affect the risk of nonadherence and to overcome the possible confounding effect of the selected factor.
The study included 315 participants, and the response rate was 95.2%. Table 1 shows the sociodemographic characteristic of the respondents. The participants were most commonly young adults (30–59 years), males, Arab ethnicity, married, employed, with a college or higher level of education, covered by health insurance, and perceived above average economic status.

### Disease characteristics

**Type of epilepsy**

About half of the participants had generalized type of epilepsy (50.5%, n = 159).

**Age at diagnosis of epilepsy**

Most of the participants were first diagnosed to have epilepsy during their childhood or adolescence period (69.1%). The mean (standard deviation [SD]) and median age at diagnosis were 16.8 (16.3%) and 11.0 years, respectively.

**Duration of the disease**

The duration was most commonly >5 years (56.8%, n = 179), followed by 1–5 years (36.8%, n = 116), only 20 respondents have <1-year duration. The mean (SD) and median durations of the disease were 16.8 (16.4) and 11.0 years, respectively.

### Antiepileptic drug therapy

Majority of participants were receiving a monotherapy regimen (76.5%, n = 241). Figure 1 shows the antiepileptic medication used by the participants. It can be seen that levetiracetam and lamotrigine were the most commonly prescribed drugs.

### Adherence to antiepileptic drugs

Using the MMAS-4, it showed that the number of participants who scored zero, 1, 2, and 3 were 223 (70.8%), 32 (10.1%), 44 (14.0%), and 16 (5.1%), respectively. None of the respondents had a score of 4. Thus, considering the earlier stated definition of nonadherence, we found that the prevalence of AEDs adherence and nonadherence were 70.8 and 29.2%, respectively.

### Factors affecting adherence

On asking the participants about factors that can affect AEDs’ adherence, forgetting to take medication was the most commonly reported factor. The relative frequencies of factors that can affect medication adherence among nonadherent participants are present in Figure 2.

### Medication side effect

Fifty-one patients (16.2% of participants) reported having medication side effects. Table 2 shows the types of medication side effects. The most common side effect was nervousness and aggressive behavior (27%).

### Association between adherence and sociodemographic factors

Table 3 shows the association between patients’ adherence and sociodemography factors. Significantly higher frequency of nonadherence was observed among the elderly and lower education level patients compared with other groups.
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Table 4 shows the association between characteristics of the epilepsy and patients’ adherence to AEDs. There was a significant association between adherence and history of seizures in the last 6 months. There was no significant difference between the mean (SD) duration of epilepsy among high adherent (17.0 years, 16.7%) and poor adherent (16.5 years, 15.7%) participants (t = 0.254, P = 0.79, CI: −3.53–4.57).

Association between adherence and therapy-related factors

The therapy-related factors studied are those concerning therapeutic regimen and type of medication used.

Table 5 shows the association between therapy-related factors and patients’ adherence to AEDs. Significantly higher adherence was found among patients who were treated by levetiracetam and clonazepam, whereas lamotrigine showed borderline adherence.

Table 6 shows the logistic regression for predictors of AED nonadherence. Factors that significantly increase the risk of nonadherence after adjusting for other factors in the models were as follows: lower education level and having a seizure within the last 6 months, whereas levetiracetam intake reduced the risk of nonadherence.

**DISCUSSION**

**Prevalence of adherence**

In this study, the prevalence of AEDs adherence among the study population was 70.8%. This is lower than another study from the United States (74%);[3] however, it is in agreement with a study from Nigeria with a recorded prevalence of 70%.[17] A slightly lower adherence rate was reported by Kassahun et al.[18] from a study in North East Ethiopia (65.5%), Gabr and Shams[4] from a study in KSA (61.7%), and Davis et al.[19] in the United States (61%). Much lower adherence rates were observed by other researchers such as Johnbull et al.[5] from Nigeria (32.6%) and Das et al.[20] from south India (29%).

The probable explanation for this variability in the prevalence of AED adherence might be related to the characteristics of the populations studied and methods for ascertaining AED adherence.

In our study, 70.8%, 25.1%, and 5.1% of the patients were ranked to have high, medium, and low adherence levels, respectively. Our patients had better adherence levels than those displayed in a study by Fadare et al.,[21] which found 17.2%, 38.3%, and 44.5% of patients having high, medium, and low adherence, respectively. Similarly, Sweileh et al.[22] found that the proportion of patients who had high, medium, and low adherence were 36%, 49.3%, and 14.7%, respectively. Recent studies reported by Pattoo et al.[23] from KSA and Yang et al.[24] from China found that the proportions of high, moderate, and low adherence for AED in a study by Pattoo et al.[23] were 48%, 34%, and 19%, respectively, whereas in Yang et al.,[24] they were 21.3%, 51.4%, and 27.3%, respectively.

**Factors associated with antiepileptic drugs adherence**

In this study, we have investigated several factors that may influence patient adherence.

**Sociodemographic factors**

Concerning age, our results showed that older participants had a significantly higher rate of nonadherence, and this is supported by studies from China[25] and the United States.[19] However, on adjusting the effect of other variables included in multiple regression model, the age was found to be a nonsignificant predictor for nonadherence. The final finding is in agreement with several studies from India,[7] Nigeria,[17] KSA,[26] and Ethiopia.[18] This could be attributed to the confounding effect of other factors associated with age.[27]
Regarding the level of education, we found that this factor is a significant predictor of poor adherence. Participants with lower education have 2.6 times higher risk for nonadherence. This is in agreement with the data from Nigeria[17] and Ethiopia. [10]

We found no significant association between other sociodemographic factors and adherence. This is in line with the findings of other researchers for gender,[5,7,17,26] ethnicity,[8] marital status,[7] and family history.[20]

**Factors related to the characteristics of the disease**

About half of our participants had generalized type of epilepsy (50.5%), which is similar to earlier reported findings from India (48.0%).[20] In addition, our participants started having the disease at an early age. In fact, about 69% had the disease during childhood and adolescence. Other researchers found that 40% of new cases of epilepsy occur before the age of 15 years.[28]

On comparing the mean age at diagnosis of disease for our patients (16.8 years) and that of other researchers, we found that our patients had a lower mean age at diagnosis compared with the data reported by Jones et al.[29] from the United Kingdom (21.8 years). This could be related to the variation in the etiological factors for epilepsy in both studies.

Concerning the duration of the disease, our data showed no difference between high and low AEDs adherent groups in mean duration of epilepsy, and
this is in agreement with a study by Gabr and Shams from the KSA. However, our result disagrees with a study by Liu et al. from China, which found that patients with a longer duration of illness had lower adherence rates.

### Table 5: The association between therapy-related factors and patients' adherence to antiepileptic drugs

| Therapy related factors | Subcategory     | Adherence |     | Nonadherence |     | P       |
|-------------------------|-----------------|-----------|-----|--------------|-----|---------|
|                         | No. | %   | No. | %   |             |       |
| Type of therapy regimen |     |     |     |     |             |       |
| Monotherapy             | 176  | 73.0 | 65  | 27.0 | 0.115 |
| Polytherapy             | 47   | 63.5 | 27  | 36.5 |       |
| Duration of treatment   |     |     |     |     |             |       |
| ≤1 years                | 132  | 73.7 | 47  | 26.3 | 0.396 |
| >1–5 years              | 77   | 66.4 | 39  | 33.6 |       |
| >5 years                | 14   | 70.0 | 6   | 30.0 |       |
| Levetiracetam           |     |     |     |     |             |       |
| Yes                     | 114  | 76.5 | 35  | 23.5 | 0.035 |
| No                      | 109  | 65.7 | 57  | 34.3 |       |
| Lamotrigine             |     |     |     |     |             |       |
| Yes                     | 88   | 65.2 | 47  | 34.8 | 0.058 |
| No                      | 135  | 75.0 | 45  | 25.0 |       |
| Lacosamide              |     |     |     |     |             |       |
| Yes                     | 18   | 62.1 | 11  | 37.9 | 0.278 |
| No                      | 205  | 71.7 | 81  | 28.3 |       |
| Carbamazepine           |     |     |     |     |             |       |
| Yes                     | 15   | 62.5 | 9   | 37.5 | 0.353 |
| No                      | 208  | 71.5 | 83  | 28.5 |       |
| Oxcarbazepine           |     |     |     |     |             |       |
| Yes                     | 15   | 75.0 | 5   | 25.0 | 0.669 |
| No                      | 208  | 70.5 | 87  | 29.5 |       |
| Clonazepam              |     |     |     |     |             |       |
| Yes                     | 9    | 100.0 | 0  | 0.0 | 0.043* |
| No                      | 214  | 69.9 | 92  | 30.1 |       |
| Vigabatrin              |     |     |     |     |             |       |
| Yes                     | 0    | 0.0  | 1   | 100.0 | 0.292* |
| No                      | 223  | 71.0 | 91  | 29.0 |       |
| Topiramate              |     |     |     |     |             |       |
| Yes                     | 3    | 60.0 | 2   | 40.0 | 0.456* |
| No                      | 220  | 71.0 | 90  | 29.0 |       |
| Ethosuximide            |     |     |     |     |             |       |
| Yes                     | 1    | 100.0 | 0  | 0.0 | 0.708* |
| No                      | 222  | 70.7 | 92  | 29.3 |       |
| Valproic acid           |     |     |     |     |             |       |
| Yes                     | 18   | 72.0 | 7   | 28.0 | 0.890 |
| No                      | 205  | 70.7 | 85  | 29.3 |       |

*Fisher’s Exact Test

### Table 6: Logistic regression for predictors of AED adherence.

| Variables                          | No. | Crude Odds Ratio (95%CI) | P value | Adjusted Odds Ratio (95%CI) | P-value |
|------------------------------------|-----|-------------------------|---------|-----------------------------|---------|
| Age                                |     |                         |         |                             |         |
| ≤10                                | 73  | 1                       |         |                             | 0.052   |
| 11-19                              | 72  | 0.53(0.24-1.13)         | 0.098   |                             |         |
| 20-59                              | 147 | 0.89(0.49-1.64)         | 0.708   |                             |         |
| ≥ 60                               | 23  | 2.61(0.99-6.91)         | 0.054   | 2.63(1.19-5.84)             | 0.017   |
| Education Level                    |     |                         |         |                             |         |
| =>College                          | 127 | 1                       |         |                             |         |
| <=Secondary                        | 43  | 2.58(1.26-5.28)         |         |                             |         |
| Having Seizure in the last 6 Months|     |                         |         |                             |         |
| No                                 | 171 | 1                       | <0.001  | 2.54(1.25-5.17)             | 0.01    |
| Yes                                | 144 | 2.55(1.55-4.20)         | 0.035   | 0.46(0.22-0.97)             | 0.041   |
| Levetiracetam                       |     |                         |         |                             |         |
| No                                 | 166 | 1                       |         |                             |         |
| Yes                                | 149 | 0.59(0.36-0.96)         |         |                             |         |
| Clonazepam                          |     |                         |         |                             |         |
| No                                 | 306 | 1                       | 0.999   |                             |         |
| Yes                                | 9   | 0                       |         |                             |         |
| Having Medication Side Effect      |     |                         |         |                             |         |
| No                                 | 472 | 1                       | <0.001  | 2.31(0.93-5.70)             | 0.07    |
| Yes                                | 51  | 3.44(1.86-6.39)         |         |                             |         |
| Lack of health information         |     |                         |         |                             |         |
| No                                 | 293 | 0.02(0.002-0.12)        |         |                             |         |
| Yes                                | 22  | 1                       | <0.001  |                             |         |

Factors related to the therapy

In this study, 76.5% of participants were prescribed monotherapy. This is in agreement with studies from India (66.1%), the United States (61%), and Malaysia (59.9%). It is worth noting here that our
result is consistent with evidence-based guidelines that recommend the use of monotherapy as an initial approach for the majority of patients with epileptic.[33] Similar to other researchers,[10,18,22,31,34] we have noticed a higher adherence rate among patients receiving monotherapy compared with those receiving polytherapy. It has been suggested that monotherapy improves adherence by offering better tolerability and avoidance of drug interaction.[19]

In this study, we found that the adherence rate was higher among participants with lower duration of treatment. This is supported by another study, in which the omission of dose was more frequent with a longer duration of treatment.[35]

In this study, most of the patients were treated by newer generation AEDs, in particular, levetiracetam and lamotrigine. Old medications such as phenytoin, carbamazepine, phenobarbitone, and valproate were used less frequently in this study. This disagrees with a study by Shegaw et al.[36] in which phenobarbital, phenytoin, carbamazepine, and sodium valproate have been used for treating 61.1%, 26.8%, 8.3%, and 3.8% of the patients, respectively. Similarly, another study revealed that carbamazepine (70.7%), sodium valproate (15.6%), and phenytoin (7.5%) were the most commonly prescribed AEDs.[21] Variation in the reported type of medication could be related to the differences in the type of epilepsy, age of patients, cost and healthcare setting policies.

Regarding medication adherence and type of medication received by our participants, the only drug that reduces the probability of poor adherence was levetiracetam. This is supported by an earlier study[37] that compared 12 months retention rate of 10 newly started AEDs used for treating 55 years or older cases.

Our results are also supported by Zhuo et al.[38] study which shows that Levetiracetam has a balanced efficacy and tolerability.

**History of seizure freedom in the last 6 months**

History of seizure freedom in the last 6 months had been used by researchers as an indicator of seizure control in patients with epileptic.[21] The current results showed that a history of seizure in the last 6 months was a significant predictor of AED adherence, and this is supported by an earlier study from the United Kingdom.[29] Tan et al.[32] found that seizure control was more common among patients with good adherence to AEDs. A study from KSA showed that patients’ adherence was significantly affected by seizure frequency,[4] and there was an increase in the frequency of seizure among nonadherent patients.

In our study, the proportion of poor adherence was significantly higher among patients who reported having seizure within the last 6 months (39.6% vs. 20.5%). This is supported by a study by Smithson et al.,[39] which explored the patients’ adherence with the occurrence of seizure within the previous 6 months. In the aforementioned study, 41% of the nonadherent participants reported having had a seizure in the previous 6 months compared with 31% of adherent participants ($P = 0.008$).

**Medication side effects**

Several side effects of AEDs were reported by participants in this study, and the most common were nervousness and aggressive behavior, followed by depression. In a study by Fadare et al.,[21] behavioral problems such as aggression and nervousness were reported by 15%–20% of the respondents, whereas in a study by Arif et al.[37] dizziness, drowsiness, and psychiatric complaints such as anxiety, irritability, depression, or behavioral changes were the most common complaints. Variation in the frequency of various side effects may be explained by a variation in the type of medication used in various studies.

In our study, poor adherence was more common among patients who had reported having medication side effect (52.6% vs. 24.6%), and this is in agreement with a study by Shegaw et al.[36] (65.7% vs. 57.4%).[34]

**Other factors (self-reported)**

**Forgetfulness:** In this study, forgetfulness was the most common reason reported by 94.6% of poorly adherent participants. This is supported by many researchers such as Hasiso and Desse[40] (75.4%), Liu et al.[25] (69.6%), Kassahun et al.[18] (53.5%), Nakhutina et al.[9] (50%), and Johnbull et al.[8] (40.7%). Al-Ramahi[40] argued that forgetfulness is a significant factor affecting the adherence of patients toward their medications, which emphasizes our finding. The WHO suggested that patients’ education should include intervention strategies that may overcome memory problems.[8]

Patients’ belief about the importance of adherence was the second most commonly stated factor. This is supported by study findings from KSA[38] and South Africa,[41] which reported lower beliefs for drug necessity among nonadherent patients. Egenasi et al.[41] concluded that patients’ beliefs about medications can influence their adherence.

Not taking the medication when got better was another explanation given by 19.6% of nonadherent respondents as a reason for their nonadherence. A similar finding was reported by a study by Gurumurthy et al.[7] in which 18.2% of patients had stopped medication.
The WHO identified a lack of education about AEDs as one of the health system–related factors that can affect adherence of patients with epileptic.\[6]\ In this study, lack of information was reported by 7% of the respondents. This is lower than a study by Shegaw et al.,\[42\] in which 60.4% of participants stated that they did not get health information from their healthcare provider.

In this study, depression was reported by 2.9% of the respondents as a factor affecting their medication adherence. This is supported by another study\[43\] that included socioeconomically diverse patients with epilepsy and found that perceived stress and depression were negatively correlated with MMAS. The authors in the previously stated study suggested screening of patients with epileptic for depression to improve AEDs adherence. In a study from China,\[43\] a significant difference in depression scores was found between the low adherence and the moderate-to-high adherence groups.

In our study, depression was self-reported, which may explain the small stated number of patients with depression.

Fear of dependence was stated by the WHO as a patient-related factor that can affect medication adherence of patients with epileptic.\[6\] Niriayo et al.,\[44\] reported that negative medication belief was a significant factor for nonadherence.

In our study, only one patient stated the expenses of medication as a factor for nonadherence. This disagrees with the studies by Niriayo et al.,\[44\] and Al-Ramahi,\[40\] where 21.5% and 16% of respondents, respectively, stated the cost as reason for nonadherence. The possible explanation for the low reporting of cost as a factor is that most of our participants (around 70%) are covered by health insurance.

**Limitations**

The results of this study cannot be generalized because the participants were selected from patients with epileptic that had attended one healthcare facility. Although, the study had used a validated tool for verification of adherence, however, because this tool is based on self-reporting of participants, there is a possible recall bias that can affect the validity of the results. Using more reliable methods, such as drug counting or plasma or serum AED levels, was not feasible in this study. We tried to overcome possible selection bias by including all patients attending the hospital during the period of data collection. High response rate in this study is in favor of better validity of the obtained data.

**Strengths**

No available data from the UAE were related to the prevalence of adherence of patients with epileptic to their medication. Moreover, to know about the factors that determine adherence to AED is very crucial for suggesting strategies to overcome these factors. This study was aimed at assessing the prevalence of AED adherence among patients attending Tertiary (Neuro Spinal) Hospital in UAE and at identifying predictors of nonadherence. We hypothesize that nonadherence is influenced by sociodemography and disease-related factors.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. WHO Fact-Sheet. Epilepsy. Key Facts. [updated on 2019 June 20; cited 2019 Nov 15]. Available from: https://www.who.int/news-room/fact-sheets/detail/epilepsy. [Last accessed on 2019 Dec 2].
2. Ettinger AB, Manjunath R, Candrilli SD, Davis KL. Prevalence and cost of nonadherence to antiepileptic drugs in elderly patients with epilepsy. Epilepsy Behav 2009;14:324-9.
3. 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;50:501-9.
4. Gabr WM, Shams ME. Adherence to medication among outpatient adolescents with epilepsy. Saudi Pharm J 2015;23:33-40.
5. Johnbull OS, Farounbi B, Adeleye AO, Ogunrin O, Uche AP. Evaluation of factors influencing medication adherence in patients with epilepsy in rural communities of Kaduna state, Nigeria. Neurosci Med 2011;2:299-305.
6. World Health Organization [Internet]. Adherence to long-term therapies: evidence for action. WHO Library Cataloguing-in-Publication Data 2003. ISBN 92 4 154599 2. [cited 2019 Nov 15]. Available from: https://www.who.int/chp/knowledge/publications/adherence_full_report.pdf. [Last accessed on 2019 Dec 2].
7. Gurumurthy R, Chanda K, Sarma G. An evaluation of factors affecting adherence to antiepileptic drugs in patients with epilepsy: a cross-sectional study. Singapore Med J 2017;58:98-102.
8. 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 Behav 2011;22:584-6.
9. Tang F, Zhu G, Jiao Z, Ma C, Wang B. Self-reported adherence in patients with epilepsy who missed their medications and reasons for nonadherence in China. Epilepsy Behav 2013;27:85-9.
10. 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:e0163040.
11. Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing compliance with antiepileptic drug regimes. Seizure 1997;6:87-93.
12. Getnet A, Woldeyohannes SM, Bekana L, Mekonen T, Fekadu W, Memeru M, et al. Antiepileptic drug nonadherence and its predictors among people with epilepsy. Behav Neurol 2016;2016:3189108.
13. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care 1986;24:67-74.
14. Benamer HT, Grosset DG. A systematic review of the epidemiology of epilepsy in Arab countries. Epilepsia 2009;50:2301-4.
15. World Health Organization, Regional Office for the Eastern Mediterranean. (2010). Epilepsy in the WHO Eastern Mediterranean Region: bridging the gap. [cited 2019 Nov 15] Available from: https://apps.who.int/iris/handle/10665/119905 [Last accessed on 2019 Dec 2].
16. Yang C, Hao Z, Yu D, Xu Q, Zhang L. The prevalence rates of medication adherence and factors influencing adherence to antiepileptic drugs in children with epilepsy: a systematic review and meta-analysis. Epilepsy Res 2018;142:88-99.
17. Ogundele DS, Dawodu DC. Adherence to anti-epileptic drugs at a tertiary health center in a developing country a cross-sectional study. Int J Sci Res Pub 2012;2:329-31.
18. Kassahun G, Moges G, Demesse B. Assessment of patients’ adherence to antiepileptic medications at Dessie referral hospital, chronic follow-up, South Wollo, Amhara region, North East Ethiopia. Neurol Res Int 2018;2018:5109615.
19. Davis KL, Candrilli SD, Edin HM. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. Epilepsia 2008;49:446-54.
20. Das AM, Ramamoorthy L, Narayan SK, Wadwekar V. Barriers of drug adherence among patients with epilepsy: in tertiary care hospital, South India. J Caring Sci 2018;7:177-81.
21. 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;8:25-36.
22. Sweeney WM, Ibhebesh MS, Jarar IS, Taha AS, Sawalha AF, Zyoud SH, et al. Self-reported medication adherence and treatment satisfaction in patients with epilepsy. Epilepsy Behav 2011;21:301-5.
23. Pattoo FH, Alshayban DM, Joseph R, Al-Musa F, Al-Jabran O, Aliaafari D. Impact of adherence to antiepileptic medications on quality of life of epileptic patients in the Eastern province of Saudi Arabia: a cross-sectional study. Imam J Appl Sci 2020;5:1-8.
24. Yang C, Yu D, Li J, Zhang L. Prevalence of medication adherence and factors influencing adherence to antiepileptic drugs in children with epilepsy from western China: a cross-sectional survey. Epilepsy Behav 2020;104:106662.
25. Liu J, Liu Z, Ding H, Yang X. Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients. Epileptic Disord 2013;15:289-94.
26. Zafar A, Shahid R, Nazish S, Aljaafari D, Alkhamsi D, Alsalman S, et al. Nonadherence to antiepileptic medications: still a major issue to be addressed in the management of epilepsy. J Neurosci Rural Pract 2019;10:106-12.
27. Ernawati I, Islamiyah WR, Sumarno. How to improve clinical outcome of epileptic seizure control based on medication adherence? A literature review. Open Access Maced J Med Sci 2018;6:1174-9.
28. Baulac M, de Boer H, Elger C, Glynn M, Kälviäinen R, Little A, et al. Epilepsy priorities in Europe: a report of the ILAE-EBE epilepsy advocacy Europe Task Force. Epilepsia 2018;59:1687-95.
29. 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;15:504-8.
30. Chauhan S, Prem Lochan Prasad PL, Bhowana Khurana B, Gahalaut P. Self-reported medication adherence to antiepileptic drugs and treatment satisfaction among paediatric patients having epilepsy: a cross sectional study from the Indian subcontinent. Sri Lanka J Child Health 2018;47:129-36.
31. Hovinga CA, Asato MR, Manjunath R, Whelless 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 Behav 2008;13:316-22.
32. Tan XC, Makmorn Bakry M, Lau CL, Tajarudin FW, Ali RA. Factors affecting adherence to antiepileptic drugs therapy in Malaysia. Neurol Asia 2015;20:235-41.
33. Kanner AM, Ashman E, Gloss D, Harden C, Bourgeois B, Bautista JP, et al. Practice guideline update summary: efficacy and tolerability of the new antiepileptic drugs I: treatment of new-onset epilepsy: report of the American Epilepsy Society and the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Epilepsy Curr 2018;18:260-8.
34. Ferrari CM, da Sousa RM, Castro LH. Factors associated with treatment non-adherence in patients with epilepsy in Brazil. Seizure 2013;22:384-9.
35. Cramer JA, Glassman M, Rienzi V. The relationship between poor medication compliance and seizures. Epilepsy Behav 2002;3:338-42.
36. Shegaw M, Kassa R, Ali Y, Addissu N. Prevalence and associated factors of antiepileptic drug nonadherence among epileptic patients attending at out patient department of Dilla University Referral Hospital, Dilla, Gedeo, SNNPR, Southern Ethiopia. Int J Biosci Med 2017;1:2.
37. Arif H, Buchsbaum R, Pierro J, Whalen M, Sims J, Resor SR Jr, et al. Comparative effectiveness of 10 antiepileptic drugs in older adults with epilepsy. Arch Neurol 2010;67:408-15.
38. Zhuo C, Jiang R, Li G, Shao M, Chen C, Chen G, et al. Efficacy and tolerability of second and third generation anti-epileptic drugs in refractory epilepsy: A network meta-analysis. Sci Rep 2017;7:2535. [cited 2019 Nov 15].
39. Smithson WH, Hukins D, Buelow J, Allgar V, Dickson J. Adherence to medicines and self-management of epilepsy: a community-based study. Epilepsy Behav 2013;26:109-13.
40. Al-Ramahi R. Adherence to medications and associated factors: a cross-sectional study among Palestinian hypertensive patients. J Epidemiol Glob Health 2015;5:125-32.
41. Egenasi C, Steinberg WJ, Rauenheimer JE. Beliefs about medication, medication adherence and seizure control among adult epilepsy patients in Kimberley, South Africa. S Afr Fam Pract 2015;57:326-32.
42. Shallcross AJ, Becker DA, Singh A, Friedman D, Jurd R, French JA, et al. Psychosocial factors associated with medication adherence in ethnically and socioeconomically diverse patients with epilepsy. Epilepsy Behav 2015;46:242-5.
43. Gruy Y, Ding XY, Lu RY, Shen CH, Ding Y, Wang S, et al. Depression and anxiety are associated with reduced antiepileptic drug adherence in Chinese patients. Epilepsy Behav 2015;50:91-5.
44. Niriyao YL, Mamo A, Kassa TD, Asgedom SW, Atey TM, Gidey K, et al. Treatment outcome and associated factors among patients with epilepsy. Sci Rep 2018;8:17354.