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## Association between antiepileptic drug side effects and medication adherence among Libyan epilepsy patients

Ensherah M. N. Ben Zekri \*  , Nabila A. Rghebi  , and Rima F. Elmezghi  

Department of Pharmaceutics, Faculty of Pharmacy, University of Tripoli, Tripoli, Libya

\* Author to whom correspondence should be addressed

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### HOW TO CITE THIS

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**Keywords:** Antiepileptic drug, cognitive complaint, epilepsy, medication adherence, side effects

**Abstract:** Treatment adherence is a critical component of epilepsy management. Antiepileptic drug side effects affect adherence and may result in the discontinuation of medication. This study aimed to investigate the association between antiepileptic drug side effects and medication adherence among Libyan patients with epilepsy while identifying predictors of adherence. A cross-sectional study was conducted at Tripoli University Hospital involving 200 adult epilepsy patients. Adherence was assessed via a self-report tool dichotomized as adherent/non-adherent if patients stopped medication due to side effects. Side effects were evaluated using the Side Effects of Antiepileptic Drugs questionnaire. Logistic regression analyzed predictors of adherence, including antiepileptic drug use, therapy regimen, and side-effect profiles, with  $p < 0.05$  declared association. The overall adherence rate was 87.0%. Higher adherence was observed in older age groups, 95.8% in patients aged 51-60, 89.4% in married patients, and 91.0% in university-educated patients. Patients on monotherapy and those seizure-free in the preceding month demonstrated better adherence (88.4% and 93.0%, respectively). Valproate users had notably low adherence (52.6%) while carbamazepine and phenytoin users showed higher adherence (89.7% and 91.7%, respectively). Cognitive complaints significantly reduced adherence (76.1% vs. 79.6%), as did aggressive behavior (58.3% adherence). Logistic regression identified two independent predictors: patients on old-generation antiepileptic drugs had 2.7 times higher adherence (AOR=2.702, 95% CI: 1.168-6.249;  $p=0.02$ ) while cognitive side effects reduced adherence by 86.4% (AOR=0.136, 95% CI: 0.031-0.596;  $p=0.008$ ). Cognitive side effects predict non-adherence, necessitating routine monitoring. Paradoxically, older antiepileptic drugs correlated with better adherence. Integrating patient-reported metrics and addressing cognitive impacts could optimize epilepsy care, highlighting gaps in side-effect management and advocating personalized strategies in clinical settings.

### Introduction

Epilepsy, a persistent neurological disease, significantly impacts brain function and is one of the most prevalent severe medical conditions, affecting 50 million individuals [1]. It crosses all boundaries of age, race, social class, and geography. In developing countries, 85.0% of individuals with epilepsy are affected, and it is estimated that about 40 million people lack access to adequate treatment [2]. Individuals with epilepsy often face serious

physical, emotional, financial, and social challenges [3]. Antiepileptic drugs (AEDs) play a crucial role in the management of epilepsy, and the ideal outcome of epilepsy treatment with AEDs is to achieve complete seizure control without any side effects. However, these drugs often come with a range of side effects, which significantly affect patients' quality of life and are linked to treatment failure in 40.0% of individuals receiving therapy [4]. The profiles of adverse effects associated with AEDs vary widely, often influencing the choice of medication due to the comparable efficacy rates among AEDs. Commonly reported side effects include cognitive difficulties, fatigue, tremors, gastrointestinal issues, osteoporosis, depression, drowsiness, dizziness, and weight fluctuations [5]. These adverse effects may require medical interventions that can range from minor treatments to expensive specialist care and potential hospital admissions [6]. In addition to healthcare costs, the financial strain on patients and their families, which includes informal caregiving expenses and lost income, can be substantial [7, 8]. Old AEDs exhibit several limitations, including inadequate response rates, considerable side effects, numerous drug interactions, and a narrow therapeutic index. Relatively newer AEDs have been prescribed to address these issues. These agents demonstrate improved tolerability, reduced potential for interactions, and reduced enzyme induction or inhibition [9, 10]. Medication adherence or the older term, medication compliance, has been defined as the extent to which patients follow the instructions they are given for prescribed treatments and their persistence in the duration of time from initiation to discontinuation of therapy [11]. Patients' adherence to the treatment regimen predicts the success of treatment and reduces the negative side effects of the disease and its severity [12, 13]. This adherence is particularly vital for individuals with epilepsy, as noncompliance with medication regimens significantly heightens the risk of experiencing additional seizures [14], increased emergency room visits due to seizure-related injuries, and a greater likelihood of motor vehicle accidents. While most individuals with epilepsy can manage their condition effectively with AEDs, the challenge of maintaining adherence remains a significant barrier to achieving optimal treatment outcomes [15]. Seizure control depends upon several factors, including adequate treatment and dosage, patients' daily activities, and adherence to antiepileptic medications [16]. The characteristics of AEDs have a significant impact on adherence to treatment, including the type of AED prescribed, whether it is prescribed as monotherapy or as a combination therapy, dosing frequency, use of brand versus generic names, and type of release formulation [16]. The relatively newer AEDs are generally thought to have fewer side effects and drug interactions, leading to improved adherence [17]. Similarly, lower dosing frequency and use of monotherapy are thought to positively impact adherence [18]. Medication side effects affect adherence and may result in the discontinuation of medications [19]. The relationship between adherence and medication satisfaction found that those who adhered more closely to their treatment were generally more satisfied with their medications. This indicates that patients who perceive their medication as effective are more likely to continue with their treatment, even in the presence of side effects [15]. Conversely, a study conducted in Brazil revealed that adverse drug effects affect quality of life and adherence to treatment [20]. Other studies also revealed that nonadherence was higher by 2.13 among the group of epileptic patients experiencing side effects as compared to the other group of patients without these side effects [21, 22]. Given the dearth of research evaluating non-adherence among Libyan patients with epilepsy, and the absence of studies specifically examining the association between AED side effects and medication non-adherence, there is a critical need to assess the current adherence status of the patients and investigate the impact of AED side effects as a key determinant of treatment adherence.

## Materials and methods

*Study design:* A cross-sectional study was conducted at Tripoli University Hospital (TUH); the largest specialized hospital in the Libyan capital, Tripoli. The study began in October 2019 and continued until the outbreak of COVID-19 in December 2019.

*Study populations and eligibility criteria:* Patients of both genders, who are diagnosed with any type of epilepsy, aged  $\geq 18$  years, have been prescribed at least one AED, and undergoing treatment for at least six months with AEDs were included in the study. The study excluded pregnant women, terminally ill patients, patients with psychiatric problems or mental illnesses, and those not able and/or not willing to take part in the study. Incomplete questionnaires and patients who do not speak either Arabic or English were also excluded.

*Study variables and outcome:* The medication non-adherence and side effects from AEDs were the primary study outcomes. Since no golden standard is available for medication adherence assessment [23], adherences to AEDs were determined by specifically asking patients whether they stopped taking their medication when they experienced side effects from the AED treatment or not. The adherence was assessed using a dichotomous response scale (i.e., yes=non adherent and no=adherent). To focus on the most commonly reported side effects, the side effects of AED treatment questionnaire (SIDAED) were used [4]. The side effect categories included four main complaints: general health, cognitive, mood, and cosmetic side effects.

*Sample size and sampling technique:* The sample size was determined using a single population proportion formula [24] as follows:  $n_i = (z\alpha/2)^2 pq/d^2$  where  $n_i$ =sample size;  $z=95.0\%$  confidence interval with  $\alpha=5\%$ ;  $P$ =estimated prevalence,  $50.0\%$ ;  $q=1-p$  and  $d$ =margin of error ( $5.0\%$ ). Substituting all the values resulted in  $n_i = (1.96)^2(0.5)(0.5)/(0.05)^2=384$ . However, we were able to collect data from only 200 epileptic patients fulfilling the inclusion criteria before the outbreak of COVID-19 and they were included in the final analysis.

*Data collection process and management:* To extract data, the questionnaire designed to be a self-report tool was distributed to the study participants. The question consisted of closed-ended questions and contained three main sections. These sections assessed sociodemographic, medication adherence, AEDs side effects, and questions related to the patient's clinical condition and antiepileptic drug use. The questionnaire was first prepared in English and translated into Arabic, the local language, by two translators to ensure that it retained its intended meaning. The questionnaire was pretested to identify potential problems and unanticipated interpretations, to any of the questions on 10 respondents having similar characteristics at the same follow-up clinic of the neurology department. A neurologist on duty was asked to help select the study participants and two pharmacists assessed in questionnaire distribution and collection. The objective of the study was explained to each patient individually. The researchers interviewed the illiterate patients who could not read or write and the rest of the participants filled in the questionnaire by themselves.

*Ethics approval and consent to participate:* A letter of permission was obtained from the University of Tripoli, based on the request and proposal of the Department of Pharmaceutics, Faculty of Pharmacy. The manager of TUH granted permission for the study to be conducted at the follow-up clinic of the neurology. Ethical clearance was secured from the Biotechnology Research Center, referenced as BEC-BTRC 34-2020. All participating patients who agreed to participate by their free will provided oral informed consent and were assured that their information would remain confidential. Participants were also made aware that their involvement was entirely voluntary, and they had the right to withdraw from the study at any time.

*Statistical analysis:* The data collected were coded, entered, and analyzed using Statistical Packages for Social Sciences v-26, and presented as frequencies and percentages. To assess the association between medication adherence and AED side effects, bivariate logistic regression analysis was used. It was used to evaluate the impact of the treatment factors as: therapy regimen (mono or polytherapy), medication used (old or relatively new AEDs), and AEDs side effect risk (high or low risk) on medication adherence.  $P < 0.05$  was used to declare association.

## Results

In this study, a cross-sectional analysis of 200 epileptic patients revealed key socio-demographic, clinical, and treatment-related factors associated with medication adherence. The overall adherence rate was 87.0% with 26 patients (13.0%) classified as non-adherent. In **Table 1**, a predominantly male cohort (54.0%) with a mean age distribution between 18 to  $\geq 71$  years was noticed among the patients. Most participants were married (66.0%), had a monthly income  $\leq 1000$  Libyan Dinar (67.5%), and attained secondary school education (40.0%) or university/diploma qualifications (33.5%). Age and education level demonstrated notable trends. The highest adherence was observed in patients aged 51-60 years (95.8%), while the youngest cohort (18-20 years) exhibited the lowest adherence (75.0%). Higher educational attainment correlated with improved adherence: 91.0% of university/diploma-educated patients were adherent, compared to 78.6% among non-educated individuals. Married patients showed higher adherence than divorced/widowed patients (89.4%, and 66.7%, respectively).

**Table 1:** Socio-demographic characteristics and adherence status of Libyan epileptic patients

Variable	Category	Frequency (n=200)	Percentage	Adherence level	
				Non-adherent, (n=26)	Adherent, (n=174)
Gender	Male	108	54	15 (13.9)	93 (86.1)
	Female	92	46	11 (12.0)	81 (88.0)
Age (years)	18-20	08	04	02 (25.0)	06 (75.0)
	21-30	35	17.5	06 (17.1)	29 (82.9)
	31-40	39	19.5	05 (12.8)	34 (87.2)
	41-50	36	18	04 (11.1)	32 (88.9)
	51-60	24	12	01 (04.2)	23 (95.8)
	61-70	33	16.5	04 (12.1)	29 (87.9)
	$\geq 71$	25	12.5	04 (16.0)	21 (84.0)
Educational level	Not educated	14	07	03 (21.4)	11 (78.6)
	Primary school	38	19	03 (07.9)	35 (92.1)
	Secondary school	80	40	14 (17.5)	66 (82.5)
	University/Diploma	67	33.5	06 (09.0)	61 (91.0)
	High education	01	0.5	0.0	01 (100)
Marital status	Married	132	66	14 (10.6)	118 (89.4)
	Not married	65	32.5	11 (16.9)	54 (83.1)
	Divorce/widow	03	1.5	01 (33.3)	02 (66.7)
Monthly income (L.D.)	$\leq 1000$	135	67.5	17 (12.6)	118 (87.4)
	$> 1000$	65	32.5	09 (13.8)	54 (83.1)

Clinically, the majority had epilepsy for 1-5 years (65.0%) and were prescribed monotherapy (77.5%), primarily carbamazepine (34.0%). Comorbidities were prevalent (52.5%), with 33.0% reporting one comorbidity. Seizure frequency varied, with 26.5% experiencing 1-3 seizures/month and 21.5% seizure-free in the preceding month. Patients on monotherapy exhibited higher adherence (88.4%) than those on polytherapy (82.2%). Seizure frequency analysis revealed that patients without attacks in the preceding year had the lowest adherence (66.7%), while those without attacks in the current month showed the highest adherence (93.0%) (**Table 2**).

**Table 2:** Clinical-related characteristics and adherence status of Libyan epileptic patients

Variable	Category	Frequency (n=200)	Percentage	Adherence level	
				Non-adherent (n=26)	Adherent (n=174)
Duration of epilepsy (years)	< 1	29	14.5	03 (10.3)	26 (89.7)
	1-5	130	65.0	17 (13.1)	113 (86.9)
	> 5	41	20.5	06 (14.6)	35 (85.4)
Medication regimen	Monotherapy	155	77.5	18 (11.6)	137 (88.4)
	Poly therapy	45	22.5	08 (17.8)	37 (82.2)
Associated comorbidities	Present	105	52.5	13 (12.4)	92 (87.6)
	Absent	95	47.5	13 (13.7)	82 (86.3)
Comorbidities	1	66	33.0	06 (09.1)	60 (90.9)
	2	31	15.5	05 (16.1)	26 (83.9)
	3	08	04.0	02 (25.0)	06 (75.0)
Seizure frequency	Did not have an attack this month	43	21.5	03 (07.0)	40 (93.0)
	1-3 times/month	53	26.5	05 (09.4)	48 (90.6)
	> 3 times/month	11	05.5	01 (09.1)	10 (90.9)
	1-3 times/year	45	22.5	07 (15.6)	38 (84.4)
	> 3 times/year	29	14.5	05 (17.2)	24 (82.8)
	Did not have an attack this year	15	07.5	05 (33.3)	10 (66.7)
	Other	04	02.0	0.0	04 (100)

In **Table 3**, among the 155 patients receiving monotherapy, carbamazepine was the most frequently prescribed antiepileptic medication (34.0%), followed by levetiracetam (16.5%) and valproate (09.5%). Phenytoin, lamotrigine, and other agents (ethosuximide, phenobarbital) were less commonly prescribed, each representing  $\leq 6.0\%$  of the total sample. Old-generation AEDs were more commonly used (54.5%) than newer agents (23.0%). Cognitive risk and behavioral risk were classified as high in 8.0%, and 24.5%, and low in 69.5%, and 53.0% of the patients, respectively.

**Table 3:** Monotherapy characteristics and adherence status of Libyan epileptic patients

Variable	Category	Frequency (n=155)	Percentage	Adherence level	
				Non-adherent (n=26)	Adherent (n=174)
Medication taken	Carbamazepine	68	34.0	07 (10.3)	61 (89.7)
	Levetiracetam	33	16.5	05 (15.2)	28 (84.8)
	Valproate	19	09.5	09 (47.4)	10 (52.6)
	Phenytoin	12	06.0	01 (8.3)	11 (91.7)
	Lamotrigine	12	06.0	04 (33.3)	08 (66.7)
	Ethosuximide	04	02.0	0.0	04 (100)
	Phenobarbital	04	02.0	0.0	04 (100)
	Gabapentin Others	01 02	01.5 01.0	0.0 0.0	01 (100) 02 (100)
Old or New	Old AEM	109	54.5	09 (8.3)	100 (91.7)
	New AEM	46	23.0	09 (19.6)	37 (80.4)
Cognitive risk	High risk	16	08.0	01 (6.3)	15 (93.8)
	Low risk	139	69.5	17 (12.2)	122 (87.8)
Behavioral risk	High risk	49	24.5	06 (12.2)	43 (87.8)
	Low risk	106	53.0	12 (11.3)	94 (88.7)

In **Table 4**, general health complaints included headache (66.5%), dizziness (44.5%), and gastrointestinal issues (35.5%). Cosmetic concerns such as hair loss (56.0%) and skin rash (25.0%) were frequent, while cognitive complaints concentration difficulties (51.5%), and memory problems (23.0%) were prominent. Mood disturbances, including irritability (31.5%) and depressive symptoms (24.0%), were also reported. Skin rash (28.0% non-adherence), aggressive behavior (41.7% non-adherence), and nausea (25.7% non-adherence) caused non-adherence, with rates exceeding 20.0%. Conversely, despite high prevalence, headache (66.5% prevalence, 85.7% adherence) and hair loss (56.0% prevalence, 88.4% adherence) demonstrated minimal disruption to adherence. Cognitive complaints, particularly memory problems (23.9% non-adherence) and concentration difficulties (20.4% non-adherence), reduced adherence.

**Table 4:** Type of side effects, complaints, and adherence status of Libyan epileptic patients

Variable	Category	Frequency (n=200)	Percentage	Adherence level	
				Non-adherent (n=26)	Adherent (n=174)
General health complaints	Fatigue and sleep problems	48	24.0	07 (14.6)	41 (85.4)
	Motor and balance problems	37	18.5	09 (24.3)	28 (75.7)
	Headache	133	66.5	19 (14.3)	114 (85.7)
	Dizziness	89	44.5	18 (20.2)	71 (79.8)
	Gastrointestinal problems	71	35.5	13 (18.3)	58 (81.7)
	Nausea	35	17.5	09 (25.7)	26 (74.3)
Cosmetic complains	Skin rash	50	25.0	14 (28.0)	36 (72.0)
	Weigh problems	22	11.0	02 (09.1)	20 (90.9)
	Problems with gums	71	35.5	08 (11.3)	63 (88.7)
	Hair loss	112	56.0	13 (11.6)	99 (88.4)
	Shaking hands	68	34.0	14 (20.6)	54 (79.4)
	Itch	75	37.5	15 (20.0)	60 (80.0)
Mood complains	Depressive mood	48	24.0	11 (22.9)	37 (77.1)
	Irritable and angry behavior	63	31.5	13 (20.6)	50 (79.4)
	Mood signs	84	42.0	14 (16.7)	70 (83.3)
	Agitated behavior	28	14.0	05 (17.9)	23 (82.1)
	Anxious behavior	34	17.0	05 (14.7)	29 (85.3)
	Aggressive behavior	12	06.0	05 (41.7)	07 (58.3)
Cognitive complains	Memory problems	46	23.0	11 (23.9)	35(76.1)
	Concentration problems	103	51.5	21 (20.4)	82 (79.6)
	Language difficulties	13	06.5	02 (15.4)	11 (84.6)
	Mental slowing	01	00.5	0.0	01 (100)

Logistic regression identified two independent predictors: the use of old-generation AEDs and cognitive complaints (**Table 5**). Patients using older-generation antiepileptic drugs have 2.7 times higher adherence compared to those on relatively newer-generation drugs ([AOR] [95% CI]: 2.702 [1.168-6.249]; p=0.020). Conversely, cognitive side effects are a major barrier to adherence, i.e.; non-adherence is 7.35 times more likely in patients with cognitive side effects. Patients reporting cognitive complaints (memory issues, confusion) have 86.4% lower adherence level ([AOR] [95% CI]: 0.136 [0.031-0.596]; P=0.008), compared to those without such side effects, **Table 6**.

**Table 5:** Logistic regression associations between adherence status, side effects, and treatment factors

Side effects	Adherence	Monotherapy or Polytherapy	New or Old	Cognitive high or low-risk	Behavioral high or low-risk
Adherence	---	0.283	0.020*	0.803	0.885
General health complains	0.773	0.350	0.484	0.230	0.889
Cognitive complains	0.008*	0.127	0.154	0.330	0.939
Mood complains	0.146	0.769	0.968	0.834	0.651
Cosmetic complains	0.998	0.697	0.130	0.998	0.534

\* Significant association by  $P < 0.05$

**Table 6:** Predictors for adherence to antiepileptic drug side effects

Predictors for adherence	B	Wald	OR [95% CI]	P value
Patients on old-generation antiepileptic	0.994	5.400	2.702 [1.168-6.249]	0.020
Patients experiencing cognitive complaints side effect	-1.992	7.013	0.136 [0.031- 0.596]	0.008

## Discussion

Although inadequate medication adherence is recognized as a primary factor contributing to AED treatment failure, this issue has not been thoroughly investigated in Libya. Therefore, the current study assessed the current adherence status of epileptic patients and investigated the impact of AED side effects as a key determinant of treatment adherence. The magnitude of non-adherence to AEDs was 13.0%, this is similar to a Saudi Arabian study (14.0%) [25] and greater than an Egyptian study (11.4%) [26]. The disparities in adherence rates between studies are related to the diverse methodologies employed to assess adherence. Even when using the same assessment instruments, such as the one used in this study (i.e., self-reported adherence), the lack of standardized, validated questionnaires contributes to inconsistent adherence data between research. The highest adherence was observed in patients aged 51-60 (95.8%). Notably, non-adherence was most prevalent in the 18-20 age group (25.0%) and among those  $\geq 71$  years (16.0%). These findings suggest age-specific adherence challenges, particularly in younger and elderly populations, warranting targeted interventions. However, these results diverge from the previous study by Gurumurthy and others [3], which reported no significant demographic differences, including age or gender, between adherent and non-adherent patients.

The present study proves the efficacy of educational status in improving medication adherence, higher educational attainment showed higher adherence rates, in which 91.0% of university/diploma-educated patients were adherent, compared to 78.6% among non-educated individuals. These results resemble the previous findings which showed that the frequency of seizures was greatly reduced and the adherence was significantly increased by patient education and medication understanding [27]. This similarity may be due to the impact of education on health awareness and adherence behavior, leading to higher adherence rates among patients with higher education levels in the current study [28]. AEDs play a crucial role in the management of epilepsy, enabling about 70.0% of patients to live without seizures. However, the challenge of inadequate adherence to these medications poses a significant obstacle to achieving lasting remission and enhancing overall functionality [2]. 65.0% of the participants had been suffering from epilepsy between one to five years. It was noted that as the duration of treatment increased, participants became more likely to be non-adherent and this is similar to a previously conducted study [2]. This lack of distinction may be attributed to a high adherence rate among patients in the

present study, which could have contributed to optimal disease management and reduced variability in clinical outcomes between the two groups. Patients with epilepsy frequently have comorbid conditions, which increase the risk of toxicity, drug interactions, and decreased adherence to treatment regimens [29]. Comorbidities were prevalent (52.5%) in the current study, with 33.0% reporting one comorbidity. In the US, data from 2021-2022 reveal that adults with active epilepsy frequently report comorbidities such as difficulty remembering (55.8%), chronic pain (40.2%), and hypertension (38.1%) [29]. The high prevalence of comorbidities emphasizes the importance of integrated care strategies and personalized treatment approaches. Therefore, healthcare providers must work in partnership with their patients to evaluate the benefits of medications while considering side effects that may impact adherence [28]. They should also take this into account when designing treatment plans, particularly for patients requiring complex or long-term medical management [29]. Currently, over three-quarters of patients are on monotherapy, while about one-quarter of the patients are on polytherapy. This aligns with a previous study which found that more than half of the patients were on AED monotherapy, with the remainder on AED polytherapy [3]. Carbamazepine emerged as the most frequently prescribed AED, taken by 34.0% of the surveyed individuals as monotherapy. This is not in line with the previous study which reported phenobarbital as the most commonly prescribed AED [3]. The current study does not demonstrate a significant difference in medication adherence or side effects between patients on monotherapy and those on polytherapy, suggesting that treatment type alone may not be a key determinant of adherence. This aligns with a previous study which similarly reported no notable difference in adherence levels between the two groups [15]. However, Gabr and Shams contrast with these results, indicating that patients on monotherapy exhibited significantly higher adherence than those on polytherapy [30]. This discrepancy has been attributed to the complexity of polytherapy regimens which involve multiple medications administered at varying times increasing the risk of missed doses [3, 15, 30]. Patients' self-reported side effects can serve as a practical screening tool in clinical settings, enabling early identification of high-risk individuals who require formal neuropsychological evaluation. This approach optimizes resource efficiency by reducing financial and time burdens while ensuring timely intervention [31]. It has been demonstrated that patients prioritize tolerability over efficacy in long-term epilepsy treatment, with treatment adherence primarily influenced by their subjective experience of side effects [32]. The relatively newer AEDs, such as lamotrigine, levetiracetam, gabapentin, and pregabalin, appear to have comparable efficacy to older agents but demonstrate superior tolerability [33]. However, cognitive complaints linked to confirmed cognitive dysfunction have been reported with nearly all older AEDs, particularly phenobarbital, phenytoin, and valproate. In this study, 54.5% of the patients were taking older AEDs (carbamazepine and valproate), and 23.0% were taking newer AEDs (levetiracetam).

Factors such as side effects and cognitive function may play a more significant role in influencing treatment adherence [34]. Our findings underscore this relationship, with 51.5% experiencing concentration difficulties, 23.0% exhibiting memory problems, and 6.5% having language difficulties. Given the significant association between adherence and cognitive complaints, these difficulties may exert a greater influence on adherence rates than the number of prescribed medications. Similarly, a study conducted in Ethiopia found that impaired concentration can lead to challenges in daily functioning, including forgetfulness regarding medication intake [35]. According to the current study, cognitive side effects are a major barrier to adherence, i.e., non-adherence is 7.35 times more likely in patients with cognitive side effects. Patients reporting cognitive complaints (memory issues, confusion) have 86.4% lower adherence levels, compared to those without such side effects. Cognitive side effects strongly predict poorer adherence, highlighting the need to monitor and manage these effects; addressing these (through patient education, alternative medications, or symptom management) could improve



outcomes. Furthermore, the classification of AEDs (older versus newer) significantly influences adherence to AEDs. Patients using older-generation antiepileptic drugs have 2.7 times higher adherence compared to those on newer-generation drugs. This higher adherence to older-generation drugs may be attributed to factors such as familiarity, dosing simplicity, cost, or fewer non-cognitive side effects compared to newer alternatives. While the relatively newer AEDs are generally associated with a lower incidence of certain side effects such as cosmetic-related adverse effects compared to older antiepileptic drugs [36], prior research, including [37], found no significant difference in the quality of life between patients using newer versus older AEDs. Pharmacists play a pivotal role in improving epilepsy management by targeting key drivers of non-adherence identified in this study, particularly cognitive and mood-related side effects [6, 38]. Through patient-tailored interventions, such as structured educational programs, collaborative optimization of AED regimens, and the implementation of adherence aids. Pharmacists can significantly reduce treatment discontinuation by recommending AEDs with improved tolerability, monitoring side effects proactively, and providing ongoing personalized support, they enhance patients' quality of life and empower individuals to sustain effective, long-term seizure control [6]. This integrated approach bridges gaps in care, ensuring therapies are both manageable and aligned with patients' unique needs.

*Conclusion:* Managing antiepileptic drug side effects remains a critical yet neglected part of epilepsy care in Libya and should be integrated into predictive models to enhance care quality. This study underscores a key opportunity for improvement in clinical practice, proposing patient-reported adherence metrics as a valuable quality indicator for optimizing epilepsy management.

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