

Unveiling the Hidden Burden: Medication-Related Problems in Epilepsy and Their Impact on Seizure Control & Quality of Life

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ABSTRACT

Background: Epilepsy is a degenerative neurological disorder marked by recurrent seizures that substantially diminish patients' quality of life (QoL). Antiepileptic medicines (AEDs), the principal treatment modality, frequently lead to various drug-related issues (MRPs) such as non-adherence, adverse drug reactions (ADRs), drug-drug interactions (DDIs), and misdosing. These MRPs adversely affect therapy efficacy by compromising seizure management and quality of life. In Iraq, there is a paucity of published research on medication-related problems in epileptic patients, indicating significant opportunities for discovery.

Objective: To ascertain the frequency and prevalence of medication-related problems (MRPs) among epileptic patients in a clinical setting in Iraq, identify the factors contributing to MRPs, and evaluate their impact on seizure management and quality of life (QoL).

Methodology: This was a cross-sectional study conducted in Dhi Qar Governorate, Iraq, from September to December 2024. This study collected data from 97 patients via formal interviews and examination of medical records. They categorized MRPs as non-adherence, adverse drug reactions (ADRs), drug-drug interactions (DDIs), and dosage mistakes. We employed descriptive statistics and logistic regression models to analyze the prevalence, contributory factors, and impacts of MRPs on seizure control and quality of life (QoL).

Results: The most prevalent medication-related problems (MRPs) were non-adherence (40.2%), adverse drug reactions (ADRs) (29.9%), drug-drug interactions (DDIs) (24.7%), and dose errors (18.6%). Polypharmacy (OR: 2.5, $p < 0.001$), age over 50 years (OR: 1.8, $p = 0.02$), and low educational attainment were all significantly correlated with medication-related problems (MRPs). Patients with MRP had much lower ratings of seizure control—only 35.1% were able to control their seizures, compared to 64.9% of people in the uncontrolled or partially controlled group. The quality of life was also diminished in individuals with persistent medication-related problems.

Conclusion: Medication-related problems (MRPs) are prevalent among individuals with epilepsy and have substantial implications for seizure treatment and overall quality of life. The efficacy of treatment depends on the prevention of MRPs via pharmacist intervention, education, and oversight. Further study is required to determine specific strategies that can reduce MRPs and enhance epilepsy care in resource-limited environments.

Keywords: Epilepsy, Medication-Related Problems, Seizure Control, Quality of Life, Antiepileptic Drugs, Non-Adherence, Adverse Drug Reactions, Drug-Drug Interactions, Polypharmacy, Pharmacist Intervention

1. INTRODUCTION

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures resulting from electrical disturbances in the brain. It impacts around 50 million individuals globally and is among the most prevalent neurological disorders on Earth (1). The condition imposes significant physical, psychological, and social burdens on sufferers, profoundly affecting their quality of life. Moreover, epilepsy incurs significant medical costs, especially in low- and middle-income countries where treatment resources are critically constrained (2).

Antiepileptic medicines (AEDs) are fundamental to epilepsy care; they aim to control seizures while minimizing side effects. The effective use of AEDs might be impeded by medication-related problems (MRPs), which are drug-related concerns that do not pertain to obtaining the desired therapeutic results. Epilepsy-associated medication-related problems include breaches of antiepileptic treatment regimens, adverse drug responses, drug-drug interactions, and dosing errors. They not only interfere with seizure regulation but also elevate hospitalization rates, diminish the quality of life, and escalate financial burdens for individuals and healthcare systems (4).

Nonadherence, the predominant medication-related problem in epilepsy management, correlates with breakthrough seizures, inadequate seizure control, and a three-fold increase in hospitalization risk (5). Adverse drug reactions, including dizziness, sleepiness, and cognitive impairment, are prevalent among users of antiepileptic drugs and frequently lead to treatment discontinuation. Polypharmacy, sometimes necessary for refractory epilepsy or concomitant conditions, complicates treatment by heightening the possibility of drug-drug interactions that may impair drug efficacy or induce toxicity. Other under-researched errors, such as dosage inaccuracies, are similarly significant, particularly among patients with intricate treatment protocols or a limited understanding of their medications (8).

Epilepsy is a common condition in Iraq, yet research on medication-related issues in patients and the effects of different treatments is limited. Given that epilepsy is a chronic disorder requiring lifetime pharmacotherapy, the identification and management of medication-related problems (MRPs) is essential. While the incorporation of clinical pharmacy services has demonstrated efficacy in improving drug utilisation, medication-related problems, and patient outcomes in several chronic diseases, its usefulness in epilepsy care has not been thoroughly examined in this region.

This study compares the quantity and categories of MRPs among epileptic patients at a clinic in Iraq. The project aims to uncover factors in MRPs and their impact on seizure control and quality of life. This research seeks to elucidate these issues to provide logical recommendations for enhancing epilepsy care, alleviating the burden of MRPs, and improving patient outcomes.

2. METHODOLOGY

Study Design

A cross-sectional observational study was conducted to evaluate medication-related problems (MRPs) in epileptic patients attending a clinical setting. The study was carried out in Dhi Qar Governorate, Iraq, over a period of four months, from September to December 2024.

Study Setting

The study was conducted in a neurology outpatient clinic at a governmental healthcare facility in Dhi Qar Governorate. This facility was chosen due to its accessibility to epileptic patients and the availability of specialized care.

Study Population

Inclusion Criteria:

- a. A neurologist diagnoses patients with epilepsy.
- b. Patients aged 18 years and above.
- c. At least one antiepileptic drug (AED) was taken by patients for a minimum of six months.
- d. The study involved patients who gave their consent to participate.

Exclusion Criteria:

- a. Patients with incomplete medical records.
- b. Patients who were pregnant or lactating.
- c. The study period included patients who did not receive regular follow-up.

Sample Size

The sample size was calculated using a prevalence-based formula, with an assumed prevalence of MRPs among epileptic patients from previous studies set at 30%, a 95% confidence interval, and a 5% margin of error. A sample size of 150 patients was determined to be statistically adequate; however, only 97 patients were enrolled due to limited study duration.

Data Collection

Data were collected through patient interviews, medical record reviews, and clinical assessments. A structured data collection form was developed and validated before use. The following data were collected:

- a. Demographic Information.

- b. Clinical Information.
- c. Medication Information.
- d. Assessment of MRPs.
- e. Non-adherence was assessed using the Morisky Medication Adherence Scale (MMAS-8).
- f. Adverse drug reactions (ADRs) were identified through patient interviews and documentation in medical records.
- g. Potential drug-drug interactions were identified using the Micromedex Drug Interaction Checker.
- h. Dosing errors and therapeutic duplications were assessed based on standard dosing guidelines for AEDs.
- i. Clinical Outcomes:
 - I. Seizure control was categorized as controlled, partially controlled, or uncontrolled based on seizure frequency.
 - II. Quality of life was assessed using a validated epilepsy-specific questionnaire.

Data Analysis

Data were analyzed using SPSS version 28. Descriptive statistics were used to summarize demographic, clinical, and medication-related variables. Frequencies and percentages were calculated for categorical variables, while means and standard deviations were calculated for continuous variables.

Prevalence of MRPs: The prevalence and types of MRPs were determined, including non-adherence, adverse drug reactions, drug-drug interactions, and dosing errors.

Factors Associated with MRPs: Logistic regression analysis was used to identify factors significantly associated with MRPs, such as polypharmacy, comorbidities, and seizure control.

Impact of MRPs on Clinical Outcomes: The relationship between MRPs and seizure control was analyzed using chi-square tests for categorical variables and independent t-tests for continuous variables.

Ethical Considerations

This study was conducted in accordance with ethical guidelines to ensure the protection and confidentiality of participants. The following ethical considerations were adhered to:

I. Ethical Approval

Ethical approval for the study was obtained from the institutional review board (IRB) or ethics committee of the respective healthcare facility in Dhi Qar Governorate, Iraq.

II. Informed Consent

All participants were provided with detailed information about the study objectives, methodology, potential risks, and benefits.

Written informed consent was obtained from each participant before data collection.

Participants were informed of their right to withdraw from the study at any time without any consequences on their medical care.

III. Confidentiality and Data Protection

All patient information was kept strictly confidential.

Personal identifiers were removed, and data were anonymized before analysis to protect patient privacy.

The collected data were securely stored and accessed only by authorized researchers.

IV. Non-Maleficence and Beneficence

The study was designed to minimize any potential harm to participants.

There were no invasive procedures, and all assessments were based on interviews and medical record reviews.

Findings from the study may contribute to improving epilepsy management and patient outcomes.

V. Scientific Integrity and Transparency

The study was conducted following ethical research principles, ensuring data accuracy, honesty, and objectivity.

Any conflicts of interest were disclosed, and the research findings were reported transparently.

3. RESULTS

Demographic and Clinical Characteristics

Age and gender:

The sample was almost evenly distributed between men and women (50.5% male, 49.5% female). There was no gender difference in epilepsy diagnosis or care during the study period.

Patients averaged 49.9 years, with patients ranging from 18 to 79 years of age, which means epilepsy occurs across all ages. The somewhat older group may serve as a testament to the chronic nature of epilepsy, which persists throughout later life.

Duration of Epilepsy:

The majority (43.3%) had been suffering from epilepsy for over 10 years, indicating a high chronic disease burden. This highlights the need for long-term drug therapy and medication-related problems (MRPs).

Number of AEDs:

Eighty-eight percent of patients used multiple AEDs. This is an aspect of epilepsy management, particularly where monotherapy does not effectively control seizures. But polypharmacy does put MRPs at higher risk.

Table 1: Demographic and Clinical Characteristics

Characteristic	Count (%)
Total Patients	97 (100%)
Gender	
- Male	49 (50.5%)
- Female	48 (49.5%)
Age	
- Mean Age ($\pm$ SD)	49.9 ($\pm$ 15.3) years
- Age Range	18–79 years
Duration of Epilepsy	
- 1–5 years	30 (30.9%)
- 6–10 years	25 (25.8%)
- >10 years	42 (43.3%)
Number of AEDs Used	
- Single AED	40 (41.2%)
- Multiple AEDs ($\geq$ 2 AEDs)	57 (58.8%)

1. Prevalence of Medication-Related Problems (MRPs)

i. Non-Adherence (40.2%):

Failure to adhere was the most prevalent MRP in 40% of patients. Forgetfulness, cost-constraint and ignorance about medication use were some of the most common causes. It reflects the need for tailored interventions including patient education, easier doses, and affordable therapy.

ii. ADRs (29.9%):

Nearly one-third of patients reported ADRs, with drowsiness and dizziness most frequent. Such adverse effects can compromise compliance and quality of life, and require close monitoring and possible dose reductions.

iii. Drug-Drug Interactions (DDIs) (24.7%):

DDIs occurred in about one-quarter of patients (particularly polypharmacy). With enzyme-dependent AEDs such as carbamazepine being involved, it calls for drug selection and medication monitoring at regular intervals by doctors.

iv. Dosing Errors (18.6%):

Nearly 19% of patients experienced dosage errors, with most errors due to underdosage. These could be associated with

incomplete knowledge of dosing schedules or patient-based modification, and may require better pharmacist-led advice.

Table 2: Prevalence of Medication-Related Problems

Type of MRP	Count (%)
Non-Adherence	39 (40.2%)
Adverse Drug Reactions (ADR)	29 (29.9%)
Drug-Drug Interactions (DDIs)	24 (24.7%)
Dosing Errors	18 (18.6%)

Details for Each MRP:

Table 3: Prevalence of various Medication-Related Problems

Non-Adherence (Total = 39)		
Specific Issue	Frequency (n)	Percentage (%)
Forgetfulness	15	38.50%
Financial constraints	10	25.60%
Lack of knowledge	8	20.50%
Fear of side effects	4	10.30%
Complex dosing schedule	2	5.10%
Total	39	100%
Adverse Drug Reactions (ADRs) (Total = 29)		
Specific Issue	Frequency (n)	Percentage (%)
Drowsiness	10	34.50%
Dizziness	7	24.10%
Gastrointestinal issues	5	17.20%
Fatigue	4	13.80%
Weight gain	2	6.90%
Mood changes	1	3.50%
Total	29	100%
Drug-Drug Interactions (DDIs) (Total = 24)		
Specific Issue	Frequency (n)	Percentage (%)
Carbamazepine with inducers	8	33.30%
Valproate with antipsychotics	6	25.00%
Phenytoin with anticoagulants	5	20.80%
AEDs with antihypertensives	3	12.50%

Multiple AED combinations	2	8.30%
Total	24	100%
Dosing Errors (Total = 18)		
Specific Issue	Frequency (n)	Percentage (%)
Underdosing	8	44.40%
Overdosing	4	22.20%
Skipping doses	4	22.20%
Taking incorrect AED timing	2	11.10%
Total	18	100%

1. Seizure Control Outcomes

Controlled (35.1%) vs. Partially Controlled (36.1%) vs. Uncontrolled (28.8%):

Only 35% of patients achieved controlled seizures, suggesting room for improvement in treatment strategies.

The partially controlled group had the highest prevalence of MRPs (non-adherence: 60%, ADRs: 34.3%). This indicates that unresolved MRPs contribute significantly to suboptimal seizure control.

Uncontrolled patients (28.8%) had lower rates of MRPs compared to the partially controlled group, possibly due to reduced engagement with therapy or other undetected factors.

Table 4: Seizure Control

Seizure Control	Count (%)
Controlled	34 (35.1%)
Partially Controlled	35 (36.1%)
Uncontrolled	28 (28.8%)

2. Relationship Between MRPs and Seizure Control

Table 5: Relationship Between MRPs and Seizure Control

Seizure Control	Non-Adherence	ADR	DDIs	Dosing Errors	Mean Age (Years)
Controlled	19 (55.8%)	6 (17.6%)	8 (23.5%)	7 (20.5%)	49.6
Partially Controlled	21 (60.0%)	12 (34.3%)	10 (28.6%)	7 (20.0%)	51.6
Uncontrolled	11 (39.3%)	6 (21.4%)	6 (21.4%)	4 (14.3%)	48.5

3. Quality of Life (QoL) Scores

Patients with controlled seizures had the highest QoL scores (76.3), while those with uncontrolled seizures had the lowest (55.2). This reflects the direct relationship between seizure control and QoL. Effective management of MRPs could enhance seizure control and, consequently, QoL.

Table 6: Quality of Life (QoL) Scores

Seizure Control	Mean QoL Score (±SD)
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Controlled	76.3 (±12.8)
Partially Controlled	64.5 (±15.4)
Uncontrolled	55.2 (±17.3)

Patients with controlled seizures reported the highest QoL scores.

QoL significantly decreased with worsening seizure control, likely due to the higher prevalence of MRPs.

4. Factors Associated with MRPs

Polypharmacy (OR = 2.5, p < 0.001):

Patients on multiple AEDs were 2.5 times more likely to experience MRPs. This confirms that polypharmacy, while sometimes necessary, increases the complexity of therapy and the likelihood of drug interactions and ADRs.

Age >50 years (OR = 1.8, p = 0.02):

Older patients were nearly twice as likely to experience MRPs. This could be due to age-related changes in drug metabolism, comorbidities, or cognitive decline affecting adherence.

Non-Adherence (OR = 3.1, p < 0.001):

Non-adherence was strongly associated with MRPs. Patients who did not adhere to their prescribed regimen were over three times more likely to experience other MRPs, including ADRs and poor seizure control.

5. Logistic Regression Analysis

Table 7: Logistic Regression Analysis

Factor	Odds Ratio (OR)	95% Confidence Interval	P-Value
Polypharmacy (≥2 AEDs)	2.5	1.8–3.5	<0.001**
Age (>50 years)	1.8	1.2–2.8	0.02*
Non-Adherence	3.1	2.1–4.6	<0.001**

- Polypharmacy (use of multiple AEDs) was the strongest predictor of MRPs (OR = 2.5, p < 0.001).
- Patients aged >50 years were 1.8 times more likely to experience MRPs (p = 0.02).
- Non-adherence had a significant association with the presence of MRPs (OR = 3.1, p < 0.001).

4. DISCUSSION

The objective of the study was to ascertain the prevalence and ramifications of medication-related problems (MRPs) in epileptic patients in Dhi Qar Governorate, Iraq. These findings provide significant insights into MRPs, their associations, and their impact on seizure management and quality of life. This is a comprehensive analysis of each result, accompanied by referenced instances.

1. Frequency of Medication-Related Issues (MRIs)

Non-adherence (40.2%), adverse drug reactions (29.9%), drug-drug interactions (DDIs) (24.7%), and dose errors (18.6%) were among the most common medication-related problems (MRPs). These results align with studies from similar situations indicating that MRPs are a crucial element in the management of chronic diseases (41).

Non-compliance: Non-adherence was identified as the predominant medication-related problem, driven by forgetfulness, budgetary limitations, and lack of knowledge. Epileptic patients worldwide reported non-adherence rates as high as 30–50% (42). Faught et al. have posited that inadequate adherence to antiepileptic drugs (AEDs) results in increased seizure frequency, diminished quality of life (QoL), and elevated healthcare expenditures (42).

Drug-drug interactions (DDIs): Adverse drug reactions (ADRs) were observed in roughly 30% of patients, with sleeplessness and dizziness being among the most prevalent adverse effects. These findings corroborate other studies indicating that antiepileptic drugs, including carbamazepine and valproate, are associated with central nervous system adverse effects (43). Adverse drug reactions significantly affect adherence and, if unaddressed, may result in treatment discontinuation.

We identified DDIs in approximately 25% of patients, particularly among those using enzyme-inducing antiepileptic drugs (AEDs). Comparable DDI rates were observed in investigations of polypharmacy-based epileptic treatment (45). AEDs adversely affect cytochrome P450 enzymes through their pharmacokinetic properties, heightening the risk of drug-drug interactions and compromising the drug's efficacy and toxicity (46).

Medication Dosing Errors: In 18.6% of patients, the dosage mistakes exceeded 65% and fell below 85%. Reports indicate that, for chronic conditions, the probability of dosing errors is elevated, typically due to patients' lack of understanding or incorrect drug prescriptions (47). Underdosing can result in subtherapeutic levels and inadequate seizure management (48).

2. Impact of MRPs on Seizure Management

Only 35.1% of patients experienced seizures that were fully managed, whereas 36.1% had uncontrolled seizures (28.8%). The elevated prevalence of MRPs in the partially managed and uncontrolled groups highlights the detrimental effects of untreated MRPs on treatment outcomes.

Non-Adherence and Seizure Management: The non-adherence rates were markedly elevated in the partially controlled group (60%) compared to the control group (55.7%). This aligns with evidence indicating that non-adherence is the primary factor contributing to compromised seizure control (50). Novakova et al. demonstrate that even slight variations from AED regimens can result in breakthrough seizures (51).

Adverse Drug Reactions (ADRs) and Seizure Management: ADRs were most prevalent in the partially controlled cohort (34.3%). Research indicates that adverse drug reactions (ADRs) may necessitate dose reduction or medication cessation, resulting in inadequate seizure management (52). Monitoring and dosage adjustments are essential for minimizing adverse drug reactions and achieving optimal patient outcomes.

Polypharmacy and Seizure Management: Polypharmacy was significantly linked to inadequate seizure control, evidenced by the higher occurrence of medication-related problems in patients utilising multiple antiepileptic drugs. There is evidence that polypharmacy raises the risk of drug-drug interactions (DDIs) and adverse drug reactions (ADRs), which makes managing seizures more difficult.

3. Quality of Life (QoL) and Seizure Management

The mean QoL score was superior in the control group (76.3) compared to the partially controlled (64.5) and uncontrolled groups (55.2). This discovery corroborates studies indicating that seizure freedom is a significant determinant of quality of life in individuals with epilepsy (55).

The diminished quality of life in the untreated group may also be ascribed to the interplay between medication-related problems and recurrent seizures. Studies have shown that individuals with untreated epilepsy are at an increased risk of experiencing psychiatric comorbidities, such as anxiety and depression, which subsequently diminish quality of life (56).

4. Factors Related to MRPs

This study also discovered the following MRP determinants:

Polypharmacy: Patients administered numerous antiepileptic drugs were 2.5 times more predisposed to experiencing medication-related problems. This aligns with evidence of polypharmacy in epilepsy management, where many drugs complicate treatment and increase the risk of drug-drug interactions (DDIs) (48). **Age:** Patients over 50 years were more prone to develop medication-related problems (MRPs) (OR = 1.8). Physiological alterations in pharmacokinetics and pharmacodynamics associated with ageing, along with comorbidities, significantly elevate this risk (57).

Non-adherence was a substantial predictor of medication-related problems (OR = 3.1). This discovery underscores the pivotal importance of adherence in diminishing medication-related problems and optimizing therapeutic outcomes (58).

5. Implications for Pharmacists:

Pharmacists can facilitate the mitigation of medication-related problems (MRPs) by medication assessments, patient education, and adherence support initiatives. Numerous studies have shown that pharmacist-led interventions substantially decrease medication-related problems and enhance treatment results in chronic diseases.

Patient Education: Adequate instruction on the use of AEDs, potential adverse effects, and compliance can empower patients and mitigate medication-related problems (MRPs). Educational sessions with participants can enhance both knowledge and adherence among individuals with epilepsy (59).

Regular Surveillance: Adverse Drug Reactions (ADRs) and Drug-Drug Interactions (DDIs) must be evaluated consistently, particularly in patients on polypharmacy. Additional resources like Lexicomp and Micromedex can assist in identifying possible interactions (60).

5. CONCLUSION

This study emphasises the extensive application of MRPs to individuals with epilepsy and their significant impact on seizure control and overall quality of life. Targeted therapeutic approaches addressing MRPs can enhance treatment results and patient satisfaction. Future research should focus on piloting and assessing pharmacist-led strategies to mitigate medication-related problems in these environments.

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