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Non-adherence to antiepileptic medications among patients in Saudi Arabia: A systematic review 2024

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Abstract:

Background:

Epilepsy is the common neurological disorder in the world, affecting approximately 50 million people. Anti-epileptic medication non-adherence can be a reason for long term hospitalization, repeated emergency seizure attacks, increased health care cost and frequent absence of work due to poor seizure control. Existed studies of anti-epileptic medication non-adherence in Saudi Arabia have reported great discrepant and inconsistent results which calls a growing demand of systematic review and meta-analysis. Non-compliance with antiepileptic drugs (AEDs) results in recurrent seizures and visits to the emergency departments, leading to an increased social and economic burden, as well as increased morbidity and mortality. Non-adherence to epilepsy medications can interfere with treatment and may adversely affect clinical outcomes, although few studies have examined this relationship. Non-adherence was found to be associated with reduced seizure control, lowered quality of life, decreased productivity, seizure-related job loss, and seizure-related motor vehicle accidents.

Aim of this review : To assess the adherence to AEDs and to identify the different factors which could affect medication adherence among patients with epilepsy.

Method: Literatures were searched from the PubMed/Medline, Science Direct, PsycINFO, and Google Scholar for grey literatures. The data were extracted using a prepared data extraction Microsoft Excel format from July 2020 to April 2024 and Saudi Digital Library (SDL), data extracted from published articles were systematically analyzed for Non-adherence to antiepileptic medications among patients in Saudi Arabia

Results:. The usability and outcome of Non-adherence to antiepileptic medications among patients in Saudi Arabia . 6 articles were selected that compliant with the theme of this present systematic review (Table 1). Among the 6 reviewed articles, articles have explained the current Non-adherence to antiepileptic medications among patients in Saudi Arabia .

Conclusion: Non-compliance with AEDs was noted in nearly half of the patients and likely to be a major cause of treatment failure. Age, recent episode of seizure, and concomitant use of other medications were significant predictors of non-compliance with AEDs. This demonstrates a need for clinicians to give more attention for the monitoring and evaluation of anti-epileptic medication adherence in the health care service.

Keywords: Non-adherence, antiepileptic, medication, patients, Saudi Arabia.

Introduction

Background

Epilepsy is a chronic disease which is rated as the second common chronic neurologic disorder worldwide in terms of disability-adjusted life years [1]. Approximately 7 in every 1,000 Saudis suffer from epilepsy with a significant social and economic burden to the patients, their families and the healthcare system [2]. Antiepileptic drugs (AEDs) are the foundation in the management of epilepsy and can achieve freedom from seizures in 70% of patients if an effective treatment plan is followed [3]. Non-adherence in epileptic patients remains the leading cause of pharmacological treatment failure and seizure recurrence [4]

Epilepsy is one of the most problematic neurological disorders [5].According to the World Health Organization (WHO), around 50 million people of all ages are affected by epilepsy worldwide, which makes it one of the most common neurological disorders [6]. Its prevalence is 7.60/1000, with an incidence reaching 67.77/100,000 [7]. Nearly 80 % of people with epilepsy (PWE) worldwide belong to middle-and low-income countries [8], with higher prevalence and incidence [9]. This disparity makes epilepsy a real public health problem in these countries [10]. The management of epilepsy requires a proper diagnosis, followed by the prescription of appropriate ant seizure medication (ASM) at an adequate dosage [11]. However, proper therapeutic follow-up and treatment efficacy depend in large part on the involvement of PWE. This involvement is represented by good ant seizure medication adherence (AMA) [12]. The poor or non-AMA can mimic drug-resistant epilepsy. Research regarding patient adherence to AEDs has focused largely on the impact of the patient-physician relationship on adherence and potential education programs intended to improve adherence [13]. Findings suggest that patients tend to be more adherent when physicians have open dialogue regarding epilepsy and its treatments [14] and when patients are comfortable speaking with their physician [15]. It is also important for physicians to not only question patients about seizure frequency and current medication use at office visits, but to probe specifically regarding adherence [16] Due to the paucity of published studies on the impact of no adherence among patients with epilepsy, this study investigates the factors associated with non-adherence to AEDs, as well as the relationship between non-adherence and patient quality of life, seizure control, and productivity.[17]

Additionally, the available questionnaires are narrowed to specific direct medication related causes without considering other possible indirect domains that hinder medication adherence in patients with epilepsy such as social reasons and cost of medications [16]

In fact, it is essential to be vigilant about all the potential barriers that could interfere with following the health care provider's recommendations. These common disadvantages of the available tools limit their use and affect the result accuracy. Therefore, there is a clear need for a specific scale that measures adherence to ASMs, covering all the potential reasons for non-adherence to optimize treatment outcomes [17].Although, many studies have been existed regarding anti-epileptic medication non-adherence of people attending outpatient department in Saudi Arabia, there is a great discrepancy and inconsistency of reported results ranging from 21.8% to 68% [18]. A full picture of magnitude of the problem is critical to develop effective intervention and for policy response that can support to improve treatment adherence of AED. This calls a growing demand of systematic review and meta-analysis regarding antiepileptic medication non-adherence and its determinants in Saudi Arabia .The studies have reported that the rate of non-adherence in epileptic patients ranges from 30% to 60% with a negative correlation between adherence and frequency of seizures [19]. Assessing no adherence to AEDs in epileptic patients and its contributing factors help to promote programs that maximize medication adherence and achieve optimal seizure control in the future .

Methodology

Aim of the study

To assess the adherence to AEDs and to identify the different factors which could affect medication adherence among patients with epilepsy in Saudi Arabia 2024 .

Study design:

Systematic reviews using Online searching engines were using databases to identify relevant articles through the included electronic databases: PubMed, EMBASE, PsycINFO, and CINAHL from July 2020 to April 2024, and Saudi Digital Library (SDL), data extracted from published articles were systematically analyzed.

Search strategy:

Online searching engines were using databases to identify relevant articles through the included electronic databases: PubMed, EMBASE, PsycINFO, and CINAHL from July 2020 to December 2024 and Saudi Digital Library (SDL), data extracted from published articles were systematically analyzed for Non-adherence to antiepileptic medications among patients in Saudi Arabia Cross-sectional studies published in English were included if they met the following criteria: (1) reported the adherence to using a validated measure; and (2) had a sample size of at least 70 patients with epileptic. The Joanna Briggs Institute critical appraisal for studies reporting prevalence data was used to assess the quality of the included studies.

Searches and Data Sources

A comprehensive search was performed to obtain studies on the adherence to antidiuretic drugs in Saudi Arabia. The databases used in the search included. The search terms used were consistent with our previous systematic review, which includes "adherence or compliance or persistence" and "antiepileptic". The full list of search terms used, and the results obtained from each database are presented. We also employed a snowballing technique and citation tracking to identify all potentially relevant studies that might not have been identified from the above databases.

Inclusion criteria:

Patients with epilepsy , patients who had taken at least one antiepileptic medication, and patients who had been followed for at least 6 months.

Exclusion Criteria

The exclusion criteria included patients who were too ill to have an interview, cognitive impairment, refused to participate, or had incomplete medical records. The patients were recruited into the study during their appointment for neurology follow-up

Data extraction

Extracted data from all the included studies , individually extracted the data of one-third of the included studies, using a modified version of The Joanna Briggs Institute Data Extraction Form for prevalence studies. The extracted data included study design, aims of the study, setting, country, number of participants and their characteristics, adherence measures including cut-off points, and the reasons for non-adherence reported by patients. The extracted data were verified.

The process of selecting the articles, which are contained in this review

We modified the study selection criteria from a previous study which reported adherence to epileptic medications , and used representative samples of the general population of epileptic medications patients. Cross-sectional studies published in English were included in our review if they met the following criteria: (1) reported the adherence to using a validated measure with a defined cut-off point to indicate adherence; and this approach of using a minimum sample size as a selection criterion has been employed in a previous the prevalence of a specific disease .

Table1: Summary of Findings of the Non-adherence to antiepileptic medications among patients in Saudi Arabia.

Author, Date, Country	Region	Study design	Study aim	Results
Alrukban et al (2024) (20)	Saudi Arabia	A cross-sectional study	To determine the rate and predictors of non-adherence to ant seizure medications in Saudi Arabia.	The most frequently rated predictor of non-adherence was poor seizure control by ASMs. This is in line with the findings of a national cross-sectional study in which a significant association between ASM non-adherence and poor seizure control (p-value = 0.002) was observed. Poor seizure control and seizure frequency were consistently found to be associated with non -adherence to ASMs in the literature . In fact, poor seizure control can result from inappropriate medication selection, sub therapeutic prescribed doses, drug–drug interactions, and most importantly non-adherence to ASMs. Doubtless, even the correct medications at the correct doses cannot be effective if the patient does not take them.If non-adherence is not recognized as a reason for the apparent medication ineffectiveness, it may lead to the unnecessary addition of another ASM or increasing the ASM dose in an attempt to manage uncontrolled seizures not published in English, and 2 studies were a validation of adherence measurement. **Conclusions** Adherence to ASMs plays a vital role in the management of epilepsy because non-adherence is associated with increased morbidity and mortality. This study reveals that adherence to ASMs is suboptimal in Saudi Arabia, and it also identifies common predictors of non-adherence to ASMs. Such outcomes will raise the awareness of health care providers about the importance of conducting adherence assessments regularly to identify non-adherent patients and their reasons for non-adherence, aiming to tailor an appropriate personalized intervention for an individual patient. Physicians' awareness of medication adherence can be effectively increased through campaigns, conferences, and clinical guidelines. Overall, non-adherent patients need to be identified, understood, and managed more carefully.

Hajji, et al (2024) (21)	Moroccan	A cross-sectional study.	To determine the proportion of non-Ant seizure Medication Adherence (non-AMA) and refusal attitude towards Epilepsy Surgery (ES) and their associated factors in Moroccan People With Epilepsy (PWE).	The lower percentage of refusal attitudes toward ES in our study could be attributed to the result of PWEs' raising awareness efforts that fit into the program of ES development previously recommended in Morocco. The nature of the doctor-patient relationship that characterizes our population gives total authority to the physician in therapeutic decisions and ethically instills the importance of absolute trust in the patient. This context seems to make the Moroccan PWE less involved in his therapeutic decisions and necessarily accept the proposal of the ES, which could underestimate the proportion of the refusal attitude of the ES in our study. The rejection of SE in our study is due to apprehension (61.2 %), confidence (24.5 %), and alleged fragility (14.3 %). The proportion of apprehension about ES is comparable to that observed in Colombia (60 %) while 86 % of PWE believe in the dangerousness of ES in the United States. In addition to some characteristics linked to epilepsy, fear of surgery and its difficult consequences was a determining reason for attitudes towards ES in the United States and Colombia. All these reasons for refusing ES stem from ignorance of the principle of this therapeutic alternative, which requires education and awareness efforts on the part of PWE. **Conclusions** This is a cross-sectional study assessing the collaborative value of PWE in the follow-up of ASM. The non-AMA and refusal attitude of ES have considerable proportions in our study but remain relatively low compared to other studies. Our results may reflect the recent efforts of the medical staff to educate and sensitize PWE during consultations, to the importance of their AMA on the one hand, and the therapeutic value of ES in DRE on the other. Associated socio-demographic and clinical factors must be taken into consideration when prescribing and monitoring the therapeutic management of PWE. The non-AMA and refusal attitude of the ES found in our study calls for intensified efforts to reduce the cases of pseudo-DRE, to develop the Doctor-PWE relationship, and to improve the involvement of the PWE in the finality of their ASM.
Alotaibi et al. (2024) (22)	Saudi Arabia	A new scale was developed	To develop and validate a multidimensional scale that measures adherence levels to	The availability of such a scale helps in identifying the adherence level to ASMs and the causes of non-adherence. The present analyses provided evidence that the ASASM-10 was a reliable and valid tool for evaluating patients' adherence to ASMs. The internal consistency of the ASASM-10 was good with Cronbach's alpha of 0.80 higher than the required value (i.e., 0.70)

			antiseizure medications and detects patients' reasons for non-adherence.	for the reliability of new scales, and it indicated excellent and acceptable evidence of internal consistency for the scale. Moreover, the ASASM-10 had slightly greater reliability than MARS (Cronbach's alpha of 0.75) . Among different available reliability estimations, Cronbach's alpha was selected in this study. It is consistently recommended to use Cronbach's alpha in the literature and by the best practice guidelines for scale development. This is due to its ease of interpretation and its ability to provide comparable results across similar studies. It is the most commonly used reliability coefficient in psychometric research, and the reference scale used in this study (MARS) also employed Cronbach's alpha for its reliability assessment. **Conclusions** The present analyses provided evidence that ASASM-10 is a reliable and valid scale for evaluating patients' adherence to ant seizure medications. It is the first available scale for assessing medication adherence in patients with epilepsy that can be utilized in clinical practice and research settings.
Kishk, et al (2023) (23)	Egypt at Kasr Al-Ainy Hospitals	cross-sectional study	To examine the clinical characteristics of adolescents with epilepsy (AWE) and highlight the differences between childhood-onset epilepsy and adolescent-onset epilepsy.	Each year, approximately 1.1 million children with epilepsy transition into adulthood. This typically occurs during adolescence, a crucial stage for both physical and psychological growth. While this period can be stressful for all individuals, young people with epilepsy may face additional challenges, including social stigma, mental health and, feelings of loneliness . One of our study's aims was to identify the differences between childhood-onset epilepsy and adolescent-onset epilepsy, A total of 136 AWE were included in the study, consisting of 82 males and 54 females with a median age of 15 and an interquartile range of 13–17. Most patients (54 %) had focal onset seizures, while the remaining 46 % had generalized onset seizures. Of the total sample, 87 (64 %) achieved seizure control for at least one year and are currently taking ASMs. However, only 60 % of the patients were found to be adherent to their ASMs. **Conclusions** Depression and self-stigma are significant barriers to adherence among adolescents with epilepsy. These findings highlight the need to involve psychiatrists and epileptologists in epilepsy transition programs.
Mahmoud et al (2022) (24)	Egypt and Saudi Arabia	A cross-sectional study	To assessment of patient's non-adherence to antiepileptic drugs	On the other hand, no significant difference in adherence due to marital or employment status either among Egyptian or Saudi patients. Another study agreed with our finding, while another one agreed with us in marital status does not affect medication adherence. Concerning employment status, some studies

			among Saudis and Egyptians, and evaluation of the association between patient beliefs about the disease and the frequency of seizures.	found that employment status significantly affected adherence to AED. Employers or students were less likely to adhere to their treatment regimen compared to those who were unemployed, and this may be justified by working or academic schedules that prevent patients from following their prescribed regimen, or may be due to the side effects, especially drowsiness that affect job or academic performance. Studies carried out in Ethiopia found that divorced and widowed patients were significantly poor adherent when compared with single patients in their marital status, which might be due to no support from their partners in adhering to the prescribed medication(s) and instructions given by health care professionals **Conclusions** Evaluation of medication adherence and improvement of the belief about the importance of medication and identification of factors affecting adherence to treatment is very important to reduce seizure frequency. These will be done by healthcare providers through educational programs to enhance the patients' belief about their medication to improve medication adherence.
Alsfouk, et al (2023), (25)	Saudi Arabia	Cross-sectional analytic study	To evaluate the rate and determinants of non-adherence to antipsychotic medications in Saudi Arabia.	Medication effectiveness is one of the biggest problems in management of chronic diseases. Many different factors can determine the effectiveness of a medication, including the appropriateness of the treatment, drug tolerance and, most important, adherence to the medication. Even the right drugs at the right doses cannot be effective if the patients do not take them. Non-adherence to medication is defined by the WHO as a situation in which a patient's behavior in taking medication is different. Out of 220 patients, 122 (55.5%) were considered non-adherent (MARS scores 6 or less). The MARS items contributing most to non-adherence were "the medication makes me feel tired and sluggish" and "forget to take the medication", 55 and 40.9%, respectively. Additionally, adverse drug effect significantly increased the risk of poor adherence in regression analysis (odds ratio = 1.97, $p = 0.028$). The model also showed that female sex, low income, cigarette smoking, substance abuse, uncontrolled disease, comorbidity, and use of Riyadh religious therapy were associated with increased risk of Prevalence and risk factors of non-adherence to antipsychotic medications in Saudi Arabia. poor adherence, but were however not statistically significant ($p < 0.05$) **Conclusion** This study showed high non-adherence rate to antipsychotic medications. Adverse drug effects and forgetting to take medications were the main patient-reported barriers to adherence. Likewise, socio demographic, clinical, and

				spiritual factors affected medication adherence. Knowing these predictors helps in early identification of patients who are predisposed to medication non-adherence and allows personalized interventions that improve adherence and treatment out com.

Results and discussion

The usability and outcome of Non-adherence to antiepileptic medications among patients in Saudi Arabia . 6 articles were selected that compliant with the theme of this present systematic review (Table 1). Among the 6 reviewed articles, articles have explained the current Non-adherence to antiepileptic medications among patients in Saudi Arabia

Poor adherence to AEDs is common in clinical practice and is associated with negative outcomes. Several studies have reported that the rate of non-adherence in epileptic patients ranges from 30% to 60% and remains the leading cause of uncontrolled seizure and recurrence [26]. In this study, of the epileptic patients were non adherent to their prescribed AEDs that appeared slightly higher than the previously reported studies on the Saudi population although it is in line with the other similar studies conducted worldwide. An old study conducted in Saudi Arabia on 104 patients concluded that 32 (30.8%) patients were non-adherent to their AEDs [27]. A recent study conducted in Riyadh concluded that 38.3% of the patients were non adherent to antiepileptic treatment [12]. A recent study from Ethiopia concluded that almost two-thirds (65.4%) of the patients were non adherent to their AEDs [19]

The association of medication non-adherence and seizure control has been documented in previous literature [28]. In a study by the authors hypothesized that general practitioners may refer patients with poor control to specialists due to an apparent failure of AED treatment when non-adherence could be the major contributor to the appearance of treatment failure [29] . Similarly, non-adherent patients in our study were more likely than adherent patients to experience a loss in seizure control and those that experienced a loss of seizure control were likely to have their treatment changed in some way. [30] The failure to consider adherence as a reason for apparent medication failure may result in an unnecessary increase in AED dosage or an addition of another AED in an attempt to control seizures [31]. This may unnecessarily expose the patient to more medication related side effects and iatrogenic complications. In order to assist physicians in identifying non-adherent patients, a standardized epilepsy management protocol should be developed that assists physicians in correctly identifying the causes of treatment failure. conditions was also associated with non-compliance in the univariate and multivariate analysis. [32] This finding calls for a reduction in inappropriate polypharmacy as complex medication regimens compromised adherence to vital medications. [33]

Conclusion

In this review, we found that there is a high burden of anti-epileptic medication non-adherence among patients attending outpatient department in Saudi Arabia. There were different and non-uniform adherence measurement techniques showing a significant variation in the reported magnitudes of anti-epileptic medication non-adherence. Presence of co-morbid illness, medication side effects and substance use or drug abuse behavior had crude association with anti-epileptic medication non-adherence. This demonstrates a need for clinicians to give more attention in the monitoring and evaluation of adherence for anti-epileptics in the health care services. We also highly recommended for the adoption of validated,

contextualized and standardized medication adherence screening tools. Furthermore, prevention, early screening and intervention of co-morbid illness, medication side effects and substance abuse behavior are vital to promote anti-epileptic medication adherence in Saudi Arabia

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