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ORIGINAL ARTICLE

Measuring of Non-Adherence of Epilepsy Patients to their Medication and its Relationship to their Beliefs about the Disease, and the Frequency of Seizures: A Comparative Study between Epilepsy Patients in Saudi Arabia and Egypt

MADIHA RABIE MAHMOUD[1-2], HIALAH ABDALLUH ALENAZI[3], MANAHEL SALEM ALMUTAIRI[3], BAYAN SULAIMAN ALBLOWI[3], OSAMA GAD ABDELAZIZ[4], HAGER MOHAMED ABDELHADY[4], SHERIF GAD ABDELAZIZ[5]

[1]*Professor of Pharmacology Dept., College of Medicine, Ha`il University, KSA.*
[2]*Professor of Pharmacology Dept., TBRI, Ministry of Higher Education and Scientific Research, Egypt.*
[3]*College of Medicine, University of Ha'il, KSA.*
[4]*Faculty of Pharmacy, Cairo University, Egypt.*
[5]*Faculty of Medicine, Ain Shams University, Egypt.*
Corresponding author: Madiha Rabie Mahmoud, Email: madihamahmoud3@gmail.com, Cell: 00966597910299

ABSTRACT

Background: Medication adherence and believes are crucial to achieving the desired goal of therapy in epileptic patient. Anti-epileptic drugs (AED) are the primary therapeutic modes for epileptic patients and have been demonstrated to control seizure, which decreases morbidity and mortality associated with epilepsy. Our aim is assessment of patient's non-adherence to anti-epileptic drugs among Saudis and Egyptians, and evaluation of the association between patient beliefs about the disease and the frequency of seizures.

Methodology: A cross-sectional study was carried out using online questionnaire among patients with epilepsy in neurology clinics either in Saudi Arabia (KSA) or Egypt. Medication adherence was assessed using a self-reported questionnaire which was designed by the authors with reference to relevant literature. The questionnaire includes patients' socio-demographic, types, and causes of epilepsy, causes of poor adherence to antiepileptic drugs and belief of patients about epilepsy. All variables were calculated using frequencies and percentages.

Results: The prevalence of non-adherence was high among epileptic Saudi patients (52.3%) compared to Egyptians (36.6%). It was reported that older age, female gender, high educational level, high family income significantly increased the patient adherence to AED, while marital and employment status didn't. Many factors causing poor adherence were forgetfulness, polypharmacy, medication complexity, feeling bad or better which more pronounced among Saudis than Egyptians.

Conclusion: Evaluation of medication adherence and improvement of the belief about the importance of medication and identification of factors affecting adherence to treatment is mandatory to reduce seizure frequency, so we recommend educational programs to enhance the patients' belief about their medication to improve medication adherence presented by the healthcare providers.

Keyword: Anti-epileptic drug, Medication adherence, Patients' beliefs, Saudi Arabia, Egypt.

INTRODUCTION

Epilepsy is a chronic and disabling neurological disease affecting individuals in all age groups impairing quality of life. [1,2] It is a debilitating illness that leads to neuropsychological impairment, frequent physical injury, social stigma, poor academic performance, reduced employment rate, and shortened lifetime. [3] Epilepsy affects approximately 50 million people and about 80% of them are found in low and middle-income countries. [1,2] Non-adherence can be defined as any deviation from the recommended timings or dosages of a prescribed treatment regimen.[4] Non-adherence may be intentional or unintentional, including premature discontinuation, forgetfulness in taking medication, taking more or less than that prescribed or at incorrect timing, and failure to refile prescription in pharmacy. [5] This contributes to reduced benefit gained from the medication,[6] increased seizure frequency, higher healthcare financial load and greater mortality.[7,8] This is in addition to poorer educational outcomes, greater risk of physical injuries, depression and anxiety, and higher levels of stigma experienced by people with epilepsy. [9] Poor adherence may be the most important cause of poorly controlled epilepsy.[10] The rate of medication adherence could be associated with many factors including belief about medications, comorbidity, number of medications, duration of therapy, age, gender, and educational level.[11,12] According to different studies, the most important predictor of medication adherence is medication belief.[13,14] Therefore, assessment of medication adherence and belief in addition to identification of factors affecting adherence is essential to improve overall epilepsy treatment outcome, [15] thereby reducing seizure frequency, reducing the mortality, and improving the quality of life in those patients.[16] This study aims to estimate the percentages of non-adherence of patients with epilepsy to treatment with AED among patients in Saudi Arabia and Egypt, as well as, to assess the association between beliefs of patients with epilepsy and extent to medication adherence & frequency of seizure.

SUBJECTS AND METHODS

This comparative study was done by collecting data from patients in neurology clinics either in Saudi Arabia or Egypt through well-done questionnaire conducted from December 2021 to May 2022. This study was carried out among epileptic patients (885); only 675 patients whose completed the questionnaire and fulfill all inclusion criteria; Saudi Arabia (306) and Egypt (369), their ages ranges from 18-65 years old. The exclusion criteria included patients who had cognitive impairment, non-epileptic patient or who were less than 18 years old. The questionnaire about patients Scio-demographic, types and causes of epilepsy, factors of poor adherence to antiepileptic drugs and belief of patients about epilepsy. Medication adherence was assessed using a self-reported questionnaire which was developed based on the review of various literature works.[17-19] Patients who took their AEDs appropriately were adherent, whereas patients who missed or stopped a dose of their AEDs within the past month were considered as non-adherent. Filling of this questionnaire is considered as an agreement for their participation. Statistical analysis was done using Package for the Social Sciences Version 25. All variables were calculated using frequencies and percentages. The p-values ≤ 0.05 were statistically significant.

RESULTS

In this research, the total number of epileptic patients were 885; only 675 patients whose completed the questionnaire; Saudi Arabia (306) and Egypt (369). About 56% of participants from females, and more than 67% from 18-30 years old, 80% from

secondary and university students, about 70% were single and divorced. The employment status was equally distributed, while the family income was low in Egypt compared to those in KSA (Table 1).

The prevalence of non-adherence was more among Saudi patients (52.3%) compared to Egyptians (36.6%, Figure 1). Poor medication adherence was observed in younger (18-30 years) participants and more pronounced in Saudis (31.6%) more than Egyptians (50.2), and adherence was directly proportion with increasing age as shown in patients` age (31-50 and > 50 years). Highly educated patients showed more adherence to AED (71.3% & 52.4%) when compared with none to middle education (30.6% & 26.8%) either in Egypt or KSA respectively. So, adherence to AED increased significantly (at $p< 0.05$) in younger age, females, high educational level, family income, while no significant difference was observed in adherence due to marital or employment status either among Egyptian or Saudi patients (Table 1).

Table 2 showed that most of participants' ages had epilepsy in age ranged from five to 25 years old. About 54.8% & 39.2% of patients with Focal epilepsy VS 29.5% & 49 with generalized epilepsy among Egyptians and Saudis respectively (Figure 2). Causes of epilepsy was varied (half of them due to blows to the head in addition to fever). Many symptoms of epilepsy, and bad effects of epilepsy on patients' life and relatives were observed. Patients' beliefs that epilepsy might improve by time was said in half of participants.

Table 1. Association between sociodemographic characteristics and non-adherence to antiepileptic medication among Egyptian and Saudi patients with epilepsy [Total n=675 Participants, n=369 (Egyptians), n= 306 (Saudis)].

Characteristics		Egyptian Participants			Saudis Participants			
Total number 369 (54.7)		Non-adherence 135 (36.6)	Adherence 234 (63.4)	P- value	Total number 306 (45.3	Non-adherence 160 (52.3)	Adherence 146 (47.7)	P- value
Gender								
Male	159 (43.1)	77 (48.4)	82 (51.6)	0.013*	138 (44.2)	110 (79.7)	28 (20.3)	0.001*
Female	210 (56.9)	58 (27.6)	152 (72.3)		168 (55.8)	50 (29.8)	118 (70.2)	
Age (years)								
18-30	249 (67.5)	124 (49.8)	125 (50.2)	0.002*	206 (67.3)	141 (68.4)	65 (31.6)	0.004*
31-50	93 (25.2)	9 (9.7)	84 (90.3)		82 (26.8)	16 (19.5)	66 (80.5)	
>50	27 (7.3)	2 (7.4)	25 (92.6)		18 (5.9)	3 (16.7)	15 (83.3)	
Level of Education								
None- Middle	72 (19.5)	50 (69.4)	22 (30.6)	0.021*	56 (18.3)	41 (73.2)	15 (26.8)	0.008*
Secondary/ University	297 (80.5)	85 (28.6)	212 (71.3)		250 (81.7)	119 (47.6)	131 (52.4)	
Marital Status								
Married	117 (31.7)	45 (38.5)	72 (61.5)	0.782	94 (30.7)	50 (53.2)	44 (46.8)	0.819
Single/ Divorced	252 (68.3)	90 (35.7)	152 (64.3)		212 (69.3)	110 (51.9)	102 (48.1)	
Employment Status								
Student	120 (32.5)	46 (38.3)	74 (61.7)	0.983	99 (32.4)	34 (34)	66 (66)	0.991
Employee	123 (33.3)	44 (35.8)	79 (64.2)		106 (34.6)	35 (33)	71 (67)	
Un-employee	126 (34.2)	43 (34.1)	83 (65.9)		101 (33)	37 (36.6)	64 (63.4)	
Monthly Income (SAR)								
< 5000	213 (57.7)	114 (53.5)	99 (46.5)	0.003*	108 (35.3)	68 (63)	40 (37)	0.020*
> 5000	156 (42.3)	21 (13.5)	135 (86.5)		198 (64.7)	92 (46.5)	106 (53.5)	

*Significant differences at P ≤ 0.05.

Table 2. Signs, symptoms and causes of epilepsy among Egyptian and Saudi patients with epilepsy [Total n=675 Participants, n=369 (Egyptians), n= 306 (Saudis)].

Question	Answer	Egyptians n (%)	Saudis n (%)
The age of being with epilepsy (years).	< 5	69 (18.7)	66 (21.6)
	5-15	123 (33.3%)	102 (33.3)
	16-25	132 (35.8%)	100 (32.7)
	26-40	36 (9.8%)	32 (10.5)
	41& above	9 (2.4%)	6 (1.9)
Types of Epilepsy.	Focal Epilepsy	202 (54.8)	120 (39.2)
	Generalized Epilepsy	109 (29.5)	150 (49)
	Uncertain Epilepsy	58 (15.7)	36 (11.8)
The cause of epilepsy.	Blows to the head	103 (27.9)	74 (24.2)
	Fever	93 (25.2)	53 (17.3)
	Genetics	40 (10.8)	42 (13.7)
	Vascular disease.	29 (7.9)	40 (13.1)
	Convulsions in childhood.	25 (6.8)	30 (9.8)
	Lack of oxygen before birth	37 (10.0)	29 (9.4)
	Meningitis.	24 (6.5)	18 (5.9)
	Congenital malformations & Brain tumors	18 (4.9)	20 (6.5)
The symptoms of epilepsy.	Involuntary and random movements	252 (68.3)	200 (65.4)
	Complete loss of consciousness	162 (43.9)	132 (43.1)
	Temporary loss of consciousness	126 (34.1)	126 (41.2)
	Stare into space	129 (34.9)	108 (35.3)
	Disturbance of vision and sensation	105 (28.5)	84 (27.5)
	psychiatric disturbances	60 (16.3)	84 (27.5)
The bad effects of epilepsy on your life.	Yes	153 (41.4)	128 (41.8)
	No	57 (15.4)	60 (19.6)
	Sometimes	159 (43.1)	124 (40.5)
The bad effects of epilepsy relatives.	Yes	159 (43.1)	136 (44.4)
	No	96 (26)	82 (26.8)
	Sometimes	114 (30.9)	94 (30.7)
Your beliefs that epilepsy might improve by time.	Yes	187 (50.7)	146 (47.7)
	No	80 (21.7)	70 (22.9)
	I don't know	102 (27.6)	90 (29.4)

Table 3. Comparison between Egyptian and Saudi patients with epilepsy about the reasons for non-adherence to AED. [Total n=675 Participants, n=369 (Egyptians), n= 306 (Saudis)].

Question	Answer	Egyptian n (%)	Saudis n (%)
Number of AED used.	Monotherapy	223 (60.4)	169 (48.7)
	Polypharmacy	146 (39.6)	157 (51.3)
Your beliefs that receiving more AED drugs caused medication non-adherence.	Yes	195 (52.8)	148 (48.4)
	No	174 (47.2)	158 (51.6)
Forgetfulness.	Yes	132 (35.8)	198 (64.7)
	No	237 (64.2)	108 (35.3)
Difficulties to remember to take AED.	No/ Rarely	234 (63.4)	146 (47.7)
	Twice/week	49 (26)	44 (14.4)
	3 Days/week	59 (26.8)	46 (15.0)
	>3 Days/week	27 (7.3)	70 (22.9)
Stop taking AED when you feel better.	Yes	119 (32.2)	190 (62.1)
	No	250 (67.8)	116 (37.9)
Stop taking AED when you feel bad.	Yes	146 (39.6)	194 (63.4)
	No	223 (60.4)	112 (36.6)
Stop taking AED because of Medications side effects.	Yes	161 (43.6)	197 (64.4)
	No	208 (56.4)	104 (35.6)
Stop taking AED because of high medicine price.	Yes	133 (36.0)	93 (30.4)
	No	236 (64.0)	213 (69.6)
Stop taking AED because of Medication complexity.	Yes	197 (53.4)	168 (54.9)
	No	172 (46.6)	138 (45.1)
Stop taking AED because of Preoccupation with life.	Yes	140 (37.9)	110 (35.9)
	No	229 (62.1)	196 (64.1)
Stop taking AED because of severe anxiety.	Strongly Agree	52 (14.1)	128 (41.8)
	Agree	68 (18.4)	80 (26.2)
	Sometimes	151 (40.9)	52 (17)
	Disagree	55 (14.9)	24 (7.8)
	Strongly Disagree	43 (11.7)	22 (7.2)
Your beliefs that receiving AED might cause anxiety & epilepsy.	No, because it protects me from the aggravation of the disease.	283 (76.7)	130 (42.5)
	No, because my life would be impossible without treatment.	156 (42.3)	42 (13.7)
	Yes, because the side effects of medications cause severe anxiety.	132 (35.8)	198 (64.7)
	Yes, because of causing dependence & addiction.	87 (23.6)	108 (35.3)
	Yes, because it might be harmful more than good.	12 (9.8)	96 (31.4)

Table 3 showed the comparison between Egypt and Saudi Arabia studying groups about reasons for non-adherence. The most effective reason for poor adherence was forgetfulness (64.7% Vs 35.8%), followed by stop taking AED when you feel better (62.1% Vs 32.2%), feel bad (63.4% Vs 39.6%), due to side effects (64.4%Vs 43.6%), polypharmacy (51.3% Vs 39.6%) among Saudi Vs Egyptian patients. However, they are equally in stop taking AED because of Medication complexity and preoccupation with life and it was vice versa in stop taking AED because of high medicine price (36%, Egyptians Vs 30.4% Saudis). All Patients beliefs that receiving more AED caused medication non-adherence. Regarding patients' beliefs about receiving AED might cause anxiety & epilepsy (76.7% or 42.3%) of Egyptians who said (no, because it protects me from the aggravation of the disease or because their life might be impossible without treatment) compared to (42.5% & 13.7%) of Saudis respectively. While 64.7%, 35.3% & 31.4% of Saudis who said (yes, because of the side effects, causing dependence & addiction & harmful more than good) compared to (35.8%, 23.6% & 9.8%) of Egyptians respectively (Figure 3).

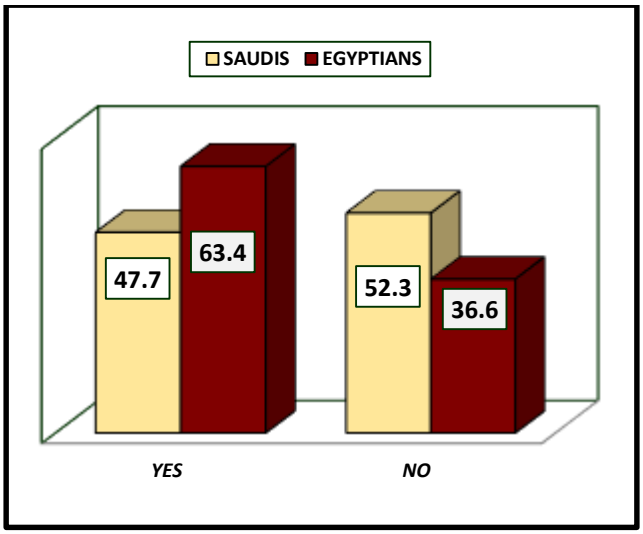

Figure 1: Prevalence of adherence and non-adherence to antiepileptic drugs among Saudis and Egyptians patients (%).

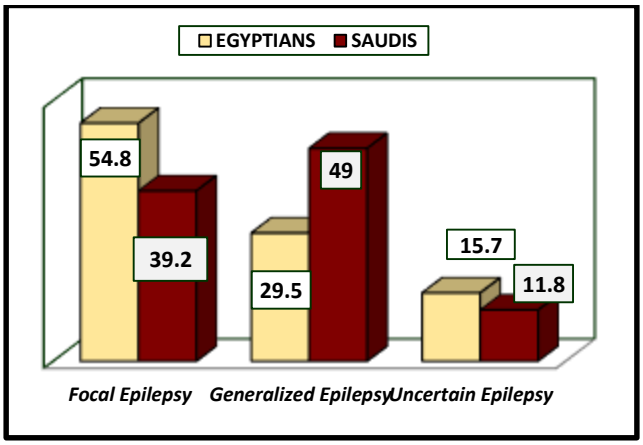

Figure 2: Types of Epilepsy among Saudis and Egyptians patients (%).

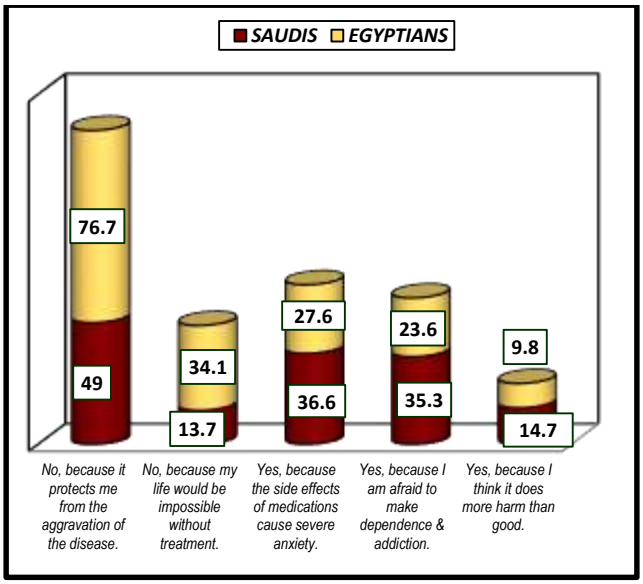

Figure 3: Patient's beliefs that receiving antiepileptics might cause anxiety & epilepsy among Saudis and Egyptians patients (%).

DISCUSSION

Medication non-adherence is a well-known significant barrier in achieving the seizure freedom for patients with epilepsy, as it poses a difficult issue for most clinicians.[20] Medication adherences can be affected by several factors including beliefs and the frequency of seizures,[21] beliefs and age.[22] Also, non-adherence to the suitable antiepileptic drug medication regimens can lead to a seizure relapse with increased serious health risk,[23] missing AED medication can lead to raise the chance of seizure recurrence.[24]

The current study involved 675 patients completed a full questionnaire (306 from Saudi Arabia and 369 from Egypt. The rate of non- adherence to AED was less among Egyptian (36.6%) than Saudi patients (52.3%), this could be explained base upon some beliefs among Saudis about AED. Our results agree with finding from WHO and other studies about the prevalence of non-adherence (20-80%),[4,25-27] which might be due to forgetfulness as found in united states and Brazil.[12,21,27] A series of studies documented low percentage of non-adherent patients, they were 18.4% in KSA,[28] 29% in USA,[29] 29.2% in UAE,[30] and 30% in India,[31] while others showed high percentages of poor-adherence 79.8%,[32] 71%, [33] 63%.[34] This high percentage of poor-adherence could be contributed to poor educational background, inadequate family support and incomplete knowledge on disease management.[33] A well, polytherapy had low adherence compared to patients on monotherapy.[32,34]

Concerning gender, most of patients from females, 56.9% (Egyptians) and 55.8% (Saudis) which came in accordance with some studies.[28,33]

Adherence to AED in female participants was significantly different from males either in Egypt (72.3%) or KSA (70.2%). On the other hand, another study conducted in Brazil agreed with our results and related this adherence because females are more accepting of the diagnosis, while male tend to prioritize work and delay seeking medical care to avoid unemployment.[35] Also, other studies agreed with us,[11,12,36] while other studies demonstrated that no significant difference was found between gender in degree of AED medication adherence.[27,28,37,38, 39]

Regarding the age of patients, poor medication adherence was observed in younger (18-30 years) participants which was more pronounced in Saudis (31.6%) more than Egyptians (50.2%), and the adherence was directly proportional to increasing age as shown in patients` age (30-50 and > 50 years). Many studies in Brazil and KSA showed that elderly patients were more adherent to AED.[35,40] A recent observation was reported that higher adherence level to AED therapy was associated with elderly patients, which could be due to youngers' preoccupation with social life, academic studies or jobs which led to forget taking their medication, and they may also think that they are healthier and do not require any treatment [[35,40]], and elderly might care about health than younger patients.[35] On the other hand, other study revealed that there were no significant differences between well and poorly controlled epilepsy in respect of patient age at diagnosis or duration of epilepsy.[27,28, 37,36,38]

Highly educated patients showed more adherence to AED when compared with non-educated or primary education level both in Egypt and KSA. These results were similar to other authors who found that patients with less education have more chance of non-adhere than the educated patients, because educated patients had an appropriate information on the disease, and importance of adherence.[33] Furthermore, because of their education level, they can interact well with health care givers and ask relevant questions.[33,35] Similar study stated that education and counseling of patients with epilepsy have shown mixed success. Intensive reminders and implementation intention interventions provided more positive effects on AEDs adherence .[29,41] However, previous studies have shown that patient understanding and perceived lack of benefit of AED were significant predictors of non-adherence.[4,12, ,26, 28,42] However, this contradiction is possibly attributed to the education level of our patients and the high scores in patients' illness perception which is similar in both the adherent and non-adherent groups which could be a result of the doctors' communication skills that were perceived to be good in both groups.[36,43]

Adherence increased significantly by increasing family income, which was in agreement with an Indian study.[42] Other study didn't agree to our results, they reported that monthly income was not found to influence the adherence to medication among their participants.[28,36,43]

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,[28,36] while another one agreed with us in marital status does not affect medication adherence.[27] Concerning employment status, some studies found that employment status significantly affected adherence to AED.[42,43] Employers or students were less likely to adhere to their treatment regimen compared to those who were unemployed,[43] 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.[44] Studies carried out in Ethiopia found that divorced and widowed patients were significantly poor adherent when compared with single patients in their marital status,[11,45] which might be due to no support from their partners in adhering to the prescribed medication(s) and instructions given by health care professionals.[11]

Regarding types of epilepsy**,** 54.8% & 39.2% of patients with focal epilepsy versus 29.5% & 49 with generalized epilepsy among Saudis and Egyptians respectively. Our study agreed with other studies[33,40] who found that partial epilepsy (52%) and generalized (48%). But other study showed that 79.2% were of generalized epilepsy and 20.8% of focal epilepsy,[45] other showed that 23.1% were of generalized epilepsy and 67.5% of focal epilepsy 9.3% with uncertain epilepsy.[31]

Concerning the number of medications received, our patients received AED as monotherapy (60.4% & 48.7%) more than polypharmacy (39.6% & 51.3%) among Egyptian and Saudi patients respectively. This agrees with the findings of another researcher who stated that patients receiving monotherapy are significantly more adherent than patient treated with polypharmacy.[18,39,40] On the other hand, no significant difference in the rate of adherence between patients on monotherapy and those on.[46]

Regarding factors affecting AEDs adherence, the current study showed that forgetfulness, patients forget taking antiepileptic drugs (64.7%) in Saudis which was more than Egyptians (35.8%). This agreed with many studies in different countries,[12,30,40,41,47] they stated that the most common reasons for non-adherence to treatment regimens were forgetting to take the medication due to lack of time. Non-adherence can generally be defined as any deviation from the recommended timings or dosages of a prescribed treatment regimen.[4, 5]

Stop taking AED due to medication complexity (about 50%) and Preoccupation with life (about 30%) either among Egyptians or Saudis. Also, Bano and Numanb (2016) stated that drugs complexity was the major factors that affected adherence,[48] and complex treatment is believed to threaten patient's adherence.[49]

Regarding patients' beliefs about receiving AED decreased medication adherence (50%). It was found that patients with poorly controlled epilepsy had beliefs about their epilepsy that were significantly different from those with well controlled epilepsy. They had a greater belief that use of medication, increased the duration of their illness and be more anxious. Epileptic patients with a negative medication belief were more likely to have uncontrolled seizure.[50] About 41.8% of Saudi patients stop taking antiepileptics due to severe anxiety from the drugs, compared to Egyptians (14.1%). Patients with poorly controlled epilepsy were more anxious and expected a longer duration of their epilepsy.[37] Patients with epilepsy are more likely to suffer from psychiatric comorbidity such as anxiety or depression.[51] Regarding patients' beliefs about receiving AED might cause anxiety & epilepsy (76.7% or 42.3%) of

Egyptians who said (no, because it protects me from the aggravation of the disease or because their life might be impossible without treatment) compared to (42.5% & 13.7%) of Saudis respectively. While 64.7%, 35.3% & 31.4% of Saudis who said (yes, because of the side effects, causing dependence & addiction & harmful more than good) compared to (35.8%, 23.6% & 9.8%) of Egyptians respectively. AED non- adherence was associated with specific beliefs about medications, being depressed or anxious, poor medication self-administration management, uncontrolled recent seizures, frequent medication dosage times, another study also showed the most common cause for poor adherence to AED therapy was the patients' beliefs that epilepsy had a spiritual or psychological cause rather than primarily being a disease of the brain.[52,26] In developing countries, epilepsy-associated stigma leads to higher treatment gaps, poor treatment outcomes, and reduced quality of life in epileptic patients.[53] Beliefs about medication and illness are potentially modifiable. In addition to beliefs, emotions and coping styles may also influence illness behaviour.[54]

CONCLUSION

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.

Informed consent Statement was made to protect their rights and ensure the security of their information. There is a phrase at the top of the questionnaire that states that completing the questionnaire constitutes acceptance to participate in this study.

Conflicts of interest: The authors have reported no conflicts of interest.

Ethical Approval: This study has been reviewed and approved by the research Ethical Committee (REC) at the University of Hail research number (H-2021-238) dated 20/12/2021. (Attached file)

Authors' contributions This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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