



ADHERENCE TO ANTI-EPILEPTIC DRUGS AND THEIR DETERMINANT FACTORS AMONG ADULT PATIENTS WITH EPILEPSY

Anas Khalil¹, Afnan Abdullah Al-Amoudi², Maha Mubarak Almutairi², Rawan Afdhal Abualola², Jana Abdullah Altaifi²

1. *Assistant Professor of Internal Medicine, Pulmonary and Critical Care Medicine, Taibah University, Almadinah Almunawwarah, KSA*
2. *Medical Intern -Taibah University- Almadinah Almunawwarah City, KSA*

ARTICLE INFO

Received:

12th Aug 2018

Received in revised form:

10th Dec 2018

Accepted:

16th Dec 2018

Available online:

26th Dec 2018

Keywords: *Anti-epileptic, Epilepsy, Brain, Medecine*

ABSTRACT

Background: One of the chronic disorders of the brain is epilepsy, it is characterized by repeated seizures. It results from an excessive electrical discharge within the brain cells, and any part of the brain can be affected. It is common in Saudi Arabia with an estimated prevalence of 6.54 per 1000 population. And, it can affect people of all ages.

Objective: To measure the level of Adherence to Anti-epileptic drugs among adult patients with epilepsy and to evaluate the personal beliefs and concerns about anti-epileptic drugs.

Methods: The study was conducted using a cross-sectional method on 80 adult patients with epilepsy using at least one anti-epileptic drug. A Morisky Medication Adherence Scale (MMAS-8) was used to assess the adherence to medications, and Beliefs about Medicine Questionnaire (BMQ) was used to assess the patients' beliefs about anti-epileptic medications.

Results: The mean Medication Adherence Scale scored by the total participants was 5.0 (SD=2.2) where 60.5% of the subjects scored above the midpoint of the medication adherence scale (MMAS-8), and 39.5 % scored below. The hypothesis testing has revealed that experiencing medications' side effects is associated with lower odds of being adherent to antiepileptic medications.

Conclusion: The hypothesis testing has revealed that there was an association between the Medication Adherence Scale and both Specific Necessity and Specific Concern. Specific necessity has shown a positive association with the Adherence Scales of P=0.24, P=0.027 while the specific concern has shown a negative association with the adherence scale of P=-0.36, P<0.001. This suggested that ensuring patients to have proper knowledge about their medications, including stressing on their importance, while dismissing the unnecessary fears and concerns would lead them to have higher adherence to their antiepileptic medications.

Copyright © 2013 - All Rights Reserved - Pharmacophore

To Cite This Article: Anas Khalil, Afnan Abdullah Al-Amoudi, Maha Mubarak Almutairi, Rawan Afdhal Abualola, Jana Abdullah Altaifi, (2018), "Adherence to Anti-Epileptic drugs and their determinant factors among adult patients with epilepsy", *Pharmacophore*, 9(6), 41-48.

Introduction

People of all ages can get affected by epilepsy, it is a brain chronic disorder [1]. It is characterized by repeated seizures which are short periods of involuntary movements that can affect any part of the body [2]. It results from an excessive electrical discharge within the brain cells, and any part of the brain can be affected [2]. The age of seizure onset commonly ranges between 26 and 28 years old and the ages of 14 and 16 years are the most sensitive age for the disease [3]. Epilepsy can be partial or generalized [2]. It can be associated with loss of consciousness, urinary or bowel incontinence and/or sensory loss [2]. Approximately 50 million people worldwide have epilepsy, making it one of the most common neurological disease globally [1]. Nearly 80% of the people with epilepsy live in low- and middle-income countries [1].

In Saudi Arabia, the prevalence of epilepsy is 6.54 per 1000 population [4]. In 1,000 consecutive Saudi nationals, the pattern of seizure and other neurological disorders was described by Al-Rajeh et al [5]. The commonest type has been epilepsies accounting for (74%) , and in the majority of the cases (63%), no specific etiology was determined⁽⁴⁾. Epilepsy may promote

Corresponding Author: Anas Khalil, Internal Medicine, Pulmonary and Critical Care Medicine Department, Taibah University, Almadinah Almunawwarah, KSA Email: anas.kalel@gmail.com

limitations, restrain activities and interfere with the occupational ability, professional goals and social integration of patients [6]. It continues to be a highly stigmatized and disabling chronic condition [7]. It requires a lifelong process of adherence to the prescriber's instructions and drug regimens [8].

Antiepileptic drugs (AEDs) are the most common treatment. It can control 70% of new epileptic patients [9].

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 [10]. Patients' adherence to the treatment regimen predicts the success of treatment, and reduces the negative side effects of the disease and its severity [11].

A one-year prospective study conducted on 104 Saudi epileptic patients attending an epilepsy clinic found that about one third of patients (30.8%) were non-adherent to their AEDs [12]. Another study of 116 adolescent patients with idiopathic epilepsy found a high percentage of non-adherence to antiepileptic drugs (38.3%) [13]. The most important factors for poor medication adherence were low level of education, forgetfulness, inability to obtain medications, fear from medications' side effects and feeling stigmatized because of their disease [12-13].

Non-adherence to medications leads to considerable morbidity, mortality, and avoidable health care costs [14]. Non-adherence to antiepileptics is the most important cause of poorly controlled epilepsy [15] and leads to 21% increase in the risk of seizures [16]. It also leads to increased absenteeism from work and, possibly increased risk of injury to oneself or others [14]. Nevertheless, adherence has been rarely discussed in consultations, and the problem of non-adherence is often hidden undisclosed by patients, and unrecognized by clinicians [17, 18].

This research study has been conducted to identify the level of adherence among adult patients with epilepsy in Al-Madinah Al-Munawwarah city, and its determinant factors to enhance their quality of life and get the optimum outcome from the therapy. [13].

Rationale

1. There have been limited numbers of researches that have studied epilepsy.
2. Based on the knowledge of the authors, there have been no studies that were specific for Al-Madinah to determine the level of adherence of epileptic patients to their medications.
3. By identifying the level of adherence and its determinant factors and adherence-related beliefs, this study can help to have a better control of epilepsy.

Objectives:

i. General objective:

To measure the level of Adherence to Anti-epileptic drugs among adult patients with epilepsy in Al-Madinah Al-Munawwarah City - Saudi Arabia

ii. Specific Objectives:

1. To identify different factors influencing medication adherence.
2. To evaluate the personal beliefs and concerns about anti-epileptic drugs.
3. If found, to identify the common side effects of anti-epileptic drugs that patients complain of.

METHODOLOGY

Study design and setting:

A cross-sectional descriptive study design was used. It was conducted at neurology outpatient clinics in King Fahad Hospital in Almadinah Almunawwarah City, Saudi Arabia during the period from May to the end of September 2018.

Sample Size:

A sample size of 80 participants were calculated at 95% confidence interval using Openepi program, a total population of 104 and a proportion of 30% were used as inputs.

Study Population:

1. Inclusion criteria:

Adult patients with epilepsy on at least one anti-epileptic drug and being followed in a neurology clinic.

2. Exclusion criteria:

Any participant who was taking anti-epileptic drugs for any reason other than epilepsy, people who stopped taking the medications, or those with learning disability or memory impairment were excluded from the study.

Sampling method:

Study participants were recruited by convenient sampling method, as all patients with epilepsy who met the inclusion criteria were asked to participate in the study in waiting rooms and clinics in the hospital.

Data collection tool:

For data collection, an existing self-administered Questionnaire was used, and the Questionnaire went through translation from English to Arabic by two different translators. The questionnaire was divided into four sections, and it included all the following items:

- 1- Socio-demographic data:** it included the age, sex, employment status, marital status, residence (Madinah/other), level of education and income.
- 2- Seizure and epilepsy history:** The patients were asked about the onset and frequency of seizures, time of the last seizure he/she had, family history of epilepsy, details of prescribed drugs including: (Name, number, and any detected side effects), and the question if she/he felt stigma [13, 19].
- 3- Assessment of medication adherence** by using **Morisky Medication Adherence Scale (MMAS-8)**: The MMAS-8 is a self-reported questionnaire that has been frequently used to assess the medication adherence because of its low levels in both cost and time expenditure [20]. The MMAS-8 has been validated in many studies in patients with diabetes mellitus, hypertension and those taking warfarin [20]. The scale consists of eight questions, first seven items having a dichotomous

answer (yes/no) that indicates the adherent or non-adherent behavior. In item 8, a patient can choose an answer on a 5-point Likert scale, expressing how often he/she does not take his medications [21]. These Questions include:

1. Do you sometimes forget to take your anti-epileptic drug?
2. People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your anti-epileptic drug?
3. Have you ever cut back or stopped taking anti-epileptic drug without telling your doctor because you felt worse when you took it?
4. When you travel or leave home, do you sometimes forget to bring along your anti-epileptic drug?
5. Did you take all your anti-epileptic drug yesterday?
6. When you feel like your symptoms are under control, do you sometimes stop taking your anti-epileptic drug?
7. Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your anti-epileptic therapy?
8. How often do you have difficulty remembering to take your anti-epileptic therapy?

Patients who scored 8 points, <8 to >6 points and ≤6 points on the scale were considered to have high, medium and low adherence, respectively [20, 21].

4- Beliefs about Medicine Questionnaire (BMQ)

This questionnaire was developed in the UK and published by Horne and Weinman (1999) [22]. Subjects answered the extent to which they agreed or disagreed with the statement on a five-point Likert scale, where 1 = strongly disagree, 2 = disagree, 3 = uncertain, 4 = agree and 5 = strongly agree, to investigate the participants' opinion for each item. The questionnaire was divided into two sections, measuring beliefs about medicines in general and beliefs about specific medications[13].

In this evaluation, items **in the specific section** will relate to the 'antiepileptic drugs', where 5 items evaluate personal beliefs about the necessity of the medications for maintaining or improving health, against 5 items evaluating concerns about the potential adverse effects of taking them. Through this study, the authors investigated how the patients weighed their concerns against their perceived benefits[23].

The **general section** consisted of the overused sub scale, i.e., the Harm-Benefit sub scale. The scores for each item in a sub scale were summed to give a total score which ranged from 4 to 20 for the Harm and Benefit scale, and ranged from 3 to 15 for the Overuse Scale. The higher scores indicated stronger beliefs in the concepts represented by the scale [13].

Data Management and analysis plan:

For the data entry and statistical analysis, statistical package for the social sciences (SPSS) version 22.0 was used. Two types of statistics were conducted. First, descriptive statistics were used where the quantitative data were shown as mean and SD, and the qualitative data were expressed as frequency and percentage. Second, the analytic statistics were used and Chi-square test was used to measure the association between the qualitative variables and if P value was less than 0.05, there was a statistically significant relationship between the two variables.

Ethical considerations:

- Ethical approval was obtained from the Scientific Research Ethics Committee at Taibah University prior to implementing the study.
- A verbal informed consent was obtained from all the participants after explaining the aim of the study.
- Privacy and confidentiality were assured as the questionnaire was filled anonymously.

Study limitation:

The main limitation of this study was the lack of enough time. This problem was overcome by extending the time for primary data collection and including more health centers.

Budget:

This study was a self-funded study. The main costs were spent for printing the questionnaires.

RESULTS

The total sample included in this study was 81 patients with a mean age of 29.8 (SD=11.1) and female to male ratio of (51.9:48.1). The mean Medication Adherence Scale scored by the total participants was 5.0 (SD=2.2) where 60.5% of the subjects scored above the midpoint of the medication adherence scale (MMAS-8) and 39.5 % scored below. The demographic and socioeconomic characteristics of the participants have been shown in Table 1 stratified by their medication adherence scale score. Those who scored above the midpoint in the Medication Adherence Scale (MMAS-8) had better education, employment and income levels compared to those who scored below the midpoint.

Table 1. Demographic characteristics of participants included in this study Stratified by their Adherence to antiepileptic drugs

Variable	Scored above the midpoint in the Medication Adherence Scale (MMAS-8)	Scored below the midpoint in the Medication Adherence Scale (MMAS-8)	Total
Sample size No. (%)	49 (60.5%)	32 (39.5%)	81 (100%)
Age in years Mean (SD) ¹ [range]	30 (11.5) [14-56]	26.8 (13.3) [15- 50]	29.8 (11.1) [14 -56]
Gender Female %	44.9	62.5	51.9
Marital Status (%) Never Married	52.9	62.5	60.5

Married	38.8	31.3	35.8
Divorced	0	6.3	2.5
Widow	2	0	1.2
Place of Residence (%)			
Al Medina	71.4	78.1	74.1
Regions governed by Al Medina	16.3	15.6	16
Other Regions	12.2	6.3	9.9
Level of education (Column N %)			
Illiterate	2	9.4	4.9
Primary school	18.4	21.9	19.8
Middle school	14.3	15.6	14.8
High school	26.5	28.1	27.2
University degree	38.8	25	33.3
Employment Status (Column %)			
Employed	26.5	12.5	21
Retired	4.1	3.1	3.7
Student	26.5	21.9	24.7
Housewife	34.7	37.5	35.8
Unemployed	8.2	25	14.8
Monthly income estimates in SAR² (Column N %)			
< 5000	34.7	53.1	42
5,000 – 10,000	46.9	25	38.3
10,000 – 20,000	12.2	9.4	11.1
> 20,000	6.1	12.5	8.6

¹SD: Standard deviation, ²SAR: Saudi riyals.

Table 2 shows the epileptic disease history of the participants stratified also by their midpoint score of the Medication adherence scale (MMAS-8). Those who scored above the midpoint of the medication adherence scale had longer duration compared to their last epileptic episode, however, when they experienced epilepsy it happened at a higher frequency compared to those who scored below the midpoint. Furthermore, those who scored above the midpoint of the Medication Adherence scale utilized a lower number of antiepileptic drug types and experienced fewer medications' side effects compared to those who scored below the midpoint. Also, those who scored above the midpoint of the Medication Adherence Scale experienced more psychological diminishing of their condition from others while also had less family history of epilepsy compared to those who scored below the midpoint.

Table 2. Epileptic disease history of participants included in this study Stratified by their Adherence to antiepileptic drugs

Variable	Scored above the midpoint in Medication Adherence Scale (MMAS-8)	Scored below the midpoint in Medication Adherence Scale (MMAS-8)	Total
Age at diagnosis in years			
Mean (SD ¹)	17.9 (12.6)	16.2 (9.8)	17.2 (11.5)
[range]	[1 - 50]	[1 - 47]	[1 - 50]
Duration of disease in years			
Mean (SD ¹)	10.8 (9.0)	11.8 (10.6)	11.2 (9.6)
[range]	[0 - 36]	[0 - 37]	[0 - 37]
Last Episode of Epilepsy (%)			
Less than a year	61.2	78.1	67.9
1 - 5 years	22.4	15.6	19.8
More than 5 years	16.3	6.3	12.3
The frequency of Epileptic Episodes (%)			
Daily	6.1	3.1	4.9
1 - 6 per week	4.1	6.3	4.9
1 -3 per month	32.7	25	29.6
1 - 11 per year	36.7	31.3	34.6
Once per a few years	20.4	34.4	25.9

Number of Medications used for Epilepsy (%)			
One	71.4	59.4	55.7
Two	20.4	25	22.2
Three or more	8.2	15.6	11.1
Experienced Medications Side Effects (%)	26.5	46.9	34.6
Have a Family history of Epilepsy (%)	12.2	25	17.3
Have experienced diminishing of his/her condition from others around them (%)	24.5	12.5	19.8

¹SD: Standard deviation

Both those who scored above and below the midpoint in the Medication Adherence Scale had approximate results in the Believe about Medicine Questionnaire (BMQ) scales. However, those who scored above the midpoint had a higher mean for the specific necessity scale, while those who scored below the midpoint had a higher mean for the specific concern scale (figure 1).

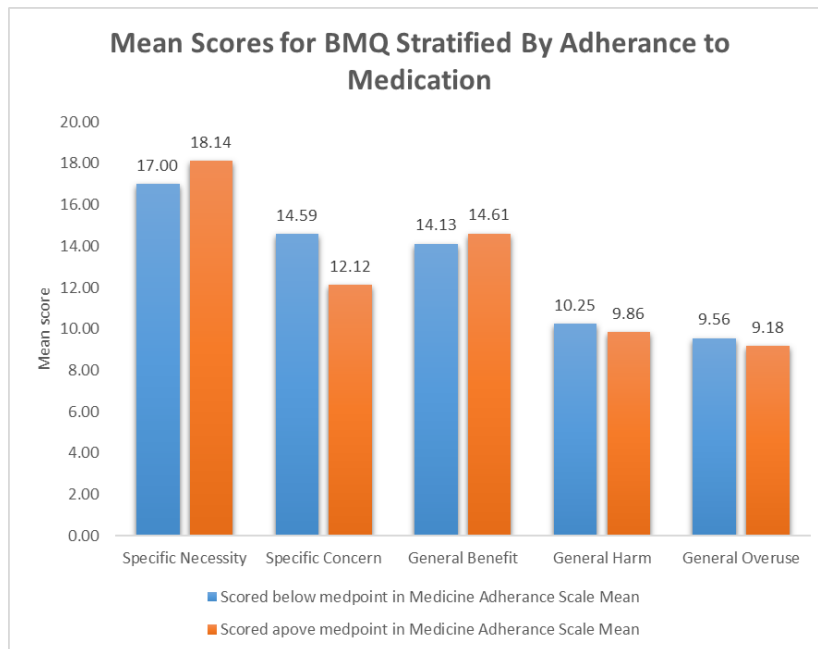


Figure 1. The mean scores for BMQ stratified by the adherence to medication

Figure 2 shows the types of anti-epileptic drugs used by all the participants. Levetiracetam had the highest ratio of use of 32% followed by both Valproic acid and Carbamazine at 23% for both.

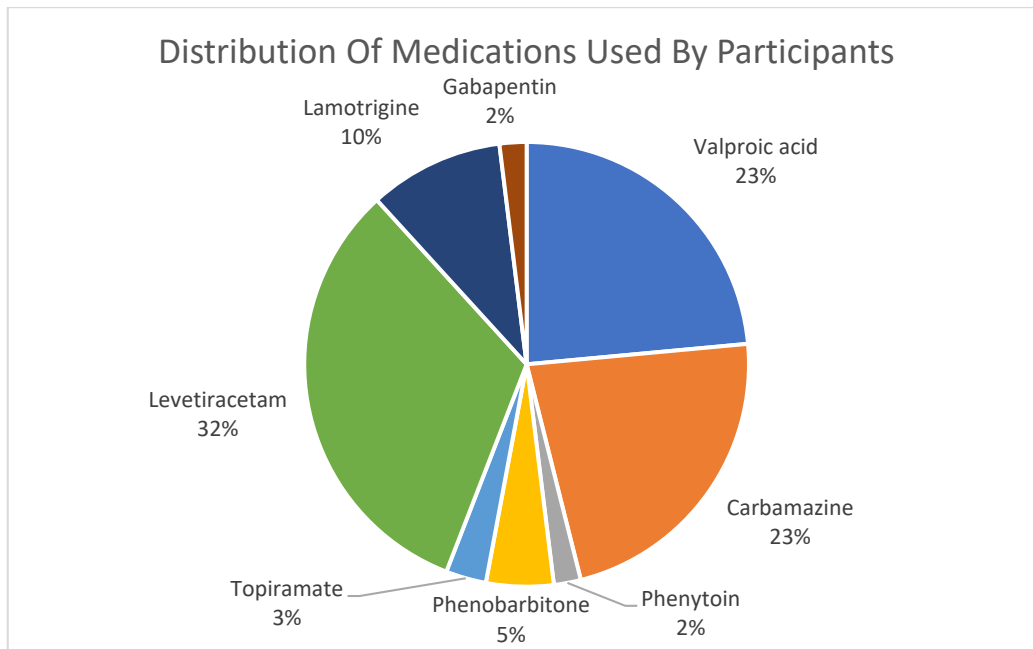


Figure 2. The distribution of anti-epileptic medications used by the participants

Being female was associated with lower odds of scoring above the midpoint in Medication adherence scale OR=0.8 (95%CI: 0.64, 0.99). The medications' side effects were also associated with lower odds of scoring above the midpoint in the Medication Adherence scale OR=0.78 (95%CI: 0.63, 0.97). The hypothesis testing has also revealed that there was enough statistical evidence to conclude that there was a difference among the income level groups in their adherence to medication scores $F(3)=2.98$, $p=0.037$. Post-hoc tests have shown that both the income groups of 5,000 – 10,000 and 10,000 – 20,000 SAR per month had higher means than below 5,000 SAR per month group. There was not enough statistical evidence to conclude any more association between the Medication Adherence scale and other factors as shown in table 3.

Table 3. The associations between different variables included in the study and medicine adherence scales

	Medication Adherence Scale (MMAS-8)
Age	
<i>b</i>	0.05
(p-value)	(0.65)
Duration of Disease in years	
<i>b</i>	-0.13
(p-value)	(0.28)
OR of being female	0.8
(CI)	(0.64 , 0.99)
OR of Having a family history of epilepsy	0.78
(CI)	(0.6 – 1.01)
OR of having medication side effects	0.78
(CI)	(0.63 , 0.97)
OR of having others diminishing the participants elliptic condition	1.1
(CI)	(0.85 , 1.42)
Place of residence	
F-value (ANOVA)	$F(2)= 0.78$
(p-value)	(0.46)
Income level	$F(3)= 2.98$
F-value (ANOVA)	(0.037)
(p-value)	
Education level	
F-value (ANOVA)	$F(4)=1.10$
(p-value)	(0.361)

While examining the associations between the Medication Adherence scale (MMAS-8) and the Believe about Medicine Questionnaire, the hypothesis testing revealed that there was an association between the Medication Adherence Scale and both

Specific Necessity and Specific Concern scales as shown in table 4. Specific necessity showed a positive association with the Adherence Scale $P=0.24$, $P=0.027$ while the specific concern showed a negative association with the adherence scale $P=-0.36$, $P<0.001$. There was not enough statistical evidence to conclude a relationship between the other Believe about Medicine scales and the Medication Adherence Scale.

Table 4. The associations between BMQ scores and medicine adherence scales

	Medication Adherence Scale (MMAS-8)
Specific Necessity	
<i>b</i> ¹	0.24
p-value)	(0.027)
Specific Concern	
<i>b</i> ¹	-0.36
(p-value)	(<0.001)
General Benefit	
<i>b</i> ¹	0.17
(p-value)	(0.10)
General Harm	
<i>b</i> ¹	-1.30
p-value)	(0.24)
General Overuse	
<i>b</i> ¹	-0.18
(p-value)	(0.08)

¹Adjusted for gender, having a history of medication side effects and income level

Discussion

In general, most of the participants in this study (60.5%) scored above the midpoint in the Medication Adherence Scale (MMAS-8). This is combatable with previously published study in other regions where most of the participants were also in adherent with their antiepileptic medications^(10, 11). Also, compared to the other previously published studies, an increase in non-adherence to anti-epileptic drugs was observed during the study among the participants up to (39.5%).

The study showed that the patients with better adherence to their medications had higher levels of income, education and employment. However, the hypothesis testing showed that there was enough statistical evidence to conclude a relationship only between the income level and the adherence to the antiepileptic drugs. This was likely because patients with better income would have access to better healthcare in terms of speed of access, frequency and quality of health services, and therefore might be more educated and self-aware about their condition and how to manage it. Nevertheless, further studies are needed to confirm the previously mentioned assumptions.

Furthermore, those who scored above the midpoint of the medication adherence scale reported that they experienced others diminishing their condition in more frequency than those who scored below the midpoint. However, the hypothesis testing did not show enough statistical evidence to conclude that there was an association between the two. This can also be related to those who scored above the midpoint of the Medication Adherence Scale having fewer episodes of epilepsy, therefore having less empathy, and also having less family history of epilepsy, therefore, having fewer people around them who are well educated about epilepsy.

The hypothesis testing showed that being female is associated with lower odds of being adherent to the antiepileptic medications.

Also, the hypothesis testing revealed that experiencing medication side effects was associated with lower odds of being adherent to the antiepileptic medications. This was likely because when you experience side effects you will be less encouraged to continue the medications. It also worth noting that those who experienced more side effects, use more drugs to manage their epilepsy. Thus, more medications can lead to higher chances of having side effects than using only one medication.

There was a positive association between the specific medication necessity scale and adherence scale, while there was a negative association between the specific concerns and the adherence scale. This suggested that giving the patients the proper knowledge about their medications including stressing out the importance of these medications while dismissing out the unnecessary fears and concerns about them would lead the patients to have higher adherence to their antiepileptic medications.

Acknowledgment

The authors would like to thank Dr.Rawan Alaofi, Dr.Duha Alahmadi, Dr. Mohammed Mohammed Alraddadi, Dr. Israa Ismail Al-Turkestany, Dr. Ghadeer Abdulrahman Almuhanha, Dr. Raneem Muneer Lamfoon, Dr. Amnah Talal Kashkari, Dr. Somaia Aloufi, Dr.Ibrahim Ismail Ibrahim, Dr. Amjad Ateek Alharbi and Dr.Abeer Furayj Aljahdali for collecting the data from the research participants. The authors would also like to thank Taibah University for sponsoring this research.

Abbreviations

AED: antiepileptic drug

BMQ: Beliefs about Medicine Questionnaire

MMAS-8: Morisky Medication Adherence Scale

Reference

1. Epilepsy. World Health Organization. 2016.
2. Russ, S.A., Larson, K., Halfon, N., 2012. A National Profile of Childhood Epilepsy and Seizure Disorder. *PEDIATRICS* 129, 256–264. doi:10.1542/peds.2010-1371 Seizure 2001;10:410–4.
3. Mosarrezaii, A. Hedayati Asl, A. & Ghafouri.A.A. 2017. Assessment of prevalence of MRI findings in epileptic patients of imam Khomeini hospital, Urmia, Iran during 2010-2011. *J Adv Pharm Edu Res.*7(4):473-478.
4. Al Rajeh S, Awada A, Bademosi O, Ogunniyi A. The prevalence of epilepsy and other seizure disorders in an Arab population: a community-based study. *Seizure.* 2001 Sep; 10(6):410-4.
5. Al-Rajeh, S., et al. "Epilepsy and other convulsive disorders in Saudi Arabia: a prospective study of 1,000 consecutive cases." *Acta neurologica scandinavica* 82.5 (1990): 341-345.
6. Gomes M.M., Filho H.S., Noe R.A. Anti-epileptic drug intake adherence. The value of the blood drug level measurement and the clinical approach. *Arq Neuro-Psiquiatr.* 1998;56:708–713.
7. Paschal, Angelia M., Sarah E. Rush, and Toni Sadler. "Factors associated with medication adherence in patients with epilepsy and recommendations for improvement." *Epilepsy & Behavior* 31 (2014): 346-350.
8. Michaud, P. A., J. Y. Frappier, and I. B. Pless. "Compliance in adolescents with chronic disease." *Archives françaises de pédiatrie* 48.5 (1991): 329-336.
9. Kwan, Patrick, and Martin J. Brodie. "Early identification of refractory epilepsy." *New England Journal of Medicine* 342.5 (2000): 314-319.
10. Shams M.E., Barakat E.A. Measuring the rate of therapeutic adherence among outpatients with T2DM in Egypt. *Saudi Pharm. J.* 2010;18(4):225–232
11. Masroor Roudsari, D. Mohammad Beigi, E. & Haghani, H. (2017), "Effect of Peer Education on the Medication Adherence and the Quality of Life of Hypertensive Patients", *Pharmacophore*, 8(3), 19-23.
12. MA Jabbar, SA Al-Shammari, Compliance in Saudi Epileptic Patients: Determinants of Compliance in Saudi Epileptic Patients. 1993; 13(1): 60-63
13. Gabr, Wael M., and Mohamed EE Shams. "Adherence to medication among outpatient adolescents with epilepsy." *Saudi Pharmaceutical Journal* 23.1 (2015): 33-40.
14. Asawavichienjinda, Thanin, Chitr Sitthi-Amorn, and Wacharin Tanyanont. "Compliance with treatment of adult epileptics in a rural district of Thailand." *Journal of the Medical Association of Thailand= Chotmaihet thangphaet* 86.1 (2003): 46-51.
15. Gomes, Marleide da Mota, Heber de Souza Maia Filho, and ROSÂNGELA APARECIDA NOÉ. "Anti-epileptic drug intake adherence: the value of the blood drug level measurement and the clinical approach." *Arquivos de neuro-psiquiatria* 56.4 (1998): 708-713.
16. Manjunath, Ranjani, et al. "Association of antiepileptic drug nonadherence with risk of seizures in adults with epilepsy." *Epilepsy & Behavior* 14.2 (2009): 372-378
17. Buelow, Janice M., and Michael C. Smith. "Medication management by the person with epilepsy: perception versus reality." *Epilepsy & Behavior* 5.3 (2004): 401-406.
18. Chen, Hsiu-Fang, et al. "The relationships among medicine symptom distress, self-efficacy, patient-provider relationship, and medication compliance in patients with epilepsy." *Epilepsy & Behavior* 19.1 (2010): 43-49.
19. Chapman, S. C. E., et al. "Patients' perspectives on antiepileptic medication: relationships between beliefs about medicines and adherence among patients with epilepsy in UK primary care." *Epilepsy & Behavior* 31 (2014): 312-320.
20. Mayet, Ahmed Y. "Patient adherence to warfarin therapy and its impact on anticoagulation control." *Saudi Pharmaceutical Journal* 24.1 (2016): 29-34.
21. Janežič, Ana, Igor Locatelli, and Mitja Kos. "Criterion validity of 8-item Morisky Medication Adherence Scale in patients with asthma." *PloS one* 12.11 (2017): e0187835.
22. Horne, Robert, and John Weinman. "Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness." *Journal of psychosomatic research* 47.6 (1999): 555-567.
23. Horne, Robert, John Weinman, and Maitteu Hankins. "The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication." *Psychology and health* 14.1 (1999): 1-24.