Original Article

Prevalence and biopsychosocial factors associated with treatment adherence among people with epilepsy in a tertiary care hospital in Riyadh, Saudi Arabia

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ABSTRACT

الأهداف: تحديد مدى الالتزام بالعلاج بين الأشخاص المصابين بالصرع (PWE) ودراسة تأثير العوامل الاجتماعية والديموغرافية والطبية والنفسية الاجتماعية على الالتزام بالعلاج.

المنهجية: تم إجراء دراسة قائمة على الملاحظة الكمية بناءً على البيانات التي تم جمعها من المرضى البالغين في عيادة الصرع، في المدينة الطبية بجامعة الملك سعود، الرياض، المملكة العربية السعودية. أكمل المرضى الاستبيانات الورقية بما في ذلك التاريخ الاجتماعي والديموغرافي والثقافي والتاريخ النفسي والتاريخ الطبي. بالإضافة إلى ذلك قمنا بتقييم الالتزام بالعلاج من خلال المقياس البصري التناظري (VAS)، وأعراض الاكتئاب بواسطة PHQ-9، وأعراض القلق من GAD7، والأعراض الجسدية بواسطة PHQ-15، وأسلوب التعلق بواسطة ECR16 والضعف الإدراكي بواسطة MOCA.

النتائج: شارك ما مجموعه 207 مريضا، بمتوسط عمر 34 سنة؛ 53.6% منهم كانوا من الإناث. كان متوسط معدل الالتزام الذي أبلغ عنه المريض لنظام العلاج 18.4%±81.6%. أظهر التحليل أحادي المتغير ارتباطات سلبية ذات دلالة إحصائية بين الاكتئاب والقلق والأعراض الجسدية والالتزام بالعلاج. ومع ذلك، أظهر تحليل الانحدار الخطي المتعدد الأعراض الجسدية فقط لتكون مؤشرًا مهمًا للالتزام بأدوية الصرع.

الخلاصة: يمكن أن تكون الأعراض/الشكاوى الجسدية بمثابة عوامل تنبؤ مهمة للالتزام بالعلاج بين الأشخاص المصابين بالصرع. هذه الدراسة هي واحدة من أولى الدراسات التي تشير إلى أهمية استهداف الأعراض الجسدية عن طريق الفحص والتدخل الطبي لتحسين مدى الالتزام بالأدوية المضادة للصرع.

Objectives: To identify the magnitude of treatment adherence among people with epilepsy (PWE) and the impact of sociodemographic, medical and psychosocial factors on treatment adherence.

Methods: A quantitative cross-sectional observational study was performed based on data collected from adult patients attending the epilepsy clinic, King Saud University Medical City, Riyadh, Saudi Arabia. Patients completed paper-based questionnaires including a sociodemographic, cultural, psychiatric history and medical history sections. In addition to that we evaluated treatment adherence by visual-analogue scale (VAS), depressive symptoms by PHQ-9, anxiety symptoms by GAD7, physical symptoms by PHQ-15, attachment style by ECR16 and cognitive impairment by MOCA.

Results: A total of 207 patients participated, with a mean age of 34 years;.53.6% were female. The mean patient-reported adherence to their treatment regimen was 81.6%±18.4%. Univariate analysis revealed statistically significant negative associations between depression, anxiety and physical symptoms and treatment adherence. However, multiple linear regression analysis only showed physical symptoms to be a significant predictor for epilepsy medication adherence.

Conclusion: Somatic (physical) complaints could be important predictors of treatment adherence in (PWE). This study is one of the first to suggest the importance of targeting physical symptoms in screening and intervention approaches to improve Antiepileptic drugs (AEDs) adherence.

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Epilepsy is one of the most common chronic serious neurological diseases and affects approximately 50 million people of all ages worldwide.[1] The estimated median prevalence of epilepsy in Arab countries is 2.3/1,000 (varying from 0.9–6.5/1,000), which is just within the range found in Europe, North America, Australia, and Asia.[2] In Saudi Arabia, the prevalence of active epilepsy is 6.54/1000 population.[3] According to global and local studies, most cases of epilepsy are idiopathic, though it may be caused by cerebrovascular accidents, head trauma, cerebral palsy and CNS infection.[1,4] The overall mortality rate for (PWE) is increased by two- to threefold compared with the general population.[1,5,6] In addition, there are high rates of psychological conditions such as depression and anxiety among (PWE).[7-10] Patients with mood disorders are more likely to be nonadherent with regard to medication.[8,11–13] The World Health Organization defines medication adherence as the extent to which a patient's behavior, in terms of taking medications, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider.[14] Anti-epileptic drugs (AEDs) are the main therapy for epilepsy to prevent seizures.[15] Indeed, up to 70% of children and adults with epilepsy can be successfully treated with AEDs.[1] However, the prevalence of significant medication nonadherence in epilepsy has been reported to vary between 26% and 79%.[16] A cross-sectional study performed locally in Riyadh, Saudi Arabia, at King Fahad Hospital found that 48.7% of patients were nonadherent regarding anti-epileptic medication. In this study, adherence was assessed by asking patients whether they ever missed or stopped their medications, with the most common factor for nonadherence being forgetfulness.[17] In another local study performed among adolescents with epilepsy conducted cross-sectionally at Riyadh National Hospital in Saudi Arabia, 38.3% were antiepileptic drugs nonadherent, and the most important factors affecting adherence to prescribed medication were the age of the mother, number of family members, number of administered drugs and seizure frequency.[18]

In general, the risk of subsequent seizures among nonadherent patients may increase by 21%.[19] Nonadherence is also associated with an increased likelihood of hospitalization and emergency room admission and with an over threefold increased risk of mortality compared to adherence.[20,21] Depression, stress and anxiety are all associated with reduced antiepileptic drug adherence.[8,11–13,22–24] Additionally, the results of another study showed that depression measured by another scale (NDDI-E) correlated with an increased risk of AED nonadherence, which led to the same result.[25] Conversely, perceived social support correlated positively with adherence.[23] In another study, however, neither depression nor family support were associated with adherence.[26] Nevertheless, these studies did not discuss the correlation between attachment style and cognitive function with treatment adherence in patients with epilepsy (PWE). However, multiple studies conducted on other diseases showed an association between attachment style especially avoidance, and reduced adherence to medical treatments.[27–29] A study at King Khalid University Hospital in Saudi Arabia has addressed the psychosocial predictors of treatment adherence in another neurological disorder, multiple sclerosis, and found that 79.47% of patients were adherent to treatment, with the most significant factor associated with nonadherence being cultural beliefs.[30] To date, there is a lack of research about the psychosocial aspects of epilepsy in Arab countries.[31] In fact, none of the local studies we found mentioned psychosocial predictors related to adherence among patients with epilepsy. Hence, this cross-sectional study aims to identify psychosocial predictors, specifically depression symptoms, anxiety symptoms, cognitive impairment, attachment style and cultural beliefs, for treatment adherence among (PWE). Addressing psychosocial problems may help to optimize care for these patients.[32] Overall, identifying barriers to AED adherence is imperative to help practitioners who are developing appropriate strategies to improve adherence rates.[20,24]

Methods.

Study design and sittings. A cross-sectional observational study was conducted with consecutive patients seen in the epilepsy clinic of King Saud University Medical City in Riyadh, Saudi Arabia, from January 2019 to January 2020.

Population. Participants were adult patients diagnosed with epilepsy who signed the consent form of the study. We included those over the age of 17 and diagnosed with primary or secondary seizure disorders more than three months prior, regardless of sex, and who completed the study questionnaire and assessment tools. We excluded those younger than 17 years and those who were unable to answer the study questionnaire or complete the assessment tools, such as those who were illiterate (who cannot read or write), those with intellectual disability (significant limitations in intellectual functioning: reasoning, learning and problem solving), and those who were unable to communicate (complete inability to use speech and language for communication).

Data collection. (PWE) attended the epilepsy clinic, where they were taken to a quiet room near the clinic to complete the questionnaires and assessment tools. The study questionnaire administered to the patients was paper-based and included the following sections: a sociodemographic, a cultural, a psychiatric history and medical history sections. The assessment tools used were as follows. Adherence was measured by using the visual analog scale (VAS) numbered from 1 to 10 as a general self-report questionnaire to assess patient adherence with care plans recommended by the treating physician,[27,33,34] A VAS score of 8 or more was considered as adherence, whereas a score of less than 8 was considered nonadherence. This cutoff score has been used in several previously published studies among various medical populations.[27,35–37] Depressive symptoms were measured by using the Arabic version of the Patient Health Questionnaire-9 (PHQ9), a 9-item scale with each item scored 0 to 3 and summed to yield a total score (range: 0–27). The PHQ9 severity cutoff point score is 10; below which is considered normal and above which indicates depression.[38] Anxiety symptoms were measured by using the Arabic version of the Generalized Anxiety Disorder 7-item scale (GAD7).

Table 1- Demographic characteristics of patients with epilepsy.

Characteristics	Total(207) 207		Adherence N=169(81.6%)		Non adherence N=38(18.4%)		*P*-value
	n	(%)	n	(%)	n	(%)	
Sex							
Male	96	(46.4)	80	(47.3)	16	(42.1)	0.559
Female	111	(53.6)	89	(52.7)	22	(57.9)	
Age, years(Mean ± SD)	34.00	(13.48)	34.45	(13.68)	32.00	(12.54)	0.313
17-44	164	(79.2)	135	(79.9)	29	(76.3)	0.368
45-59	31	(15.0)	23	(13.6)	8	(21.1)	
>=60	12	(5.8)	11	(6.5)	1	(2.6)	
Nationality							
Saudi	199	(96.1)	162	(95.9)	37	(97.4)	0.550
Non Saudi	8	(3.9)	7	(4.1)	1	(2.6)	
Marital status							
Married	104	(50.2)	87	(51.5)	17	(44.7)	0.590
Single	93	(44.9)	75	(44.4)	18	(47.4)	
Divorced	9	(4.3)	6	(3.6)	3	(7.9)	
Widow	1	(.5)	1	(.6)			
Education level							
University	114	(55.1)	92	(54.4)	22	(57.9)	0.003*
High school	72	(34.8)	65	(38.5)	7	(18.4)	
Intermediate school	12	(5.8)	8	(4.7)	4	(10.5)	
Primary school	9	(4.3)	4	(2.4)	5	(13.2)	
Occupation							
Employed	81	(39.1)	67	(39.6)	14	(36.8)	0.572
Unemployed	114	(55.1)	91	(53.8)	23	(60.5)	
Retired	12	(5.8)	11	(6.5)	1	(2.6)	
Family income							
Less than 5000	38	(18.4)	30	(17.8)	8	(21.1)	0.596
5000-10000	60	(29.0)	49	(29.0)	11	(28.9)	
10000-15000	54	(26.1)	42	(24.9)	12	(31.6)	
More than 15000	55	(26.6)	48	(28.4)	7	(18.4)	
Residency							
Inside Riyadh	161	(77.8)	133	(78.7)	28	(73.7)	0.502
Outside Riyadh	46	(22.2)	36	(21.3)	10	(26.3)	
Duration of epilepsy(Mean ± SD)	11.95	(9.29)	12.19	(9.40)	10.92	(8.82)	0.450

*Significant *p*-value

Table 2 - Past psychiatric history of patients. Reasons of not seeing a psychiatrist in the past:

Suggested reasons:	n	(%)	order
I do not suffer psychologically and I do not need a psychiatrist	158	(81.4)	1st
I suffer psychologically, but I need psychological and social support inside the epilepsy center, not going to psychiatric clinics outside the center	9	(4.6)	2nd
I suffer psychologically, but I think I do not need a psychiatrist	6	(3.1)	3rd
I suffer psychologically, but I avoid seeing a psychiatrist for fear of society's perception	5	(2.6)	4th
I suffer psychologically but I do not have access to a psychiatrist	3	(1.5)	
I did not think about it	3	(1.5)	
I do not need a psychiatrist because I suffer for short period	2	(1.0)	
I suffer psychologically, but I did not think that I would go to a psychiatrist	2	(1.0)	
Because I think what I feel is the effects of epilepsy medications	2	(1.0)	
Because I think I only need care from my family	1	(.5)	
I fear from psychiatric medications side effects	1	(.5)	
I left it because I did not benefit from it	1	(.5)	
I got help from a life coach	1	(.5)	

Table 3 - Medical history of patients by adherence status.

Variables	Total		Adherence		Non adherence		*P*-value
	n	(%)	n	(%)	n	(%)	
Chronic illnesses							
Hypertension	8	3.9	7	4.1	1	2.6	0.550
Diabetes Mellitus	6	2.9	6	3.6	0	0	0.291
Asthma	12	5.8	10	5.9	2	5.3	0.876
Cardiovascular Diseases	4	1.9	4	2.4	0	0	0.441
Eczema	1	.5	1	.6	0	0	0.816
Hematological diseases	1	.5	0	0	1	2.6	0.184
Thyroid diseases	1	.5	1	.6	0	0	0.816
Osteoporosis	2	1.0	2	1.2	0	0	0.660
Systemic Lupus Erythematosus	1	.5	1	.6	0	0	0.816
Psoriasis	1	.5	1	.6	0	0	0.816
Rheumatoid	2	1.0	1	.6	1	2.6	0.334
Number	168	81.2	135	79.9	33	86.8	0.321

The GAD7 scoring system is as follows: 5-9 indicates mild anxiety, 10-14 moderate anxiety and 15-21 severe anxiety.[39] We used the Arabic version of the PHQ-15 to assess physical symptoms,[30] with 15 items scoring 0 (not bothered at all) to 2 (bothered a lot). Scores on the PHQ-15 range from 0 to 30, with a score 15 or above indicating a greater physical symptom burden. Physical symptoms listed on the PHQ-15 include headache, back pain, and gastrointestinal symptoms.[40,41] Attachment style was assessed by using the Arabic version of the Experiences in Close Relationships 16-item scale (ECR16).[30,37] The ECR16-item scale has been validated against the longer ECR-32.[42] The ECR16 yields two separate scores: a total anxious (ECR16-Anx) and a total avoidant (ECR16-Avoid) attachment score based on the scoring of eight items for each attachment style. Each attachment score ranges from 8 to 56, with higher anxious or avoidant attachment scores representing greater attachment insecurity. Cognitive impairment was evaluated by using the Arabic version of the Montreal Cognitive Assessment (MOCA). Scores on the MOCA range from 0 to 30. A score of 26 and above is defined as normal; a score below indicates cognitive impairment.[43]

Bias. There is possible recall bias due to the use of self-reported tools.

Study size. Two hundred seven participants fulfilled the criteria and agreed to participate in this study from January 2019 till January 2020.

Ethical considerations. Ethical approval was obtained from the institutional review board at the Faculty

Table 4 - Patient psychiatric examinations by adherence status.

Variables	Total		Adherence		Nonadherence		*P*-value
	n	(%)	n	(%)	n	(%)	
PHQ9 Score							
Crude mean (± SD)	6.31	(5.51)	5.91	(5.26)	8.13	(6.28)	0.024
Adjusted* mean (± SE)	6.97	(0.48)	5.91	(0.40)	8.13	(0.99)	0.034
PHQ9 depression groups							
Normal (0–9)	160	(77.3)	136	(80.5)	24	(63.2)	0.021
Depression (≥10)	47	(22.7)	33	(19.5)	14	(36.8)	
GAD7							
Crude mean (± SD)	6.37	(4.91)	5.95	(4.63)	8.21	(5.69)	0.027
Adjusted* mean (± SE)	7.05	(0.43)	5.95	(0.35)	8.21	(0.90)	0.014
GAD7 anxiety groups							
Mild anxiety	66	(31.9)	55	(32.5)	11	(28.9)	
Moderate anxiety	35	(16.9)	25	(14.8)	10	(26.3)	
Severe anxiety	16	(7.7)	11	(6.5)	5	(13.2)	
PHQ15							
Crude mean (± SD)	8.19	(5.46)	7.69	(5.23)	10.39	(5.98)	0.006
Adjusted* mean (± SE)	9.00	(0.45)	7.69	(0.38)	10.40	(0.88)	0.005
PHQ15_CAT							
Minimal	63	(30.4)	55	(32.5)	8	(21.1)	<0.001
Low	70	(33.8)	59	(34.9)	11	(28.9)	
Medium	44	(21.3)	39	(23.1)	5	(13.2)	
High	30	(14.5)	16	(9.5)	14	(36.8)	
ECRM16anxiety							
Crude mean (± SD)	27.68	(10.68)	27.24	(10.85)	29.61	(9.79)	0.219
Adjusted* mean (± SE)	28.38	(0.96)	27.24	(0.83)	29.61	(1.60)	0.246
ECR16 avoidance							
Crude mean (± SD)	25.04	(8.24)	25.23	(8.07)	24.21	(9.04)	0.027
Adjusted* mean (± SE)	24.73	(0.74)	25.23	(0.62)	24.21	(1.47)	0.503
MOCA score							
Crude mean (± SD)	22.41	(4.06)	22.48	(4.08)	22.11	(4.03)	0.609
Adjusted* mean (± SE)	22.29	(0.37)	22.48	(0.31)	22.11	(0.67)	0.609
MOCA cognitive function groups							
Normal	56	(27.1)	45	(26.6)	11	(28.9)	0.771
Cognitive impairment	151	(72.9)	124	(73.4)	27	(71.1)	

*Mean values were adjusted for age and sex

of Medicine at King Saud University in Riyadh. The interviewer informed all participants about the purpose of the research, why they were chosen, all potential risks and benefits and that they had the choice to participate in the study. If they agreed to participate, they signed a written consent form.

Statistical analysis. Data were analyzed by using Statistical Package for Social Studies (SPSS 22; IBM Corp., New York, NY, USA). Continuous variables are expressed as the mean±standard deviation and categorical variables as percentages. The t-test was applied for continuous variables. The chi-square test and Fisher's exact test were utilized for categorical variables. Adjusted mean values of the examined psychiatric scores were calculated using general linear regression models with adherence status as a fixed factor. Age and sex were treated as covariates. A multivariate stepwise linear regression model was run to detect potential independent predictors. A p-value <0.05 was considered statistically significant.

Results. The sociodemographic characteristics of the study participants based on adherence status are shown in **Table 1**. A total of 207 patients participated in the study, with a mean (±SD) age of 34 (±13.48) years and an epilepsy duration of 11.95 (±9.29) years. Females represented more than half of the sample, at 53.6%. The vast majority (96.1%) of the respondents

Table 5 - Correlation between epilepsy medications polypharmacy and adherence status.

Variables	Total		Adherence		Nonadherence		*P*-value
	Number	%≥	Number	(%)	Number	(%)	
Polypharmacy							
yes polypharmacy	60	29.27	49	(29.34)	11	(28.95)	0.962
No polypharmacy	145	70.73	118	(70.66)	27	(71.05)	
Levetiracetam							
Yes	115	55.56	90	(53.25)	25	(65.79)	0.160
No	92	44.44	79	(46.75)	13	(34.21)	
Valproic Acid							
Yes	21	10.14	17	(10.06)	4	(10.53)	0.931
No	186	89.86	152	(89.94)	34	(89.47)	
Carbamazepine							
Yes	58	28.02	46	(27.22)	12	(31.58)	0.589
No	149	71.98	123	(72.78)	26	(68.42)	
Lamotrigine							
Yes	24	11.59	23	(13.61)	1	(2.63)	0.040*
No	183	88.41	146	(86.39)	37	(97.37)	
Phenytoin							
Yes	4	1.93	4	(2.37)	0	(0.00)	0.441
No	203	98.07	165	(97.63)	38	(100.00)	
Topiramate							
Yes	5	2.42	3	(1.78)	2	(5.26)	0.228
No	202	97.58	166	(98.22)	36	(94.74)	
Clonazepam							
Yes	1	0.48	1	(0.59)	0	(0.00)	0.816
No	206	99.52	168	(99.41)	38	(100.00)	
Lacosamide							
Yes	5	2.42	5	(2.96)	0	(0.00)	0.359
No	202	97.58	164	(97.04)	38	(100.00)	
Phenobarbital							
Yes	1	0.48	1	(0.59)	0	(0.00)	0.816
No	206	99.52	168	(99.41)	38	(100.00)	

Significant *p*-value

were Saudi, half (50.2%) of them were married, and 55.1% had a university educational level. The majority of the patients responded positively to the VAS, with an adherence rate of 81.6%. There were no significant ($p>0.05$) differences between the 2 groups (adherence, nonadherence) regarding any of the assessed demographic characteristics mentioned above, except for educational level, with a p-value of 0.003.

The prevalence of chronic diseases (hypertension (HTN), Diabetes Mellitus (DM), asthma, cardiovascular disease (CVD), hematological diseases, thyroid diseases, Systemic Lupus Erythematosus (SLE), psoriasis, and rheumatoid among the studied subjects was not high; asthma was the most prevalent at 5.8%. There was no significant difference between the 2 groups in terms of the prevalence of any of these chronic diseases, as all p-values were >0.05. In total, 27.5% of the sample had a family history of epilepsy, though this results was nonsignificantly (p-value=0.829) higher among the nonadherence group, at 28.9%, than in the adherence group, at 27.2%. Most (77.3%, 78.3%) of the participants did not think that epilepsy was related to psychological stresses or evil eye, black magic, or Jinn. The vast majority (98.1%, 94.7) of respondents denied any mental illness before or after epilepsy, and only 5.8% reported seeing a psychiatrist because of their epilepsy. The majority of the subjects (94.2%) reported not seeing a psychiatrist; their main reason was that they were not suffering psychologically and therefore no need for a psychiatrist (81.4%). Only 38.6%

Table 6 - Univariate analysis examining the relationship between variables and Visual Analogue Scale of treatment adherence.

Variables	Beta	Standard error	*P*-value
Age	0.015	0.008	0.068
Sex (female vs male)	-0.199	0.226	0.380
Disease duration	0.020	0.012	0.109
PHQ9	-0.052	0.020	0.011
GAD7	-0.064	0.023	0.005
PHQ15	-0.071	0.020	0.001
ECR-Anxious	-0.017	0.011	0.104
ECR-Avoidant	-0.008	0.014	0.548
Family history of epilepsy	-0.026	0.253	0.918
Supernatural belief	-0.099	0.274	0.719
Past psychiatric illness	-0.220	0.821	0.789
Marital status (married vs not married)	0.203	0.226	0.369
Education (bachelor or higher vs lower than Bachelor's degree)	-0.042	0.227	0.854
Employment status(unemployed vs employed)	-0.177	0.231	0.445
MOCA score	-0.011	0.028	0.704

reported feelings of psychological change after their epilepsy diagnosis. The use of psychiatric medications and attending psychological sessions among patients diagnosed with psychiatric illness after epilepsy were reported by only 27.3% and 30%, respectively. When we compared the adherence and nonadherence groups in terms of all the previously addressed points, the differences were not significant. These data are shown in **Table 2 & 3**.

The patients' psychiatric examinations by adherence status are shown in **Table 4**. The prevalence of depression among the studied population according to the PHQ-9 score (≥10) was 22.7%, and this prevalence was significantly higher among the nonadherence patients than the adherence patients, at 36.8% vs. 19.5%, respectively, with a *p*-value of 0.021. The total crude mean (±SD) score for the PHQ-9 was 6.31 (±5.51), which was significantly higher among the nonadherence group, at 8.13 (±6.28), than the adherence group, at 5.91 (±5.26), with a *p*-value of 0.024. Similar findings were obtained when the adjusted mean was calculated. For the GAD7, nonadherence patients had significantly higher crude and adjusted means, at 8.21(±5.69) and 8.21(±0.90) compared to 5.95(±4.63) and 5.95(±0.35) in the adherence group, with p values of 0.027 and 0.014, respectively. The severity of anxiety was also higher in the nonadherence group, but the difference was not significant (p=0.119).

Similar results were obtained with the PHQ15, for which a highly significant difference was found in both the crude and adjusted mean scores of somatic symptoms, being higher in the nonadherent patients, at 10.39 (5.98) and 10.40 (0.88) vs. 7.69 (5.23), and 7.69 (0.38), respectively. Additionally, the severity of somatic symptoms differed significantly between the two groups (p<0.001); it was high in 36.8% of the nonadherence group and 9.5% of the adherent group.

Table 7 - Multivariate regression analysis examining the relationship between variables and Visual Analogue Scale of treatment adherence.

Variables	Estimate	Standard error	*P*-value
Age	0.132	0.008	0.058
Sex	0.046	0.238	0.533
PHQ9 Score	-0.012	0.030	0.910
PHQGAD7 Score	-0.052	0.035	0.624
PHQ15	-0.218	0.028	0.020

There were no significant differences between the two groups regarding the crude and adjusted mean scores of anxious ECR16; however, the crude ECR16 avoidance score was significantly higher in the adherence group (25.23; ±8.07) than in the nonadherence group (24.21; ±9.04), with a *p*-value of 0.027.

The prevalence of cognitive impairment according to the MOCA scale was 72.9%, which was no significantly higher in the adherence group (73.4%) than in the no adherent group (71.1%). The crude mean (±SD) MOCA score was 22.41 (±4.06), indicating moderate cognitive impairment among the study participants, and the adjusted MOCA score was 22.29 (±0.37), with a nonsignificant difference between the two groups in both cases.

Epilepsy medications by adherence status and the correlation between polypharmacy and adherence status are shown in **Table 5**. Polypharmacy was prevalent in 29.27% of the patients. In general, there were no significant differences between the two groups for any of the assessed antiepileptic medications, except for lamotrigine (p=0.040), which was used by a higher percentage of adherent patients, at 13.61%, than no adherent patients, at 2.63%.

Univariate analysis revealed statistically significant negative associations between the psychological variables (PHQ-9 (p=0.011), GAD-7 (p=0.005), and PHQ15 (p=0.001)) and (AED) adherence. On the other hand, none of the demographic or epilepsy-specific questions correlated significantly with medication adherence (all *p*-values >0.05), as shown in **Table 6**.

Table 7 shows the findings of multiple linear regression analysis. Only PHQ15 was significantly associated with (PWE) adherence to medications, and

this association was negative (Beta=-0.218, and *p*-value 0.020)

Discussion. This study examined several psychosocial factors and their impact on treatment adherence in (PWE) in Saudi Arabia. In this study, we identified the percent of treatment adherence among patients with epilepsy. We found two studies performed in Saudi Arabia that measured treatment adherence in (PWE).[17,18] We also identified the impact of psychosocial predictors on epilepsy treatment adherence, including depression symptoms, anxiety symptoms, cognitive impairment, attachment style and cultural beliefs. The rates of nonadherent patients in this study were lower than those in studies performed locally in Saudi Arabia[17,18] as well as studies performed globally[22,23,26,30] This might be explained by positive physician-patient relationships and simplified drug regimens.[14]

The results of this study show that patient age is a significant predictor of epilepsy medication adherence. For example, the older is the patient, the higher is the possibility of compliance. This is consistent with previous data showing that AED adherence appears to be more likely to occur with age. This may be explained by the fact that a patient realizes that the medication's benefits may possibly improve over time.[24] In addition, lamotrigine use was associated with higher adherence rates than other antiepileptic medications, probably due to its fewer sedative and cognitive side effects.[44–47]

However, no association between attachment style and AED adherence in epilepsy patients was found. The conclusion that avoidant relationships are not a significant predictor factor for nonadherence is in fact consistent with a previous study performed in an Multiple sclerosis (MS) patients in Saudi Arabia,[30] though it does contrast with data showing a strong association with poor medication adherence in diabetes and hepatitis patient populations.[27,28] Moreover, in our univariate analysis, depression and anxiety symptoms were associated with nonadherence, but this association was not present in multivariate analysis. On the other hand, only physical symptoms were a significant predictor of poor medication adherence. Such physical symptoms can be explained in the context of somatic symptom disorder, especially because previous research in epilepsy has demonstrated a two- to fivefold increase in physical (somatic) symptoms compared to the general population.[48,49] In this case, the patient may faultily perceive symptoms as troubling side effects and decide to stop taking medication. The other explanation for these symptoms is the actual potential side effects of the (AED).[50] Differentiating between these two is challenging.

This study has some limitations, the cross-sectional nature of the study makes it difficult to ascertain causality between psychosocial predictors and nonadherence. As our patients were recruited through convenience sampling, the findings should be generalized to the Saudi population with caution. Additionally, the study did not include other factors that might affect adherence, such as beliefs about their medications and side effects or the way patients manage their medications.[24] It is well known that there are no gold standard methods for measuring medication adherence.[24] Furthermore, another limitation was reliance on a self-report measure for medication adherence, which increases the risk of bias, either due to faulty memory or efforts to appear responsible.

In conclusion, although our study showed a low percentage of nonadherence in a tertiary medical care center, the nonadherence issue continues to be a serious problem in epilepsy patients and deserves more investigation. We identified a significant relationship between the presence of physical symptoms and nonadherence in a sample of patients from Saudi Arabia. This finding highlights the importance of screening and possibly managing epilepsy patients for any comorbid physical symptoms. More studies on AED adherence in different geographical and cultural settings are needed.

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Ethical Consent

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.