Sleep quality, daytime sleepiness, and insomnia in patient with epilepsy: *A single center experience from Saudi Arabia*

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ABSTRACT

الأهداف: قياس عبء الأرق و النعاس النهاري المفرط (DTS) و تأثيرهما على جودة النوم بالإضافة لدراسة عوامل الخطورة المؤدية إلى ضعف جودة النوم.

المنهجية: أجرينا دراسة مقطعية على 218 مريضاً مصاباً بالصرع من خلال استبيانات تم التحقق من صحتها وترجمتها مسبقًا لتقييم جودة النوم والأرق و النعاس النهاري المفرط باستخدام مؤشر جودة النوم بيتسبرغ، ومؤشر شدة الأرق، ومقياس إبوورث للنعاس، على التوالي.

النتائج: اتضح أن حوالي 75% من المشاركين بالدراسة لديهم جودة نوم سيئة. 42.2% لم يكونوا يعانوا من الأرق، بينما 37.6% يعانون من أرق خفيف، 17.9% يعانون من أرق متوسط و 2.3% يعانون من أرق شديد. فيما يخص النعاس النهاري المفرط: ما يقارب من 64.2% من المشاركين كان لديهم نوم طبيعي، و 17.8% لديهم نعاس نهاري متوسط بينما 16.9% و 0.9% من المشاركين إما يحتمل أو يجب عليهم التماس العناية الطبية لحل هذه المشكلة. بالمقارنة مع الأشخاص الذين ينامون بشكل طبيعي كان المرضى الذين يعانون من الأرق السريري أكثر عرضة بنسبة 5.45 مرة لسوء جودة النوم، في حين أن المرضى الذين يعانون من نعاس نهاري متوسط ولديهم توصية للحصول على رعاية طبية كانوا أكثر عرضة بنسبة 6.84 و 44.15 لسوء جودة النوم. كان المرضى الذين يحدث لهم نوبات الصرع كل شهر أكثر عرضة 2.51 مرة لسوء جودة النوم مقارنة بالمرضى الذين يعانون من نوبات الصرع سنوًيا.

الخلاصة: اوضحت الدراسة ارتفاع معدل انتشار ضعف جودة النوم، والأرق، والنعاس النهاري المفرط في العينة التي تم دراستها من مرضى الصرع السعوديين.

Objectives: To measure the burden of insomnia and daytime sleepiness (DTS) and their effects on sleep quality, and the risk factors of poor quality of sleep.

Methods: We conducted a cross-sectional study of 218 epilepsy patients. We administered well-validated and previously translated questionnaires to assess sleep quality, insomnia, and DTS using the Pittsburgh Sleep Quality Index, Insomnia Severity Index, and Epworth Sleepiness Scale, respectively.

Results: Approximately 75% of participants reported poor sleep quality. Moreover, 42.2% did not have insomnia, while 37.6%, 17.9%, and 2.3% had subthreshold insomnia and clinical insomnia of moderate and severe severity, respectively. Roughly 64.2% of participants had normal sleep, 17.8% had an average amount of DTS, and 16.9% and 0.9% may and should seek medical attention, respectively. Compared to normal sleepers, patients with clinical insomnia were 5.45 times likely to experience poor sleep quality, whereas patients with an average amount of DTS and who were recommended to seek medical attention were 6.84 and 44.15 times likely to experience poor sleep quality, respectively. Patients who had seizures every month were 2.51 times likely to experience poor quality sleep, compared to patients who had seizures annually.

Conclusion: We found a higher prevalence of poor quality of sleep, insomnia, and excessive DTS in our sample of Saudi epilepsy patients.

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Epilepsy is a common chronic condition with an incidence of 61.4/100,000 person-years. Approximately 13 million people experience disability-related years lost and 0.5% of the total disease burden is attributed to epilepsy.[1] In Saudi Arabia, with a population of 30 million, the prevalence of epilepsy is

6.54 per 1,000, similar to the prevalence in many other countries.[2] Sleep disorders such as poor sleep quality, daytime sleepiness (DTS), and insomnia are commonly found in patients with epilepsy.[2-4] Poor quality of sleep and excessive DTS has been reported in 1.5-41.1% of patients suffering from epilepsy, compared to 3-18.1% in healthy people.[2,5] Moreover, the burden of DTS ranges between 20-26.5% among patients with epilepsy.[4] Factors such as type (focal versus generalized or both), frequency, timing, and number of episodes for seizures may contribute to poor quality of sleep among these patients.[6] Additionally, the main treatment strategy of epilepsy is antiseizure medications (ASMs), which may induce sleep disorders and poor sleep quality.[6,7]

Overall, there is a complex relationship between epilepsy and sleep disruptions.[8] Research suggests that sleep disorders are found in a substantial percentage of patients with epilepsy, but there are variations in the burden of these disorders.[6] Sleep disturbances may aggravate seizures and some people may develop seizures due to altered sleep.[9] Sleep disturbances may have adverse effects on seizures, which may negatively affect sleep and exaggerate some sleep disorders.[10] In addition, sleep disturbances may affect overall quality of life and physical and mental health; therefore, it is important to have a better understanding of how sleep disorders may be implicated in epilepsy.[11,12] Providing a timely diagnosis and treating sleep disturbances in patients with epilepsy is expected to improve epilepsy management. Therefore, measuring the burden of sleep disturbances, such as insomnia and excessive DTS, and their effect on sleep quality in patients with epilepsy is crucial.

There are no previous studies have been conducted in Saudi Arabia to address sleep profiles using validated tools to estimate the prevalence of poor sleep quality, DTS, and insomnia. In the present study, we aimed to assess the occurrence of sleep disturbances and DTS, and their impact on sleep quality and to measure the risk factors of poor sleep quality. We used three validated and reliable questionnaires that were translated into Arabic: Pittsburgh Sleep Quality Index (PSQI),[13] Insomnia Severity Index (ISI),[14] and Epworth Sleepiness Scale (ESS).[15,16] These assessments have been validated in heterogenous Arabic samples in different countries in the Middle East.[17-21]

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Methods. *Study design and participants.* The current study was a descriptive cross-sectional survey administered to all epilepsy patients attending the outpatient clinic from October 2020 to March 2021 at King Fahad Medical City (KFMC) in Riyadh, Saudi Arabia. The KFMC research institution's scientific committee reviewed and approved the study.

Participants were required to be at least 18 years old and be diagnosed with epilepsy for at least 1 year. Exclusion criteria were diagnosis of a primary sleep disorder or cognitive impairment, working nights or shift work, and any chronic comorbidities. Patients provided written consent to participate, and confidentiality was assured throughout the study period.

Data collection instruments. We administered well-validated and translated assessments. Arabic versions of these tools have been used in epileptic samples, as well as patients with diabetes, hypertension, cancer, dermatological concerns, and healthy adults in Saudi Arabia.[16,22-27]

The PSQI was administered to evaluate the sleep habits of all participants during the past month. Scores were an aggregate of seven components, each scored 0 (no difficulty) to 3 (severe difficulty). Total scores ranged 0-21, with higher scores 5 or more indicating poorer or worse quality of sleep.

The ISI comprised seven questions, which were summed to obtain a total score. Participants with scores of (0-7, 8-14, 15-21, and 22-28) were considered to have "no clinically significant insomnia", "subthreshold insomnia", "moderate clinical insomnia", and "severe clinical insomnia", respectively.

The ESS was used to measure subjective sleepiness. The test comprises eight situations in which we rate the patient's tendency to become sleepy on a scale of 0 (no chance of dozing) to 3 (high chance of dozing). The participant's total score is a sum of the eight questions, and participants are categorized into one of four categories: unlikely abnormal sleepiness (score 0-7), average DTS (score 8-9), excessive sleepiness that may require medical attention (score 10-15), and excessive sleepiness and that requires medical attention (score 16-24).

In addition to these 3 questionnaires, sociodemographic and clinical characteristics were collected, including gender, education level, type of epilepsy, presence of nocturnal seizures, neuroimaging findings, epilepsy duration, age of onset, and number of antiepileptics medications.

Statistical analysis. Frequencies and proportions were used to describe our sample for variables such as marital status, education, presence of any comorbidities, type of epilepsy, and frequency of epilepsy. Chi-squared or

Table 1 - Socio-demographic and clinical characteristics of patients with epilepsy (n =218).

Characteristics	Total	
	n	(%)
Age (years)		
18 to 27	94	(43.1)
28 to 38	87	(39.9)
39 to 49	25	(11.5)
50 to 60	12	(5.5)
Gender		
Female	113	(51.8)
Male	105	(48.2)
Education		
No education or primary	18	(8.3)
Intermediate	15	(6.9)
Secondary	69	(31.7)
University or post university	116	(53.2)
Marital status		
Single	120	(55)
Married	92	(42.2)
Separated/divorced	6	(2.8)
Employment status		
Employed	64	(29.4)
Retired	7	(3.2)
Unemployed	95	(43.6)
Student	52	(23.9)
Comorbidity		
None	212	(97.2)
Some type of comorbidity	6	(2.8)

Table 2 - Clinical characteristics of patients with epilepsy.

Clinical characteristics	Total	
	n	(%)
Type of epilepsy		
Focal	130	(59.6)
Generalized	80	(36.7)
Both	8	(3.7)
Onset of epilepsy		
Infancy	18	(8.3)
Childhood	65	(29.8)
Adolescent	43	(19.7)
Adulthood	92	(42.2)
Timing of seizure		
Predominantly nocturnal	151	(15)
Predominantly daytime	566	(56.2)
Both	291	(28.9)
Frequency of seizure		
Annually	79	(36.2)
Monthly	89	(40.8)
Weekly	25	(11.5)
Daily	15	(6.9)
Long time ago or once	10	(4.6)
Cause of epilepsy		
Genetic	77	(35.3)
Structural	105	(48.2)
Metabolic/infectious/non-lesional	18	(8.3)
Under investigation	18	(8.3)
ASMs		
Monotherapy	84	(38.5)
Polytherapy	134	(61.5)
Drug response		
Drug responsive	90	(41.3)
Drug resistant	117	(53.7
NA/not fitting	11	(5)
The proactive factor for seizure		
Lack of sleep	47	(21.6)
Stress	33	(15.1)
Non-compliance to ASMs	51	(23.4)
No specific reason	66	(30.3)
More than one factor	21	(9.6)
Brain MRI		
Normal	87	(39.9)
Abnormal	110	(50.5)
Not available/not done	21	(9.6)

ASMs=antiseizure medications; MRI=magnetic resonance imaging

Fisher's exact tests were used to evaluate the association between categorical or binary variables and sleep quality. Similarly, a bivariate logistic regression analysis was conducted to establish the risk factors of poor sleep quality. Before the multivariable regression analysis, we checked various determinants for multicollinearity. Finally, a multivariable logistic regression analysis was performed to establish the adjusted effect of each risk factor or predictor of poor sleep quality. We presented the findings of multivariable regression using crude (OR) and adjusted odds ratios with 95% confidence intervals (CIs). Correlation between sleep quality and insomnia or DTS was determined using Pearson correlations and the coefficient of determination (R2). In addition to A p-value of less than 0.05 was deemed statistically significant. SPSS (version 23.0; IBM, Armonk, NY, USA) was used to analyze the data.

Results. *Socio-demographic characteristics.* A total of 218 patients were enrolled in our study. The mean age of the patients was 30.37 years (±9.69, range=42 years). Approximately half (43.1%) of the patients were aged 18-27 years and only 5.5% were 50-60 years. Likewise, half of the patients were male (51.8%) and a similar proportion (50.0%) of them were unmarried.

Table 3 - Sleep quality in relation to daytime sleepiness and insomnia.

Characteristics	Sleep quality						P-Value	Crude OR	95% CI	
	Total		Good		Poor					
	n	(%)	n	(%)	n	(%)				
ISI interpretation										
No insomnia	92	(42.2)	44	(80)	48	(29.4)		1		
Subthreshold insomnia	82	(37.6)	10	(18.2)	72	(44.2)	<0.0001	6.60	3.03	14.37
Clinical insomnia	44	(20.2)	1	(1.8)	43	(26.4)		39.42	5.21	298.44
ESS interpretation										
Normal	140	(64.2)	45	(81.8)	95	(58.3)		1		
Average amount of DTS	39	(17.9)	8	(14.5)	31	(19)	0.002	1.84	0.78	4.31
May or should consider seek medical attention	39	(17.9)	2	(3.6)	37	(22.7)		8.76	2.02	37.98

CI = confidence interval; DTS-daytime sleepiness; ESS-Epworth Sleepiness Scale; ISI-Insomnia Severity Index; OR-odds ratio.

Table 4 - Correlations among sleep quality, daytime sleepiness, and insomnia (n = 218).

Characteristics	PSQI total score	ESS score	ISI score
PSQI total score			
Pearson Correlation	1	.329**	.654**
Sig. (2-tailed)		.000	.000
ESS score			
Pearson Correlation	.329**	1	.407**
Sig. (2-tailed)	.000		.000
ISI score			
Pearson Correlation	.654**	.407**	1
Sig. (2-tailed)	.000	.000	

Notes: ** Correlation is significant at p<.001, ESS-Epworth Sleepiness Scale; ISI-Insomnia Severity Scale; PSQI-Pittsburgh Sleep Quality Index

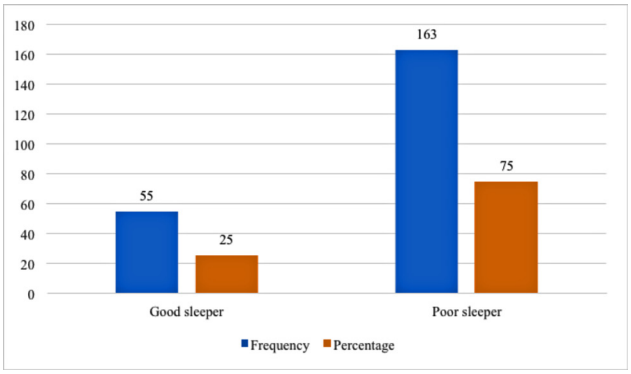

Figure 1 - Prevalence of poor sleep quality among patients with epilepsy using PSQI.

Finally, roughly half our patients (53.2%) had university or post-university degrees; however, 43.6% were unemployed. **Table 1&2** shows the sociodemographic and clinical characteristics of the participants.

Clinical characteristics. In terms of subtype, 59.6% of participants had focal epilepsy and 36.7% had generalized epilepsy. Almost half the patients (42.2%) had epilepsy onset in adulthood, 40.8% reported having seizure episodes monthly, and 48.2% reported their cause of epilepsy being structural. Roughly two-thirds (61.5%) of participants used polytherapy and almost half (53.7%) were found to be drug-resistant. Finally, only 2.8% of participants had any comorbidities. **Table 1&2** shows the socio-demographic and clinical characteristics of the participants.

The PSQI, ISI, and ESS scales. Seventy-five percent of patients demonstrated poor sleep quality, as measured by the PSQI scale (mean score = 6.97 ± 3.29; **Figure 1**).

Likewise, the mean score for ISI was 9.14 (± 6.18), indicating subclinical insomnia. We found that 42.2% of our participants did not have insomnia, 37.6% had subthreshold insomnia, and 17.9% and 2.3% had clinical insomnia of moderate and severe severity, respectively.

Next, the mean score for ESS was 5.69 (±3.981), and we found that 64.2% of participants demonstrated normal sleep, 17.8% had an average amount of DTS, 16.9% excessive sleepiness that may need medical attention, and 0.9% should seek medical attention for their significant DTS.

Sleep quality, DTS, and insomnia. Among the participants with poor sleep quality, 29.4% had no insomnia, compared to 80% of the patients with good quality of sleep, indicating a significant difference (p<0.001). Roughly 26.4% of the patients with poor

Table 5 - Risk factors of poor sleep quality among patients with epilepsy.

Age (years)	AOR	95% CI	
18 to 27	1		
28 to 38	1.353	0.523	3.504
39 to 49	0.497	0.117	2.102
50 to 60	5.715	0.808	40.443
Employment status			
Employed	1		
Retired	0.37	0.03	5.07
Unemployed	0.63	0.25	1.59
Student	1.03	0.29	3.60
Onset of epilepsy			
Infancy	1		
Childhood	3.47	0.81	14.94
Adolescent	0.82	0.19	3.56
Adulthood	1.88	0.47	7.50
Frequency of seizure			
Annually	1.00		
Monthly	2.51	1.00	6.25
Weekly	2.05	0.53	7.86
Daily	2.27	0.34	15.29
A long time ago or once	2.53	0.35	18.27
ASMs			
Monotherapy	1		
Polytherapy	0.64	0.28	1.49
Brain MRI			
Normal	1		
Abnormal	0.64	0.28	1.48
Not available /not done	1.67	0.46	6.08
ISI interpretation			
No insomnia	1		
Subthreshold insomnia	0.94	0.31	2.84
Clinical insomnia	5.45	1.02	29.14
ESS interpretation			
Normal	1		
The average amount of DTS	6.837	2.779	16.822
May or should consider medical attention	44.149	5.184	375.977

ASMs-antiseizure medications, AOR-adjusted odds ratio, CI-confidence interval, DTS-daytime sleepiness, ESS-Epworth Sleepiness Scale, ISI-Insomnia Severity Index, MRI-magnetic resonance imaging

quality had clinical insomnia as opposed to only 1.8% of the patients with good quality of sleep (p<0.001). Likewise, 58.3% of patients with poor quality of sleep were found to have normal sleep, compared to 81.8% of patients with good quality of sleep (p<0.002). Moreover, 18% of patients with poor sleep quality reported an average amount of DTS, compared to the 14.5% of patients with good quality of sleep, indicating a significant difference. Similarly, a greater proportion of patients with poor sleep quality (22.7%) were found to seek medical attention, compared to only 3.6% of patients with good sleep quality. Significance values of subjective sleep quality compared with sample demographic and clinical characteristics are presented in **Tables 1, 2 and 3**.

Correlation among sleep quality, DTS, and insomnia. **Table 4** shows the correlations among sleep quality, DTS, and insomnia using Pearson correlations. A statistically significant positive correlation was found between PSQI total and ESS scores (r=0.329, r^2=0.106, p<0.001; **Figure 4**). Similarly, a positive and strong correlation was found between PSQI total and ISS scores (r=0.654, r^2=0.428, p<0.001; **Figure 2**). Finally, a moderate and positive correlation was found between ISI and ESS scores (r=0.407, r^2=0.166, p<0.001; **Figure 4**).

Predictors of sleep quality. **Tables 4 and 5** demonstrate the regression analysis findings, revealing the risk factors of poor sleep quality. Patients with subthreshold insomnia were 6.60 times likely to report poor sleep quality compared to patients with no insomnia (OR=6.60; 95% CI: 3.03-14.37). Moreover, patients with clinical insomnia were 39.42 times likely to experience poor sleep quality compared to patients with no insomnia (OR=39.42; 95% CI: 5.21-298.44); however, 95% CIs were imprecise and wide.

Similarly, patients with an average amount of DTS were 1.84 times likely to have poor quality sleep compared to patients with normal sleep (OR=1.84; 95% CI: 0.78-4.31) and patients who were recommended to seek medical attention were 8.76 times likely to experience poor quality sleep compared to patients with no insomnia (OR=8.76; 95% CI: 2.02-37.98); however, 95% CIs were imprecise and wide. Other factors such as education, employment, marital status, type of therapy, drug resistance, type of epilepsy, causes of epilepsy, frequency, and timing of seizure were not found to be risk factors of poor sleep quality in the bivariate analysis.

The multivariable analysis (**Table 5**) found 3 significant factors after adjusting for age, employment status, the onset of epilepsy, ASMs, and brain magnetic resonance imaging: seizure frequency, insomnia, and DTS. With respect to ISI interpretation, we found that patients with subthreshold and clinical insomnia were 0.94 and 5.45 times likely to have poor quality sleep compared to patients with no insomnia, respectively (OR=0.94, 95% CI: 0.31-2.84; OR=5.45, 95% CI: 1.02-29.14, respectively); however, 95% CIs were imprecise and wide. Similarly, we found that patients with an average amount of DTS were 6.84 times likely

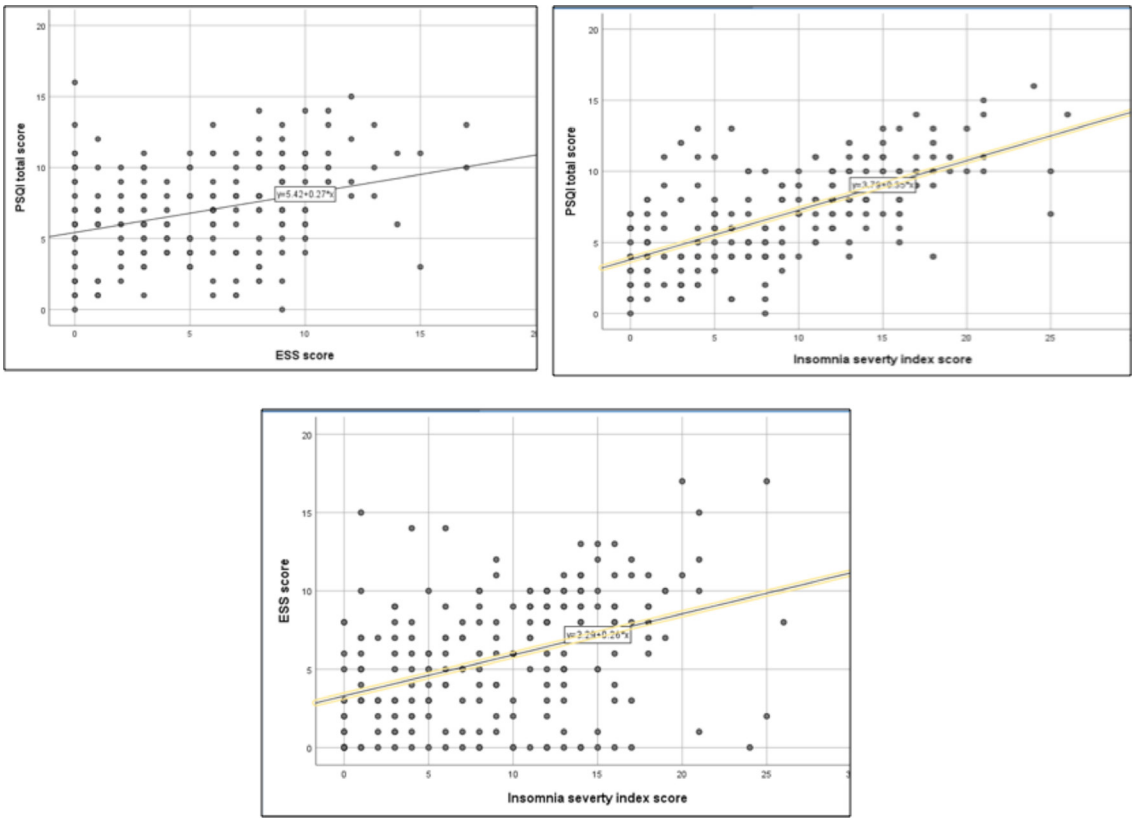

Figure 2 - Epilepsy awareness score distribution among participants.

to have reduced sleep quality compared to patients with normal sleep (OR=6.84; 95% CI: 2.79-16.82). We also found that patients recommended to seek medical attention for their insomnia were 44.15 times likely to have poor quality sleep compared to patients with no insomnia (OR=44.15; 95% CI: 5.18-375.98); however, 95% CIs were imprecise and wide. Finally, with respect to seizure frequency, we found that patients who had monthly seizure episodes were 2.51 times likely to have poor quality sleep compared to patients who had seizure episodes annually (OR=2.51; 95% CI: 1.00-6.25).

Discussion. In the current cross-sectional study, we aimed to estimate the occurrence of sleep disorders and their effects on sleep quality in patients with epilepsy, as well as the prevalence of DTS and insomnia in these patients and the risk factors of poor sleep quality.

We found that 75% of participants reported poor sleep quality, with 37.6% having subthreshold insomnia, 17.8% having an average amount of DTS, and roughly 18% were recommended to seek medical attention. Compared with the existing literature, our sample demonstrated a relatively higher prevalence of insomnia (24.6-34% of patients in the previous research), but a comparable prevalence of excessive DTS (16.9-28% in previous research).[11,28-30] Notably, one study conducted in India found that roughly 25% of patients with epilepsy suffer from sleep disorders.[31]

While assessing the impact of socio-demographic, clinical characteristics, and sleep disturbances, we found that none of the socio-demographic and clinical factors (e.g., gender, comorbidities, education, employment status, type of therapy, drug resistance, type of epilepsy, and causes of epilepsy) significantly differed between poor and good sleepers.

Our analysis and findings regarding the lack of effect of socio-demographic and clinical factors are consistent with other studies conducted in different countries. Previously conducted studies have not found any differences in the quality of sleep by age, gender, or type of epilepsy.[32-35] In addition, factors such as frequency of seizure, insomnia, and DTS were positively associated with poor quality of sleep (**Table 5**).

We found positive relationships between excessive DTS and poor sleep quality and insomnia and poor sleep quality, suggesting that patients with epilepsy with

insomnia and excessive DTS suffer from poor sleep quality. No relationship was found between ASMs and sleep quality, which is consistent with another study;[36] however, ASMs may still affect sleep quality. Some studies have demonstrated that DTS in patients with epilepsy may improve after reducing the frequency of ASMs and that older medications may negatively affect sleep compared to newer drugs.[37-39]

The current cross-sectional study is the first conducted in Saudi Arabia that has attempted to estimate the prevalence of poor sleep quality, DTS, and insomnia in patients with epilepsy. We administered reliable Arabic versions of well-validated assessments to estimate the prevalence of poor sleep quality, DTS, and insomnia in our participants; therefore, our findings may be comparable to studies conducted in other countries. the limitation of the present study is its cross-sectional nature; therefore, we cannot establish a relationship between factors such as insomnia and excessive DTS with poor sleep quality. Secondly, the 3 assessments that were used in our present study are subjective in nature and rely on participant responses; therefore, our findings may be biased due to the lack of objective sleep measures like polysomnography. Moreover, our sample size was relatively smaller than other studies, suggesting imprecise results for important factors of poor sleep quality. We recommend that more studies be conducted in different hospitals in Saudi Arabia with larger sample sizes, allowing results to be generalized to other study settings with a higher degree of confidence. We also did not assess the impact of sleep hygiene on sleep quality since we excluded patients who worked night shifts. Such factors may be important predictors of sleep quality and should be assessed in the future. Lastly, we included all patients with epilepsy and did not have a control group to which we could have compared the prevalence of insomnia and excessive DTS; however, our present study should be considered a foundation for future studies in Saudi Arabia.

Conclusion. We found a relatively higher prevalence of poor sleep quality, insomnia, and excessive DTS in patients with epilepsy in Saudi Arabia. Almost two-thirds of the patients with epilepsy suffered from poor sleep quality, demonstrating a high prevalence. Factors such as seizure frequency, insomnia, and excessive DTS were found as significant and important risk factors of poor sleep quality in the present study. Although we did not find any differences in sleep quality by socio-demographic and clinical factors, it is possible that we may have missed some important factors due to our limited sample size. Therefore, future studies should clarify and explore this issue further.

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