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Depression and poor sleep: neglected prevalent issues among adult epileptic patients

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Abstract

Background Psychiatric comorbidities, and sleep disorders, are prevalent in adults with epilepsy (AWE). Good control of epilepsy can help AWE lead a normal fruitful life and incorporate in daily activities as others. This study aims to assess the frequency, risk factors of depression, and poor sleep quality among patients with epilepsy and examine their relation with epilepsy control.

Methods This cross-sectional study was accomplished during the period from January to October 2023 involving 179 AWE. All were exposed to complete history taking: stressing on personal data, evaluation of medication adherence using the modified Morisky scale, sleep quality using the Pittsburgh Sleep Quality Index, and depressive symptoms evaluated by the Zagazig Depression Scale.

Results Depression was reported in 22.2% of studied patients; while 44.4% had poorer epilepsy control. Poor sleep quality was reported in 35.2% of epilepsy patients and was associated with non-adherence and poor seizure control. Depression increased the risk of poor control by about 16-folds. Non-adherence was associated with depression and poor sleep quality and was one of the predictors of poor epilepsy control.

Conclusion Depression and poor sleep quality can impair the outcome of PWE and also there is a strong association between depression and poor sleep quality among PWE and both impair seizure control.

Keywords Epilepsy, Depression, Sleep quality, Non-compliance

Background

Epilepsy, the most common neurological disorder, is categorized by paroxysmal, recurring, and transient central nervous system malfunction in the form of excessive discharge of brain neurons [1]. Epilepsy affects more than 50 million individuals globally; 80% of them habitat low- and middle-income countries. Up to 70% can lead a seizure-free life if they are properly treated [2]. In Arab countries, the estimated prevalence is about 6.9 per 1000 people [3]. Psychiatric comorbidities, like anxiety, mood, and psychotic disorders, are frequent comorbidities in patients with epilepsy (PWE) with rates reaching three times higher than the general population [4]. Depression is one of the most common comorbidities that impair the quality of life in PWE [5].

The lifetime hazard of depression encountered in the general population is 15–18%, with about 20% suffering one episode at some point in their lifetime [6]. From one-third to one-half of PWE develop a depressive symptom that undermines optimal seizure control [7]. Comorbid depression in PWE can be justified via various theories, neurobiological like a hyperactive hypothalamic–pituitary–adrenal axis (HPA), neuroinflammatory (IL-6, IL-2, IL-1b, tumor necrosis factor-a and interferon-g) [8], neurotransmitter disturbance (norepinephrine and

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serotonin) [9] anatomical aberrations (paralimbic structures and prefrontal cortex) [10], and the social load of disease itself [11].

Commonly, PWE suffers from daytime sleepiness and impaired sleep quality. The interplay between epilepsy and sleep dysfunction is complex. Sleep deprivation can exacerbate fits that occur mostly during sleep [12]. The effect of epilepsy on sleep can be linked to the same pathophysiological process triggering epilepsy, the effect of the seizure itself, antiepileptic therapy, or a combination of those factors [13].

This study was done to assess the frequency, risk factors of depression, and poor sleep quality among PWE and examine their relation with the control of epilepsy.

Methods

A cross-sectional study was accomplished at the epilepsy and neurology outpatient clinic during the period from January to October 2023 on patients with definite diagnoses of different types of epilepsy according to the classification of the International League against epilepsy [14].

Based on that depression prevalence among AWE was 70.3% [11], and the attendance rate of PWE in the Neurology outpatient clinic, at Zagazig University Hospital is 400 patients/6 months, the sample size was calculated to be 179 patients at a confidence level of 95%, power of study 80% and effect size 1.0 using OpenEpi software. The sample was recruited via a systematic random technique (every third patient was included).

The following patients were excluded: patients with brain disorders such as metabolic encephalopathy, CNS infections, head trauma, electrolyte disturbance, brain tumor, patients on anxiolytics or anti-depression medication, patients with system failure or malignancies, patients with substance abuse, and patients with severe intellectual disability that can interfere with scale application.

Study tools

All patients were exposed to complete history taking: stressing on personal data that involved assessment of socio-economic status (SES) using a questionnaire created by El-Gilany and colleagues which scores as follows: socio-demographic score < 50% (low), score 50%– < 75% (middle), and score ≥ 75% (high) after modification [15]. Also, present, past, and family history, age of onset, type of seizure, frequency, semiology of seizures, and history of status epilepticus were collected.

The level of seizure control was assessed grounded on the frequency, and type of seizures that took place in the previous 12 months and categorized as the following Table 1.

Table 1 Level of seizure control [16]

Level	Fits frequency and type in the past 12 months
Good	no seizures
Partial	1–20 focal, 1–4 complex partial, 1 GTC, 1–20 absence, or 1–20 myoclonic seizures
Poor	20 focal, > 4 focal with impaired awareness, > 1 GTC, > 20 absence, or > 20 myoclonic seizures

GTC generalized tonic–clonic

Morisky Medication Adherence Scale (The MMAS-8): an eight-item scale that is utilized to evaluate compliance with medication. It is constructed as seven yes/no questions while the last one is a five-point Likert measure. Adequate adherence is set at ≥ 6 [17]. The Arabic version used was developed by Ashur and colleagues and they reported that it had adequate internal consistency ($\alpha = 0.70$) and moderate split-half reliability ($r = 0.65$) [18].

Assessment of depression was done using the Zagazig Depression Scale (ZDS) which is a reliable 52-item self-rating Arabic scale to measure a wide spectrum (17 domains) of depressive manifestations. Each question has yes/no answer. Answer 'yes' is scored as 1 and 'no' is scored as 0 with scores ranging from 0 to 52. It has adequate internal consistency (Cronbach's alpha 0.82). Scores: 0–9 mean "no symptoms", 10–19 "mild depression", 20–29 "moderate depression", and ≥ 30″ severe depression" [19].

Pittsburgh Sleep Quality Index (PSQI) was used to estimate the quality of sleep during the previous month. It consists of 19 questions covering seven component subscales: sleep latency, duration, disturbance, daytime dysfunction, habitual sleep efficiency, subjective sleep quality, and use of sleep medications, and. Entire score arrays from 0 to 21. The higher the scores, the lesser the quality of sleep with an accepted cutoff for poor quality at ≥ 8 [20]. The Arabic version of Suleiman et al. [21] was used (Cronbach's α of the Arabic version is 0.74).

A pilot study was conducted on 10% of the total sample (18 patients) to assess the study tools' practicability and simplicity of scales and estimate the time required to complete each scale. Study tools were appropriately clear, so no modification was done hence, patients involved in the pilot study were included in field work. Upon accepting sharing in the study, informed oral consent was obtained from patients. All were subjected to detailed history taking, full clinical examination, and then filling in the study scales (it took approximately 30 min to complete the questionnaires) in a private room.

Statistical analysis

Statistical analysis was accomplished using the software SPSS (Statistical Package for the Social Sciences) version 26. Categorical data was designated using absolute frequencies. Shipro-Wilk test was utilized to check data distribution normality. Quantitative data was represented using mean ± standard deviation/median (interquartile range) based on the type of data distribution. Independent sample t-test was used to compare the means of two groups while the Mann–Whitney test was used for not normally distributed data. For categorical variables, chi-square (χ^2) and Fisher's exact tests were used. Ordinal data between the two groups were compared using chi-square for the trend test. To evaluate risk factors for depression and epilepsy control, Binary backward Wald regression analysis was done. *P* value < 0.05 is considered significant while $p \leq 0.001$ is statistically highly significant.

Results

This study included 179 AWE aged from 20 to 65 years. Males constituted 54.7%, 46.9% were on middle SES, 44.7% had partial seizures, 72.6% had idiopathic epilepsy and 55.9% reported that seizures can occur anytime per day. Disease duration ranged from 7 to 30 years (Table 2).

ZDS total score ranged from 1 to 33 with a median of 7. A larger percentage of patients (77.7%) reported no depressive symptoms. PSQI total score ranged from 3 to 18 with a median of 6 and accordingly, 35.2% had poor sleep quality. According to MMS-8, 27.9% were non-compliant (Table 3).

Concerning the total score of ZSD among male and female patients, males ($n=98$) had a median value of 7 and IQR (5–9) versus a median value of 7 and IQR (4–10.5) in females ($n=81$) with a statistically non-significant difference ($Z=-0.159$, $p=0.874$). Median (IQR) of PSQI in males [6(4–8)] versus in females [6(4–9)] with a statistically non-significant difference ($Z=-0.053$, $p=0.958$) (Fig. 1). Good seizure control prevailed in 58% of male patients versus 42% in females (Fig. 2).

A statistically significant relation was found between depression and age, disease duration, SES, therapy, poor sleep quality, and non-compliance. Depression was associated with younger age, longer disease duration, lower SES, dual and multiple drug therapy, poor sleep quality, and non-compliance. There is a statistically non-significant relation between depression and either gender, type of epilepsy, time of fits, or etiology. There is a statistically significant relation between poor sleep quality and disease duration, SES, depression, and non-compliance. Poor sleep quality was associated with longer disease duration, lower SES, depression, and non-compliance.

Table 2 Distribution of the studied patients according to baseline data

	N **= 179**	**%/ range**
Sex		
Male	98	54.7%
Female	81	45.3%
Male sex	98	54.7%
Age [mean ± SD]	43.88 ± 13.19	20–65
Disease duration (median [IQR])	12(10–20)	7–30
Social class:		
Low	35	19.6%
Middle	84	46.9%
High	60	33.5%
Type of epilepsy:		
Partial	80	44.7%
Generalized	60	33.5%
Unknown	39	21.8%
Etiology:		
Symptomatic	49	27.4%
Idiopathic	130	72.6%
Time:		
Anytime	100	55.9%
Nocturnal	49	27.4%
Day time	30	16.8%
Therapy:		
Mono	49	27.4%
Double	79	44.1%
Multiple	51	28.5%
Control of seizures:		
Good	100	55.9%
Partial	49	27.4%
Poor	30	16.8%

Table 3 Distribution of the studied patients according to depression, sleep quality and compliance to treatment

	N **= 179**	**%/Range**
ZDS [median (IQR)]	7(4–9)	1–33
Depression:		
Normal	139	77.7%
Mild	22	12.3%
Moderate	8	4.5%
Severe	10	5.6%
PSQI [median (IQR)]	6(4–8)	3–18
Poor sleep	63	35.2%
Non-compliance (< 6)	50	27.9%

ZDS Zagazig Depression Scale, *PSQI* Pittsburgh Sleep Quality Index

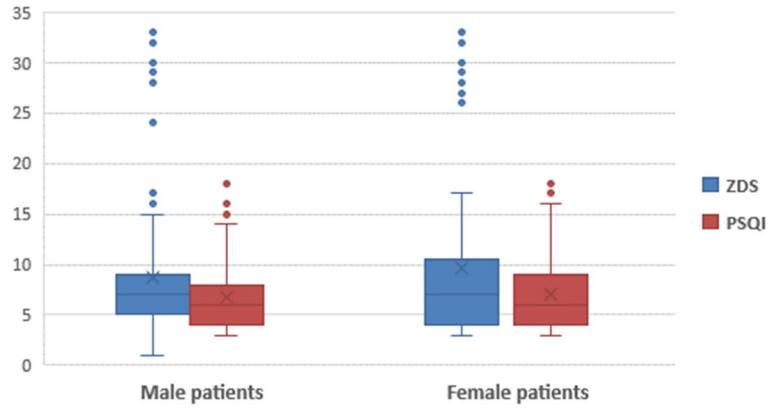

Fig. 1 Boxplot showing ZDS and PSQI scores among male and female PWE

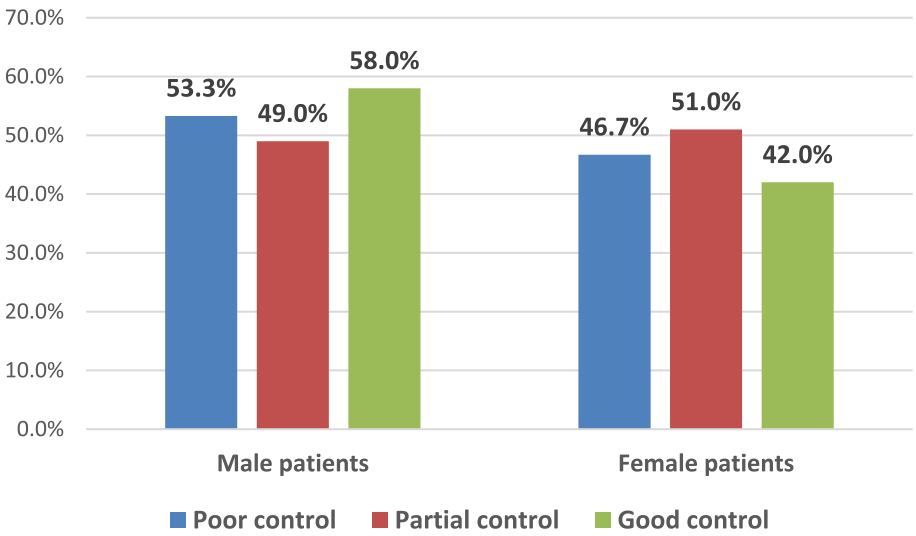

Fig. 2 Multiple bar chart showing relation between gender and seizure control

There is a statistically non-significant relation between depression and either age, gender, therapy, type of epilepsy, time of fits, or etiology (Table 4).

Multivariate analysis revealed that low SES, receiving double multiple drug therapy, poor sleep quality, and non-significantly independently increased the risk of depression by 3.866, 4.151, 5.68, 3.384, and 3.749-folds respectively. Middle SES non-significantly independently increases the risk of depression by 2.686-folds. Multivariate analysis of poor sleep quality revealed depression, and non-compliance significantly independently increase the risk of poor sleep quality by 2.997 and 3.644-folds respectively. Low SES non-significantly independently increases the risk of depression by 2.997-folds. Middle SES non-significantly independently decreases the risk of poor sleep quality (AOR = 0.651) (Table 5).

There is a statistically significant relation between control of epilepsy and disease duration, socioeconomic class, therapy, poor sleep quality, depression, and non-compliance. Poorer control was associated with longer disease duration, lower SES, double drug therapy, poor sleep quality, depression, and non-compliance. There is a statistically non-significant relation between control of epilepsy and either age, gender, type of epilepsy, time of fits, or etiology (Table 6).

Low SES, receiving double drug therapy, depression, and non-compliance significantly independently increase the risk of partial and poor control by 41.301, 59.666, 16.365, 3.26, and 15.673-folds respectively. Multiple drug therapy non-significantly independently increases risk by 6.501-folds. Middle SES non-significantly independently decreases risk (Table 7).

Table 4 Relation between depression, sleep quality, and the studied parameters

	Depression ***N*** **= 40 (%)**	χ^2	***p***	**Poor sleep quality** ***N*** **= 63(%)**	χ^2	***p***
Age (mean ± SD)	40.2 ± 12.19	2.022[b]	0.045*	42.21 ± 12.12	1.255[b]	0.211
Sex *n* (%):						
Male	19 (47.5%)	1.092	0.296	34 (54%)	0.024	0.877
Female	21 (52.5%)			29 (46%)		
Duration [median (IQR)]	18(12–23)	−4.239[a]	< 0.001**	18(11–22)	−3.712[a]	< 0.001**
Social class:						
Low	18 (45%)	19.369[c]	< 0.001**	25 (39.7%)	13.445[c]	< 0.001**
Middle	16 (40%)			21 (33.3%)		
High	6 (15%)			17 (27%)		
Type of epilepsy:						
Partial	13 (32.5%)	1.393	0.238	23 (36.5%)	1.911	0.385
Generalized	18 (45%)			26 (41.3%)		
Unknown	9 (22.5%)			14 (22.2%)		
Etiology:						
Idiopathic	25 (62.5%)	2.657	0.103	49 (77.8%)	1.298	0.255
Symptomatic	15 (37.5%)			14 (22.2%)		
Time:						
Anytime	23 (57.5%)	0.103	0.748	35 (55.6%)	0.632	0.729
Nocturnal	11 (27.5%)			19 (30.2%)		
Day time	6 (15%)			9 (14.3%)		
Therapy:						
Mono	4 (10%)			13 (20.6%)	0.805[c]	0.37
Double	19 (47.5%)	9.032[c]	0.003*	32 (50.8%)		
Multiple	17 (42.5%)			18 (28.6%)		
Poor sleep quality	27 (67.5%)	23.568	< 0.001**			
Depression				27 (42.9%)	23.568	< 0.001**
Non-compliance	26 (65%)	35.158	< 0.001**	34 (54%)	32.735	< 0.001**

χ^2 chi-square test

[a] Mann–Whitney test

[b] Independent sample *t* test

[c] Chi-square for trend test

*$p < 0.05$ is statistically significant

**$p \leq 0.001$ is statistically highly significant

Discussion

Depression is a growing problem affecting all age groups regardless preexisting comorbidities that necessitates screening all individuals for depression once per year. Having a chronic disease such as epilepsy potentially adversely affects body image besides job performance and satisfaction with life. Hence, epilepsy can vastly increase the risk of depression.

The prevalence of depression in the current study was 22.3% which was to a large extent less than that reported in a former Egyptian study by Sehlo and colleagues [11] who stated that 70.3% of PWE had depression. This can be attributed to the difference in situations of both studies and also a difference in screening questionnaires used. They studied depression prevalence during COVID-19 which was a stressful event for the overall general population. A previous meta-analysis reported a wide variance in depression prevalence from 5.09 to 85.5% [22].

Impaired sleep quality was reported in 35.2% of PWE. Previous studies reported a prevalence of 53.6%, and 65.5% among PWE [23] and [24] respectively. A previous study by Çilliler and Güven reported that poor sleep quality and depression were reported in 42.7% and 74.7% of PWE respectively.

Depression was associated with younger age but with longer disease duration. We suggested that longer disease duration can be disappointing to patients who

Table 5 Multivariate regression analysis of factors associated with depression among epilepsy patients

		β	*P*	AOR	95% C.I	
					Lower	Upper
Depression	High SES		0.092			
	Low SES	1.352	0.036*	3.866	1.092	13.693
	Middle SES	0.988	0.084	2.686	0.876	8.235
	Drug therapy (mono)		0.038*			
	Drug therapy(double)	1.423	0.03*	4.151	1.143	15.072
	Drug therapy(multiple)	1.737	0.012*	5.68	1.475	21.882
	Poor sleep quality	1.219	0.01*	3.384	1.342	8.533
	Non-compliance	1.322	0.006*	3.749	1.464	9.6
Poor sleep quality	High SES		0.042*			
	Low SES	0.844	0.121	2.325	0.799	6.767
	Middle SES	-0.429	0.299	0.651	0.29	1.464
	Depression	1.098	0.015*	2.997	1.239	7.251
	Non-compliance	1.293	0.003*	3.644	1.57	8.46

AOR adjusted odds ratio, *CI* confidence interval, *SES* socioeconomic status

*$p < 0.05$ is statistically significant

thought that their fits would change with time and younger age still have constraints when comparing their lifetime with their mates without epilepsy.

Non-compliance was a common factor that was associated with depression, and poorer control in univariate and multivariate analysis in line with Sehlo and colleagues and Hesdroff and coworkers [11, 25]. This can be explained as a positive feedback mechanism as non-compliance increases the opportunity for poor seizure control and increasing rate of fits and ER visits which can increase the sense of poor mastering of one's life hence feeling helpless with increasing opportunity to develop depression. Depression, itself, with loss of interest, can make a patient feel that medication has no benefit; accordingly, he will be non-compliant.

Poor sleep quality was also associated with non-adherence in agreement with the study by Adem and colleagues [24].

Poor sleep quality is significantly related to depression in both uni and multivariate analysis which can be one of the depressive symptoms or a result of epilepsy or medications that adversely affect mental health. Sleep deprivation is a recognized precipitating factor for seizures as increases neuronal excitability. This comes in agreement with previous studies [23, 26, 27].

Poor sleep quality was related to poor seizure control in univariate analysis which agreed with those who reported that poor sleep quality is linked with more recurrent seizures [28].

A previous study by Çilliler and colleagues reported that poor sleep quality and depression were reported in 42.7% and 74.7% of PWE respectively [28].

Receiving more than a single drug increases the risk for depression, poor sleep quality, and poorer epilepsy control in agreement with Planas Bellave et al. [23]. This can be attributed to adverse effects of drugs, psychological perception of being far from seizure control, and financial issues that may impair sleep quality, precipitate depression hence impair disease control.

Socioeconomic class and financial crisis since the COVID-19 lockdown followed by the Russian-Ukrainian war that aggravated poverty among lower SES, can affect seizure control, increase the prevalence of depressive symptoms even in apparently healthy individuals, and impair sleep quality as noted in the current study. Financial burden can hinder an adequate supply of AEDs and drive patients to skip one dose of a certain drug or even one drug to make medications sustain longer which leads to suboptimal fit control. It may lead to working extra shifts or receiving inadequate meals to combat an imbalance in income versus expenditure. This finding comes in agreement with other studies [11, 29].

Suboptimal epilepsy control was detected in 44.1%. A previous study stated that 53.4% of PWEs were uncontrolled [30]. In that study, low medication adherence is a risk factor for poor control in agreement with the current study.

Poor disease control was associated with lower SES in harmony with previous studies [21, 31, 32], which conveyed that low SES was associated with poorly controlled disease. This can be attributed to that epilepsy itself is associated with a lower employment rate. Also, PWE within lower SES can not afford the cost of medication or regular follow-up visits. Also, lower SES was a predictor

Table 6 Relation between epilepsy control and the studied parameters

	Good control *N* = 100 (%)	Partial/poor control *N* = 79 (%)	χ^2	*p*
Age (mean ± SD)	45.14 ± 13.62	42.29 ± 12.52	*t*(1.44)	0.152
Sex *n* (%):				
Male	58 (58%)	40 (50.6%)	0.967	0.325
Female	42 (100%)	39 (49.4%)		
Duration[median (IQR)]	10(8–12)	18(13–22)	*Z*(− 7.163)	< 0.001**
Social class:				
Low	4 (4%)	31 (39.2%)	17.689	< 0.001**¥
Middle	58 (58%)	26 (32.9%)		
High	38 (38%)	22 (27.8%)		
Type of epilepsy:				
Partial	47 (47%)	33 (41.8%)	2.16	0.34
Generalized	29 (29%)	31 (39.2%)		
Unknown	24 (24%)	15 (19%)		
Etiology:				
Idiopathic	77 (77%)	53 (67.1%)	2.181	0.14
Symptomatic	23 (23%)	26 (32.9%)		
Time:				
Anytime	56 (56%)	44 (55.7%)	0.031	0.859
Nocturnal	28 (28%)	21 (26.6%)		
Day time	28 (28%)	14 (17.7%)		
Therapy:				
Mono	43 (43%)	6 (7.6%)	9.219	0.002*¥
Double	28 (28%)	51 (64.6%)		
Multiple	29 (29%)	22 (27.8%)		
Depression	4 (4%)	36 (45.6%)	43.95	< 0.001**
Poor sleep	17 (17%)	46 (58.2%)	32.89	< 0.001**
Non-compliance	6 (6%)	44 (55.7%)	54.146	< 0.001**

χ^2 chi-square test, *Z* Mann–Whitney test, *t* independent sample *t* test

*$p < 0.05$ is statistically significant

**$p \leq 0.001$ is statistically highly significant

¥ Chi-square for trend test

Table 7 Multivariate regression analysis of factors associated with partial and poor disease control

	β	*P*	AOR	95% C.I	
				Lower	Upper
High SES		0.011*			
Low SES	2.919	0.01*	41.301	1.987	172.78
Middle SES	− 0.375	0.461	0.608	0.254	1.861
Drug therapy (mono)		< 0.001**			
Drug therapy (double)	5.179	< 0.001**	59.666	8.928	398.739
Drug therapy (multiple)	1.915	0.06	6.501	0.923	645.795
Depression	2.795	< 0.001**	16.365	3.458	77.455
Non-compliance	2.752	< 0.001**	15.673	3.859	63.651

*$p < 0.05$ is statistically significant

**$p \leq 0.001$ is statistically highly significant, *AOR* adjusted odds ratio, *CI* confidence interval, *SES* socioeconomic status

for depression and poor sleep quality which in turn impaired disease control.

Being a common disease frequently encountered in primary health care (PHC), family physicians should be aware of such problem that undermines patient outcomes. So early regular screening for sleep abnormalities and psychiatric disorders done at PHC, with early referral to a psychiatrist and neurologist can lead to better outcomes at the level of both the patient and the overall health system.

There are some limitations in this study. The most significant is the cross-sectional design so a causal relation can not be proved. Also, there was no control group, a relatively small sample size, and patients did not perform polysomnography as objective evaluation of sleep quality are other limitations. In the current study, we not only investigate the frequency of both depression

and poor sleep quality but also examine their relation to seizure control which was objectively assessed.

Conclusion

Both depression and poor sleep quality seem as if fire lies there underneath the ashes that can impair the outcome of AWE. Depression, and poor sleep quality among PWE are inter-related on one hand and both impair disease control on the other hand. We recommend screening PWE for depression and sleep disorders at regular intervals especially in times of crisis either financial or wars to early diagnose such problems, to provide timely management, to improve both quality of life and care, and to perform training programs for family and primary health care physicians on necessity of screening and early diagnosis of poor seizures control, depression, sleep abnormalities among PWE.

Abbreviations

PWE	Patients with epilepsy
SES	Socioeconomic status
GTC	Generalized tonic colonic
ZDS	Zagazig Depression Scale
MMAS	Morisky Medication Adherence Scale
PSQI	Pittsburgh Sleep Quality Index

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Authors' contributions

SF, AA, HE, LA, and RH carried out this work. AA and HE designed the study shared in interviewing patients, data analysis and manuscript writing. SF and RH collected the patients, gathered clinical data, and shared in manuscript writing. LA was responsible for the evaluation of depression among patients. All authors were involved in drafting the article or revising it critically for important. All authors read and approved the final manuscript.

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Availability of data and materials

Data and materials supporting the results of this article are included within the article (and its additional file(s)).

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Ethics Committee of the Faculty of Medicine, Zagazig University (ZU-IRB #10247/25–12-2022). Written informed consent was obtained from all study participants after explaining the details and benefits as well as risks to them. Surrogate consent from the patient's legal guardian or designated health proxy was permitted in cases where the patient did not have decision-making capacity.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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