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High risk of anxiety and depression in caregivers of adult patients with epilepsy and its negative impact on patients' quality of life

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ABSTRACT

Objective: The objective of this study was to assess the anxiety and depression of caregivers of adult patients with epilepsy (PWE) and evaluate its effect on patient quality of life (QOL).

Method: One hundred sixty pairs of adult PWE and their caregivers were enrolled in our study. Quality of life in adult PWE was evaluated with the Quality of Life in Epilepsy Inventory-31 scale (QOLIE-31). Symptoms of anxiety and depression in caregivers were assessed with the Hamilton Anxiety Rating Scale (HAM-A) and the Hamilton Depression Rating Scale (HAM-D) respectively. Correlation and stepwise multiple liner regression analyses were used as statistical analysis.

Results: Of the caregivers, 41 (31.30%) had anxiety symptoms (HAM-A scores > 6) and 44 (33.59%) had depression symptoms (HAM-D scores > 6). Caregiver anxiety was significantly associated with poorer adult PWE QOL scores in four of the seven subscales and the QOLIE-31 total score. Caregiver depression was significantly associated with poorer adult PWE QOL in all seven subscales as well as the QOLIE-31 total score. Caregiver depression was an independent predictor of the QOLIE-31 total score and five subscales: seizure worry, emotional wellbeing, energy/fatigue, cognitive, and medication effects.

Conclusion: Caregivers of adult PWE are at high risk of experiencing anxiety and depression. Caregiver psychological status, especially depression, was an independent predictor of poorer QOL for adult PWE.

1. Introduction

Epilepsy is one of the most common neurological disorders, with the prevalence rate being second only to stroke [1]. The abrupt and repetitive nature of seizures can lead to many serious psychological problems, including stigma, and patients with epilepsy (PWE) sometimes conceal their condition from their neighbors, relatives, and even families, which can cause feelings of isolation and self-abasement [2]. Seizures impact upon PWE in various ways: restrictions from driving, worries of seizure onset in public settings, low marriage rates, low education levels, and low participation rates in entertainment activities [3,4].

Depression and anxiety are the most common psychological comorbidities in PWE. Psychological comorbidity in PWE relating to depression has a prevalence of 12–50%, and for anxiety a prevalence of 4.3–52.1% [5–8]. Recently, the psychological status in caregivers of patients with chronic disease has been receiving increasing attention. Previous studies have shown that caregivers of PWE are at high risks of experiencing depression and anxiety comorbidity, even reaching up to 50%, and 58%, respectively [9–13].

Quality of life (QOL) is an important component in the clinical management of PWE [14]. Previous studies have indicated that psychological comorbidities in PWE, such as anxiety, depression, and sleep disorders have a significant impact on QOL [15–20]. Several studies have also shown that caregiver psychological comorbidities, depression and anxiety in particular, are significantly correlated with QOL in child and adolescent PWE [12,21–23]. Caregivers of child and adolescent PWE are most typically their parents, whereas caregivers in adult PWE could be the spousal partner, parent, offspring, sibling, or any other individuals. Although the caregivers of adult PWE play a less important role than those of child and adolescent patients, caregivers still have a profound effect on adult PWE. However, the relationship between caregiver anxiety and depression with adult PWE QOL has not been fully investigated to date.

In this study, we assessed caregiver anxiety and depression. We examined the correlations between adult PWE QOL with their caregivers'

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anxiety and depression, as well as clinical and demographic characteristics, such as age at seizure onset, epilepsy duration, seizure severity, current number of antiepileptic drugs (AEDs), caregivers sex, caregivers age, relationship to patients, and whether they were a single caregiver.

2. Materials and methods

2.1. Study population

Participants were 160 pairs of adult PWE and caregivers, who regularly attended the Epilepsy Center in Henan Provincial People's Hospital between March 2017 and March 2018. Patient inclusion criteria were as follows: a diagnosis of epilepsy according to the criteria of the International League Against Epilepsy [24], and age above 18 years old. Patient exclusion criteria were the presence of significant cognitive deficits meaning that the questionnaires could not be completed, severe organic brain disease, and the presence of acute symptomatic seizure. Caregivers' exclusion criteria were the presence of significant cognitive deficits meaning that the questionnaires could not be completed. Overall, 29 pairs of adult PWE and their caregivers, who provided invalid questionnaire responses, were excluded. Therefore, 131 pairs of adult PWE and their caregivers were included in the analysis. This study was approved by the Ethics Committee of Henan Provincial People's Hospital. Informed consent was obtained from each patient and their caregiver.

2.2. Questionnaires

The Hamilton Anxiety Scale (HAM-A) [25] and Hamilton Depression Scale (HAM-D) [26] were used to evaluate anxiety and depression in caregivers. We used Chinese versions of the HAM-D and HAM-A, which were assessed to have satisfied validity and reliability [27]. The HAM-A includes 14 symptoms, with each symptom rating from 0 (absent) to 4 (severe); HAM-A scores range from 0 to 56, with higher scores representing more severe anxiety. Scores of 0–6 are considered normal; scores of 7–13 are considered possible anxiety; 14–20 are considered probable anxiety; 21–29 are considered definite anxiety, and above 29 are considered severe anxiety. The HAM-D includes 7 sections with 17 questions, ten questions rating from 0 (absent) to 4 (severe) and seven questions rating from 0 to 2. The scale scores range from 0 to 54, with higher scores reflecting more severe depression. Scores of 0–6 are considered normal; scores of 7–16 are considered mild depression; 17–24 are considered moderate depression, and above 24 are considered severe depression.

The Quality of Life in Epilepsy Inventory-31 scale (QOLIE-31) Chinese version was used to assess the QOL in PWE, which has been demonstrated to be valid and reliable in Chinese people with epilepsy [28]. The inventory of QOLIE-31 contains seven domains: seizure worry, overall quality of life, emotional wellbeing, energy/fatigue, cognitive, medication effects, and social function. The total score was calculated by assigning different percentages to the seven scores, ranging from 0 to 100, with higher scores indicating better QOL.

The Seizure Severity Scale [29] was completed by two neurologists at each assessment. It divides seizure severity into three groups: (1) group one includes patients with no seizures of any type in the past year; (2) group two includes patients with ≤20 simple partial seizures, ≤20 absence or myoclonic seizures, ≤4 complex partial seizures or ≤1 generalized tonic–clonic seizure in the past year, (3) group three includes patients with any amount beyond group two. We define group one, two, and three as the group of mild, moderate, and severe severity, respectively.

2.3. Statistical analysis

Analyses were conducted using IBM SPSS Statistics for Windows v.21.0 (IBM Corp. Armonk, NY, U.S.A.). Descriptive variables were expressed as mean ± standard deviation, and categorical variables were expressed as frequencies and percentages. Pearson correlation/Spearman's rank correlation coefficient was used to assess the association between demographic characteristics and caregivers' anxiety and depression scores with adult PWE QOL scores. Pearson correlation analysis was used for normally distributed data, and Spearman's rank correlation coefficient was used for ranked or abnormally distributed data. Stepwise multiple linear regression modeling was used to identify the independent risk factors for adult PWE QOL. In all tests, a p value less than 0.05 was considered as statistically significant.

3. Results

3.1. Demographic characteristics of patients and caregivers

The clinical and demographic characteristics of the 131 patients are shown in Table 1. The mean age of patients was 29.35 ± 11.85 years (range 18–66 years), and 58 (44.27%) patients were female. The mean age at seizure onset was 20.56 ± 12.40 years (range 0.5–58 years). The mean duration of epilepsy was 8.87 ± 9.33 years (range 1–43). Only 27 (20.61%) patients were in remission for longer than one year, and 60 (45.80%) patients were treated with monotherapy.

The mean age of caregivers in our study was 39.78 ± 9.69 years (range 21–64 years), and 54 (41.22%) caregivers were female. The relationships between caregiver and the patient were spouse (n = 44; 33.59%), parent (n = 63; 48.09%), offspring (n = 12; 9.16%), and 'other' (n = 12; 9.16%). In total, 103 (78.63%) of patients had only one caregiver, and 28 (21.37%) had more than one caregiver.

3.2. Description of the caregivers' psychological status

The scores of HAM-A and HAM-D that reflect caregivers' depression and anxiety severity are shown in Table 2. The mean HAM-A and HAM-D scores of caregivers were 24.58 ± 6.25 and 24.52 ± 6.69, respectively. Anxiety symptoms were reported by 41 (31.30%) caregivers, in which 18 (13.74%) experienced possible anxiety, 10 (7.63%) experienced probable anxiety, 11 (8.40%) experienced definite anxiety, and two (1.53%) experienced severe anxiety. In the caregivers, 44 (33.59%) had depression symptoms, in which 30 (22.90%) experienced mild depression, 12 (9.16%) experienced moderate depression, and two (1.53%) experienced severe depression symptoms.

Table 1
Clinical and demographic characteristics of adults PWE (n = 131).

Variables	N (%)/mean ± SD
Female	58 (44.27%)
Age (years)	29.35 ± 11.85
Age at seizure onset	20.56 ± 12.40
Epilepsy duration	8.87 ± 9.33
Number of AEDs	
0	12 (9.16%)
1	60 (45.80%)
2	44 (33.59%)
≥3	15 (11.45%)
Seizure severity	
Mild	27 (20.61%)
Moderate	13 (9.92%)
Severe	91 (69.47%)
QOLIE scores	
Seizure worry	32.21 ± 18.82
Overall quality of life	46.63 ± 13.36
Emotional wellbeing	37.16 ± 21.46
Energy/fatigue	38.03 ± 21.83
Cognitive	36.04 ± 20.97
Medication effects	28.58 ± 17.59
Social function	33.90 ± 22.94
QOLIR-31 total score	36.70 ± 16.39

PWE: patient with epilepsy; AEDs: antiepileptic drugs; QOLIE: quality of life in epilepsy inventory-31; QOL: quality of life.

Table 2
The severity of anxiety and depression in caregivers of adult PWE ($n = 131$).

Anxiety severity	HAM-A score	N (%)
No anxiety	0–6	90 (68.70%)
Possible anxiety	7–13	18 (13.74%)
Probable anxiety	14–20	10 (7.63%)
Definite anxiety	21–29	11 (8.40%)
Severe anxiety	>29	2 (1.53%)
Depression severity	HAM-D score	N (%)
No depression	0–6	87 (66.41%)
Mild depression	7–16	30 (22.90%)
Moderate depression	17–24	12 (9.16%)
Severe depression	>24	2 (1.53%)

PWE: patient with epilepsy; HAM-A: the Hamilton Anxiety Scale; HAM-D: the Hamilton Depression Scale.

3.3. Correlation analysis of demographic characteristics and caregiver psychological status with adult PWE QOL

Correlations between demographic characteristics and caregiver psychological status with adult PWE QOL are shown in Table 2. Caregiver anxiety was significantly correlated with poorer adult PWE QOL in the QOLIE-31 total score ($r = -0.178$, $p = 0.042$) and four subscales: seizure worry ($r = -0.286$, $p = 0.001$), overall quality of life ($r = -0.240$, $p = 0.006$), emotional wellbeing ($r = -0.186$, $p = 0.033$), and energy/fatigue ($r = -0.203$, $p = 0.020$). Meanwhile, caregiver depression was strongly correlated with poorer adult PWE QOL in the QOLIE-31 total score ($r = -0.294$, $p = 0.001$) and in all subscales: seizure worry ($r = -0.294$, $p = 0.001$), overall quality of life ($r = -0.183$, $p = 0.036$), emotional wellbeing ($r = -0.277$, $p = 0.001$), energy/fatigue ($r = -0.301$, $p = 0.000$), cognitive ($r = -0.260$, $p = 0.003$), medication effects ($r = -0.210$, $p = 0.016$), and social functions ($r = -0.188$, $p = 0.031$).

Age at seizure onset ($r = 0.209$, $p = 0.017$), epilepsy duration ($r = 0.175$, $p = 0.045$), and adult PWE have only a single caregiver($r = 0.187$, $p = 0.038$) had a significant correlation with the social function subscale. Adult PWE with female caregivers had a significant correlation with the emotional wellbeing ($r = 0.180$, $p = 0.039$) and energy/fatigue ($r = 0.199$, $p = 0.023$) subscales. Number of AEDs, caregivers' age, and caregiver relationship with patients had no correlation with adult PWE QOL.

3.4. Stepwise multiple linear regression analysis on QOL in adults PWE

The QOLIE-31 and subscales were regarded as dependent variables, and the demographic characteristics of patients and their caregivers, as well as the HAM-A and HAM-D scores of caregivers, were added into the stepwise multiple linear regression model as independent predictors. The results of stepwise multiple linear regression for QOLIE total score and seven subscales are presented in Table 3. The stepwise regression for the total scores produced a two-variable model ($R^2 = 0.116$, $F = 8.359$, $p < 0.001$), including caregiver depression ($B = -0.387$, $\beta = -0.293$, $p = 0.001$) and age at seizure onset ($B = 0.226$, $\beta = 0.171$, $p = 0.042$). Caregiver depression symptoms were independent predictors for five of the seven subscales, which were seizure worry ($R^2 = -0.455$, $\beta = -0.300$, $p = 0.000$), emotional wellbeing ($R^2 = -0.473$, $\beta = -0.273$, $p = 0.001$), energy/fatigue ($R^2 = -0.529$, $\beta = -0.301$, $p = 0.000$), cognitive ($R^2 = -0.439$, $\beta = -0.260$, $p = 0.003$), and medication effects ($R^2 = -0.307$, $\beta = -0.216$, $p = 0.012$).

Caregiver anxiety was an independent predictor for the subscales of overall quality of life ($B = -0.287$, $\beta = -0.240$, $p = 0.006$). Seizure severity was an independent predictor for the subscales of seizure worry ($R^2 = 4.704$, $\beta = 0.204$, $p = 0.014$) and medication effects ($R^2 = 4.353$, $\beta = 0.202$, $p = 0.018$). (See Table 4.)

4. Discussion

Psychiatric comorbidities, such as anxiety and depression, are common in patients with epilepsy and significantly impact epilepsy treatment and QOL [15,30,31]. Furthermore, psychiatric comorbidities in parental caregivers are significantly related to the QOL in child and adolescent patients [32–34]. The present study adds to this literature by demonstrating that, independent of patient and family factors, caregiver psychopathology, especially depression, has a significant association with QOL in adult PWE. These findings highlight the importance of addressing caregiver psychiatric comorbidities in not only child PWE, but also adult PWE.

In our study, we found that caregiver anxiety and particularly depression were significantly related to poorer QOL in adults PWE. Analyses showed that caregiver depression and age at seizure onset were independent predictors for QOL in adult PWE. Other demographic characteristics, such as epilepsy duration, seizure severity, having a female caregiver, and whether or not the PWE had a single caregiver correlated with several QOL subdomains in adult PWE. Number of AEDs, caregiver

Table 3
The correlation analysis of variables associated with QOL in adults PWE ($n = 131$).

		Seizure worry	Overall QOL	Emotional wellbeing	Energy/fatigue	Cognitive	Medication effects	Social function	QOLIE-31 total score
Age at seizure onset	r	0.164	0.139	0.051	0.007	0.133	0.144	0.209	0.172
	p-value	0.062	0.113	0.565	0.933	0.131	0.102	**0.017**	**0.049**
Epilepsy duration	r	0.009	−0.070	0.089	0.072	−0.033	0.175	0.029	0.021
	p-value	0.920	0.424	0.312	0.417	0.706	**0.045**	0.746	0.811
Number of AEDs	r	−0.005	−0.149	−0.073	−0.031	−0.114	−0.058	−0.107	−0.113
	p-value	0.956	0.089	0.407	0.729	0.194	0.514	0.223	0.200
Seizure severity	r	0.151	0.152	0.111	0.103	0.004	0.203	0.138	0.130
	p-value	0.086	0.083	0.206	0.241	0.961	**0.020**	0.116	0.139
Caregivers age	r	−0.097	−0.063	−0.058	−0.073	−0.095	−0.152	−0.056	−0.092
	p-value	0.269	0.476	0.513	0.404	0.280	0.083	0.522	0.297
Caregivers sex	r	0.032	0.105	0.180	0.199	0.152	0.062	0.089	0.151
	p-value	0.715	0.232	**0.039**	**0.023**	0.083	0.479	0.311	0.086
Relationship to patients	r	0.070	0.107	0.160	0.158	0.027	0.010	0.131	0.100
	p-value	0.428	0.226	0.068	0.071	0.759	0.909	0.135	0.254
Single caregiver	r	0.082	0.102	0.081	0.081	0.074	0.021	0.187	0.087
	p-value	0.350	0.246	0.359	0.355	0.403	0.808	**0.033**	0.321
Caregivers anxiety	r	−0.286	−0.240	−0.186	−0.203	−0.169	−0.092	−0.036	−0.178
	p-value	**0.001**	**0.006**	**0.033**	**0.020**	0.053	0.297	0.680	**0.042**
Caregivers depression	r	−0.294	−0.183	−0.277	−0.301	−0.260	−0.210	−0.188	−0.294
	p-value	**0.001**	**0.036**	**0.001**	**0.000**	**0.003**	**0.016**	**0.031**	**0.001**

QOL: quality of life; AEDs: antiepileptic drugs; the boldface p-values are significant at $\alpha < 0.05$.

Table 4
The stepwise multiple linear regression model analysis.

	B[a]	Std. Error	β[b]	p-Value
Seizure worry				
Caregivers depression	−0.455	0.124	−0.300	0.000
Seizure severity	4.704	1.889	0.204	0.014
Age at seizure onset	0.274	0.124	0.180	0.030
Overall quality of life				
Caregivers anxiety	−0.287	0.102	−0.240	0.006
Emotional wellbeing				
Caregivers depression	−0.473	0.145	−0.273	0.001
Relationship to patient	4.070	2.020	0.169	0.046
Energy/fatigue				
Caregivers depression	−0.529	0.148	−0.301	0.000
Cognitive				
Caregivers depression	−0.439	0.144	−0.260	0.003
Medication effects				
Caregivers depression	−0.307	0.120	−0.216	0.012
Seizure severity	4.353	1.822	0.202	0.018
Social function				
Age at seizure onset	0.414	0.155	0.224	0.009
Caregivers depression	−0.356	0.155	−0.193	0.023
Seizure severity	4.984	2.360	0.178	0.037
QOLIE-31 total score				
Caregivers depression	−0.387	0.110	−0.293	0.001
Age at seizure onset	0.226	0.110	0.171	0.042

[a] B is the unstandardized regression coefficient, represents the association between the predictor and outcome variable.

[b] β is the standardized regression coefficient, illustrates a comparison of the effect of different predictors.

age, and caregiver relationship to patients were not found to have a statistically significant association with adult PWE QOL.

In our study, the proportions of caregivers who experienced anxiety and depression symptoms were 31.30% and 33.59%, respectively. The prevalence rate of anxiety and depression in our study is consistent with those from previous studies [35]. Previous studies have reported that the prevalence of anxiety and depressive disorders in PWE to be 20–50% [6,36,37], and a meta-analysis revealed that major depressive disorder affects 21.9% of patients in epilepsy clinics [38]. A previous study has shown that decreased activity of serotonin, norepinephrine, dopamine, and GABA facilitate the kindling process of seizure foci, and the decrease of these neurotransmitters is a pivotal pathogenic mechanism of depressive disorders (DDs), which indicated that DDs and epilepsy may share common pathogenic mechanisms that facilitate the occurrence of one in the presence of the other [39]. There have been other studies indicated that genetic background contributes substantively to the comorbidity of anxiety and depression with audiogenic seizures propensity [40]. In this study, we found that the prevalence rate of anxiety and depression symptoms in caregivers of PWE were similar to those found in PWE, which indicates that caregivers of PWE are under similar pressure and experiencing psychological difficulties comparable to those of patients. With this in mind, clinicians should not only focus on psychological problems in adult PWE but also pay more attention to psychological problems experienced by their caregivers.

Previous studies shown that, in caregivers of child and adolescent PWE, 21–47% of the parents suffer anxiety symptoms, while 33–55% of the parents suffer depression symptoms [9,41]. Our study showed similar depression and anxiety rates in the caregivers of adult PWE. The vast majority of former studies have focused on parents as caregivers of child and adolescent PWE. Some previous studies focused on parental anxiety and depression in children and young people who underwent surgery [42,43]. While in this study, we illustrated that the caregivers of adults PWE suffered similar psychological problems as those of child and adolescent caregivers. This topic has been ignored for a long period.

In our study, we showed that caregiver depression is widely related to poorer QOLIE across all subscales and the QOLIE-31 total score. Moreover, in the regression analysis, caregiver depression was an independent predictor for the QOLIE-31 total score and for five of the subscale scores (seizure worry, emotional wellbeing, energy/fatigue, cognitive, and medication effects). Very few studies have concentrated on the caregivers of adult PWE, while several former studies have reported that depression in caregivers is associated with low QOL in child and adolescent PWE, which were consistent with the results of our study [12,36,44]. In our study, caregiver anxiety was related to poorer QOLIE-31 total score and in four of the subscales (seizure worry, overall QOL, emotional wellbeing, and energy/fatigue), while in the regression analysis, caregiver anxiety was an independent predictor for the overall QOL subscale.

Our study shows that seizure severity was an independent predictor for the seizure worry, medication effects, and social function subscales. This means that the more serious seizure severity, the higher the scores for seizure worry, medication effects, and social function subdomains. Two previous studies have found that seizure severity has a relationship with the QOLIE, consistent with the findings from our study [45,46].

In the regression analysis, age at seizure onset was an independent predictor for the total QOL scales, social function, and the seizure worry subscales. Moreover, age at seizure onset was the strongest predictor for the social function subscale. In other words, the older the age at seizure onset, the better social function and QOL were reported to be. As we progress in age, our intelligence increases and social abilities develop. Epilepsy, especially the refractory epilepsy syndromes, can induce brain injury, even mental retardation. Therefore, seizure onset at an older age allows our intelligence and social function to develop before the brain damage may be sustained, and therefore, enable patients to embrace a better QOL.

Our data illustrate that adult PWE with female caregivers have better emotional wellbeing and energy/fatigue scores than those with male caregivers. A previous study has reported that parental gender has no significant association with the QOL in pediatric PWE [47]. Parents tend to pay similar attention to their children but female family members tend to be gentler, thoughtful, and more comprehensive. In our study, the caregivers were not only the parents of patients, but also other relations, including spouse and offspring. This may account for these different outcomes. We also found that adult PWE with more than one caregiver had better social functions than those with a single caregiver. An old Chinese proverb says that “there is strength in numbers”; thus, a greater number of caregivers may take better care of the patient.

Finally, a major limitation of our study is that it was conducted in a tertiary hospital. Patients in our epilepsy center were probably more severe than those in primary hospitals. Furthermore, data on medications for anxiety or depression as control group were lacking, which could be considered in further study.

5. Conclusion

Caregivers of adult PWE are at high risk of experiencing anxiety and depression. Caregiver psychological status, especially caregiver depression and age at seizure onset in patients were independent predictors for poorer QOL in adult PWE. Thus, we suggest that clinicians pay more attention to the psychological status of caregivers, especially in relation to depression symptoms, in order to provide further professional advice and medication by way of intervention to benefit caregivers and to improve adult PWE QOL.

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Conflict of interest

The authors do not report any conflict of interest.

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