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Original Article

# Risk factors for sleep disturbances and low quality of life in adolescents with epilepsy

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## *Abstract*

***Background*** Epilepsy impacts health-related quality of life (QoL) and increases sleep disturbances. Duration of medication use, recurrent seizures, number of anti-epileptic drugs (AEDs), abnormal electroencephalography (EEG), and comorbidities are factors that might affect sleep and QoL in adolescents with epilepsy.

***Objective*** To analyze risk factors related to sleep disturbances and QoL in adolescents with epilepsy.

***Methods*** This analytical-observational study was performed in epilepsy outpatients treated between January -June 2024, of adolescent age, and had used AEDs for more than a year. Quality of life was evaluated using the *Pediatric Quality of Life Inventory*™ (PedsQL™) - Epilepsy Module, and sleep disturbances were evaluated using the *Sleeping Disturbance Scale for Children* (SDSC) questionnaire. Fisher's and Kolmogorov-Smirnov analyses were performed along with logistic regression for multivariate analysis.

***Results*** Forty-eight patients participated in this study. Subjects' mean age was 12.69 (SD 2.4) years and 54.2% of subjects were male. Mean duration of medication use was 2 years with the minimum interval of the last seizure episode occurring 1 week before observation. More than half of the patients (60.4%) had abnormal EEGs. Most patients were treated with monotherapy AED (81.3%). Seventy five percent of patients had low QoL and 47.9% had sleep disturbances. In multivariate analysis, adolescents with abnormal initial diagnosis EEGs had 19.1 times higher risk of sleep disturbances (95%CI 3.3 to 110.4; P= 0.001) than those with normal EEGs. Among patients with abnormal EEGs, sleep disturbances increase the risk of low QoL (OR 1.6; 95%CI 0.93 to 2.73; P=0.015) .

***Conclusion*** Abnormal EEG was a significant risk factor for sleep disturbances and low QoL in adolescent epilepsy patients.

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***Keywords:*** *epilepsy; quality of life; sleep disturbances; pedsQL; SDSC*

Epilepsy is a chronic disease that requires regular taking of medications with many side effects.[1] The target of therapy in epilepsy are seizure control with minimal adverse effects.[1] However, epilepsy and AEDs also can impact children's health-related quality of life (QoL).[1-4] Limitations related to their illnesses influence the life function of children with epilepsy, which can be exacerbated during adolescence.[2]

Prolonged duration and number of AEDs used concurrently may lead to decreased attention span and sleep quality in epilepsy patients.[5] Complexity of the etiology, type of seizure, and comorbidities were also reportedly related to difficulties having good quality sleep that led to low QoL.[1,3,6] Although previous studies have investigated the relationship between sleep and epilepsy in children, the association between sleep and epilepsy must be further evaluated to analyze factors related to sleep disturbances and QoL in adolescents with epilepsy.

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## Methods

We performed an observational study between January - June 2024 of adolescent epilepsy outpatients aged 10-18 years and who used AEDs for more than a year. Epilepsy diagnosis was established by history of seizures, clinical manifestation, physical examination, standard EEG, and brain CT scan. Quality of life was evaluated using the PedsQL$^{TM}$ - Epilepsy Module and sleep disturbances were evaluated using the the *Sleeping Disturbance Scale for Children* (SDSC) questionnaire.

The possible risk factors for outcomes were collected from medical records: age classification (early, middle, late), duration of treatment (<3 years, >3 years), seizure period within 1 year (controlled, uncontrolled), type of therapy (monotherapy, polytherapy), monotherapy using valproic acid (present, absent), type of seizure (generalized, focal), epilepsy syndrome (idiopathic, symptomatic), first EEG result (normal, abnormal), and comorbidities (present, absent). Age classification was defined as early for subjects aged 10-14 years, middle for those 15-16 years, and late for those 17-18 years. Controlled seizure was defined as being seizure-free within the previous one year.

The subjects were also grouped into idiopathic or symptomatic groups. The symptomatic group had a definite cause for epileptic seizures or had developmental delay without a definite cause or etiology, which was called cryptogenic. The idiopathic group had no cause for epilepsy, other than a possible hereditary predisposition.[7] The QoL was defined as low for PedsQLTM score <70%. Sleep disturbance was defined as a total SDSC questionnaire score of >39.

Data were analyzed with Fisher's and Kolmogorov-Smirnov tests, as well as and logistic regression. The odds ratios (OR) and 95% confidence intervals (CI) are reported.

## Results

A total of 48 adolescents with epilepsy (26 boys and 22 girls) were included in this study. Six subjects (12.5%) were early adolescents, 30 (62.5%) were middle adolescents, and 12 (25%) were late adolescents. Twelve subjects (25%) had treatment >3 years, 35 (72.9%) had uncontrolled seizures, 9 (18.8%) had polytherapy, 44 (91.7%) had generalized seizures, 40 (83.3%) had idiopathic epilepsy, and 18 (37.5%) had comorbidities. Thirty-nine subjects used monotherapy, which were valproic acid (72.9%), carbamazepine (4.2%), clobazam (2%), and phenytoin (2%). The comorbidities were obesity (14.5%), cerebral palsy (10.4%), psychiatric problems (6.3%), mild malnutrition (4.2%), and acute lymphoblastic leukaemia (2.1%).

Most subjects had low QoL (75%). The most common problems were in executive function (97.2%), followed by cognitive function (91.7%), impact on their daily life (94.4%), sleep/fatigue (66.7%) and mood behavior (66.7%) (**Table 1**). The SDSC questionnaire revealed that all subjects with sleep disturbances had problems starting/maintaining sleep duration, sleep-wake transition, and excessive somnolence (**Table 2**).

Compared to the group with normal EEG result at the time of initial diagnosis, adolescents who then had abnormal EEGs had significantly higher risk of low QoL (OR 7.8; 95%CI 1.7 to 34.8; P=0.006) and sleep disturbances (OR 22.3; 95%CI 4.2 to 119.2; P<0.001). Those with comorbidities also had a significantly higher risk of low QoL (OR 1.6; 95%CI 1.2 to 2.2; P=0.002) and sleep disturbances (OR 5.2; 95%CI 1.5 to 18.7; P=0.016). Bivariate analysis revealed that polytherapy increased risk of sleep disturbances (OR 0.08; 95%CI 0.009 to 0.7; P=0.009), but was did not significantly associated with QoL. Subjects who had undergone treatment for ≤ 3 years showed lower QoL (54.1%) (**Table 3**).

Multivariate analysis revealed that abnormal EEG at the time of initial diagnosis was not a significant risk factor for low QoL (OR 0.2; 95%CI 0.038-to 1.044; P=0.032) (**Table 4**), however it is increasing risk for sleep disturbances (OR 19.1; 95%CI 3.3 to 110.4; P=0.00) (**Table 4**). But comorbidities and therapy type did not retain their statistical significance, with regards to sleep disturbances.

Considering the limited sample size, we used matching variable analysis for the abnormal EEG result group (n=21) to determine the risk of low QoL in adolescent with sleep disturbances. It revealed that in abnormal EEG group, patients with sleep disturbances had a significantly higher risk of

**Table 1**. Characteristics of subjects' QoL assessed by PedsQLTM

| Quality of life | (N=48) |
|---|---|
| Normal, n (%) | 12 (25.0) |
| Low, n (%) | 36 (75.0) |
| Impact | 34 |
| Cognitive function | 33 |
| Sleep/fatigue | 24 |
| Executive function | 35 |
| Mood behavior | 24 |

**Table 2**. Characteristics of sleep disturbances in subjects assessed by SDSC

| The SDSC results | (N=48) |
|---|---|
| No disturbances, n (%) | 25 (52.1) |
| Sleep disturbances, n (%) | 23 (47.9) |
| Initiating/maintaining | 23 |
| Breathing disorder | 9 |
| Disorders of arousal | 12 |
| Sleep-wake transition | 23 |
| Excessive somnolence | 23 |
| Hyperhydrosis | 19 |

**Table 3**. Analysis of possible risk factors for low QoL and sleep disturbances (N=48)

| Characteristics | Quality of life | | | | Sleep disturbances | | | |
|---|---|---|---|---|---|---|---|---|
| | Low (n=36) | Normal (n=12) | OR (95%CI) | P value | Yes (n=23) | No (n=25) | OR (95%CI) | P value |
| Sex, n | | | | | | | | >0.05 |
| Male | 18 | 8 | 0.5 | >0.05 | 13 | 13 | 1.2 | |
| Female | 18 | 4 | (0.1 to 1.9) | | 10 | 12 | (0.4 to 3.8) | |
| Age, n | | | | | | | | |
| Early | 5 | 1 | | | 11 | 19 | | |
| Middle | 21 | 9 | | >0.05 | 8 | 4 | | >0.05 |
| Late | 10 | 2 | | | 4 | 2 | | |
| Duration, n | | | | | | | | |
| ≤3 years | 26 | 10 | 0.52 | >0.05 | 16 | 20 | 0.5 | >0.05 |
| >3 years | 10 | 2 | (0.09 to 2.8) | | 7 | 5 | (0.1 to 2.1) | |
| Seizure period, n | | | | | | | | |
| Uncontrolled | 26 | 9 | 1.1 | >0.05 | 17 | 18 | 0.9 | >0.05 |
| Controlled | 10 | 3 | (02 to 5.1) | | 6 | 7 | (0.2 to 0.3) | |
| Type of therapy, n | | | | | | | | |
| Polytherapy | 9 | 0 | 0.7 | >0.05 | 8 | 1 | 0.08 | 0.009 |
| Monotherapy | 27 | 12 | (0.6 to 0.9) | | 15 | 24 | (0.009 to 0.7) | |
| VPA Monotherapy | | | | | | | | |
| Present | 24 | 11 | 0.18 | >0.05 | 4 | 22 | 0.17 | 0.022 |
| Absent | 12 | 1 | (0.02 to 1.57) | | 19 | 3 | (0.04 to 0.76) | |
| Type of seizure, n | | | | | | | | |
| Focal | 4 | 0 | 0.9 | >0.05 | 3 | 1 | 3.6 | >0.05 |
| Generalized | 32 | 12 | (0.7 to 0.9) | | 20 | 24 | (0.4 to 37.4) | |
| Epilepsy syndrome, n | | | | | | | | |
| Idiopathic | 30 | 10 | 1 | >0.05 | 17 | 23 | 0.3 | >0.05 |
| Symptomatic | 6 | 2 | (0.1to 0.7) | | 6 | 2 | (0.04 to 1.4) | |
| EEG results, n | | | | | | | | |
| Abnormal | 26 | 3 | 7.8 | 0.006 | 21 | 8 | 22.3 | 0.000 |
| Normal | 10 | 9 | (1.7 to 34.8) | | 2 | 17 | (4.2 to 119.2) | |
| Comorbidities, n | | | | | | | | |
| Present | 18 | 0 | 1.6 | 0.002 | 13 | 5 | 5.2 | 0.016 |
| Absent | 18 | 12 | (1.2 to 2.2) | | 10 | 20 | (1.5 to 18.7) | |

developing low QoL (OR 1.6; 95%CI 0.93 to 2.73; P=0.015) when compared to subject with abnormal EEG and without sleep disturbance.

## Discussion

In our study, parental interviews using PedsQL™-Epilepsy Module and the SDSC questionnaire revealed that 75% of adolescents with epilepsy had

**Table 4**. Multivariate logistic regression to identify risk factors

| Risk factors | Variables | OR (95%CI) | P value |
|---|---|---|---|
| Quality of life | Abnormal EEG | 0.2 (0.038 to 1.044) | 0.032 |
| | Comorbidities | 0.0 (0.00 to - ) | 0.998 |
| Sleep disturbance | Abnormal EEG | 19.1 (3.3 to 110.4) | 0.001 |
| | Comorbidities | 2.8 (0.5 to 14.9) | 0.220 |
| | Type of therapy | 0.1 (0.09 to 1.34) | 0.084 |
| | Valproic Acid | 0.6 (0.06 to 6.86) | 0.740 |

low QoL [mean 62.2 (SD 11)] and almost half of them had sleep disturbances.

Previous studies in pediatric population reported that epilepsy impacted physical, emotional, social and occupational function, causing low QoL.[8-10] Longer epilepsy duration, shorter duration of previous seizure episodes, severity, and increased number of AEDs had correlations with low total PedsQLTM-Epilepsy Module results and subdomains.[11]

Our results were similar to those of a previous study in the sub-domains: 87.5% had executive function problems, 77.1% had difficulties in cognitive function, and their physical and social activities were negatively impacted (77.1%). Also, half of them had problems with sleep/fatigue (50%) and mood behaviour (50%).[12]

We focused our study population only on adolescent patients. In our study, low QoL was highest in middle-aged adolescents (43.7%), in contrast to Saudi Arabian study that reported higher QoL score in adolescents compared to children.[3]

Our subjects' mean age was 12.69 (SD 2.4) years. Approximately 75% of our subjects were treated with AEDs for <3 years. Because of our small sample size, the duration of treatment may have not a significant association with QoL.[2,3] However, the result was similar to that of an Egyptian study,[11] in which the duration of epilepsy was not significantly associated with patient QoL, but the percentage of subjects who had undergone treatment for ≤ 3 years showed lower QoL (54.2%).

Sleep disturbances are common in children and adolescents, and the risk increases in those with epilepsy.[13] A study reported a 67.7% prevalence of sleep disturbances in children,[6] which was slightly lower than that of another study by Ong *et al.*[14] In our study, with small sample size, 47.9% of children had sleep disturbances. All subjects with sleep disturbances had problems to initiating sleep or maintaining sleep duration, sleep-wake transition, and had excessive somnolence. Similarly, a previous study reported SDSC sub-domain (initiating sleep or maintaining sleep duration, sleep-wake transition, excessive somnolence) results of 63.2%, 23.8%, 7.9%, respectively.[6] In addition, Furones *et al.*[15] reported 47.7%, 53%, 44.4%, respectively.

A previous multivariate analysis revealed that generalized seizure type increased the risk of sleep disturbances by 5.2 times compared to focal seizure type.[6] Generalized genetic epilepsies and neural sleep pathways share similar thalamocortical networks, therefore, several neurotransmitters that regulate sleep also modulate seizures. Younger age onset of seizures experienced more severe sleep disturbance (P=0.027).[16] However, in our study, age, type of seizure, duration of treatment, and seizure period were not significantly associated with sleep disturbances.

In our study, most patients were treated with monotherapy using valproic acid (VPA) (72.9%). The VPA is capable in altering sleep structures by inhibiting cortical synchrony to reduce seizure frequency. It causes prolonged N1 sleep stage in non-rapid eye movement (NREM), shortened rapid eye movement (REM) sleep, decreased sleep efficiency (SE), increased awakenings, and a reduced number of REM phases, all of which can increase incidence of somnolence/daytime sleepiness.[17]

In our study, abnormal EEG (OR 22.3; 95%CI 4.2 to 119.2; P=0.000), comorbidities (OR 5.2; 95%CI 1.5 to 18.7; P=0.016), polytherapy (OR 0.08; 95%CI 0.009 to 0.7; P=0.009), and VPA use (OR 0.17; 95%CI 0.04 to 0.76; P=0.022) showed significantly increased risk of sleep disturbances in adolescents. Multivariate analysis revealed that abnormal EEG was the only variable associated with increased risk of sleep disturbances, with 19.1 times higher risk compared to patients with normal EEG (95%CI 3.3 to 110.4; P=0.001). Because of the bidirectional relationship of

sleep disturbances and QoL, we specifically analyzed the abnormal EEG group, in 29 subjects with abnormal EEG it was revealed that 26 (89.7%) had low QoL and 21 (72.4%) had sleep disturbances. Patients with abnormal EEG at the time of initial diagnosis with sleep disturbances had a 1.6 times higher risk of developing low quality of life than abnormal EEG of adolescents without sleep disturbances (95%CI 0.93 to 2.73; P=0.015).

There were some limitations in our study. In addition to the small sample size, we did not evaluate some factors that might be related to sleep disturbances such as bed/room sharing, sleep hygiene, history of sleep disturbances, and AED compliance.[15] The strength of our study was that we specifically evaluated quality of life and sleep disturbances in adolescent epilepsy patients.

In conclusion, adolescents with epilepsy are at risk of having sleep disturbances, especially those with abnormal EEG results at the time of initial diagnosis, which can be associated with low quality of life. Therefore, these patients should undergo regular assessments of sleep disturbance to implement early interventions to maximize the quality of life in adolescents with epilepsy. Further study to evaluate the relationship between sleep and QoL in patient with epilepsy is needed, including sleep hygiene and interventions to improve QoL.

## Conflict of interest

None declared.

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