Factors Associated with Caregiver Sleep Quality Related to Children with Rare Epilepsy Syndromes

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Objective To evaluate the impact of pediatric sleep disturbances and night-time seizure monitoring of children with rare epilepsy syndromes on the sleep quality and mental health of caregivers.

Study design A cross-sectional study was conducted using caregiver entered data from the Rare Epilepsy Network on pediatric sleep disturbances and Patient Reported Outcomes Measurement Information System measures for caregiver fatigue, sleep disturbance, sleep-related impairment, depression, anxiety, companionship, and cognition. Logistic regression was used to examine associations between risk factors and caregiver sleep quality.

Results Non-Hispanic white mothers comprised 83% of the 742 respondents in this study. After adjusting for covariates, difficulty falling asleep, excessive daytime sleepiness, frequent night-time awakenings, and very restless sleep in children were associated with fatigue (aOR 95% CI, 1.5-2.2), sleep-related disturbance (aOR 95% CI, 1.7-2.6) and sleep impairment (aOR 95% CI, 1.5-2.4) in caregivers. Caregiver anxiety (aOR 95% CI, 3.6-6.0) and depression (aOR 95% CI, 2.8-6.0) were also highly associated with their fatigue and sleep quality, whereas companionship (aOR 95% CI, 0.3-0.4) and higher caregiver cognition (aOR 95% CI, 0.1-0.2) were protective. In addition, sharing a room or bed or using methods that require listening for seizures were significantly related to sleep disturbance and fatigue in the caregivers.

Conclusions In rare epilepsies, pediatric sleep disturbances and night-time seizure monitoring are significantly associated with caregiver fatigue and poor sleep quality. In addition to the intense caregiving needs of children with rare epilepsies, fatigue and poor sleep quality in caregivers may contribute to or result from mental health problems. *(J Pediatr: X 2020;2:100021)*.

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Pediatric epilepsy, a common neurologic disorder,[1,2] is associated with substantial burdens on both affected children and their caregivers.[3,4] Similar to other childhood chronic illnesses,[5,6] altered sleep patterns, such as frequent night-time checking and co-sleeping, have been reported in caregivers of children with epilepsy.[7-9] Individuals with rare epilepsies (eg, Dravet syndrome, Lennox-Gastaut syndrome) may suffer from higher risks for psychiatric disorders,[10,11] somatic disorders, and drug-resistant seizures[12,13] compared with the general epilepsy population, which may further alter a caregiver's sleep pattern and impair their sleep quality.

Sleep deprivation is among the most common seizure triggers in those with epilepsy. Nocturnal seizures disrupt sleep and increase daytime drowsiness in patients, also increasing the risk of daytime seizures. Nocturnal seizures are a risk factor for sudden unexpected death in epilepsy (SUDEP).

For children aged 0-17 years who live with a rare epilepsy, SUDEP is estimated to account for at least 0.22 deaths per 1000 patient-years,[14] which may underestimate the incidence of SUDEP.[15,16] Of note, the incidence of SUDEP can be substantially higher in children with rare epilepsies (eg, Dravet syndrome) compared with the general epilepsy population,[17,18] possibly owing to refractory seizures and medical complexity. It has been consistently reported that SUDEP occurs much more often at night than in daytime,[19] which may be related to the relatively poor supervised environment at night and the severity of nocturnal seizures.[20,21] Nocturnal monitoring has been suggested to have a protective effect against SUDEP,[22,23] although the data are limited to 1 case control study. In addition to monitoring for nocturnal seizures to record frequency, providing necessary

PROMIS	Patient-Reported Outcomes Measurement Information System
REN	Rare Epilepsy Network
SUDEP	Sudden unexpected death in epilepsy

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*List of organizations of the Rare Epilepsy Network is available in the **Appendix**.

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interventions (such as a rescue medication), or comforting the child, caregivers who are aware of SUDEP may be more inclined to monitor their children during sleep, which may in turn impair their own sleep quality.

Nonetheless, compared with extensive investigations on sleep disorders in individuals with epilepsy, caregiver sleep quality is understudied. We therefore conducted this cross-sectional study to examine risk factors for caregiver sleep disturbance, fatigue, and sleep-related impairment, focusing on children with rare epilepsies. Based on current understanding of nocturnal seizure burden, seizure worry, and SUDEP, we hypothesized a priori that caregiver perceived mental burden and strategies of nocturnal monitoring would negatively affect their sleep. In addition, we examined the association between pediatric sleep disturbances and caregiver sleep quality.

Methods

This study used a cross-sectional design in examining survey data from the Rare Epilepsy Network (REN). The REN was initiated by members of the Epilepsy Leadership Council to establish a registry of individuals with rare epilepsy syndromes or rare disorders with a high incidence of epilepsy. After informed consent was obtained, data in the REN were collected from caregivers of affected individuals or from cognitively able affected adults at both baseline and follow-up visits. In this study, we used only the caregiver data from 742 parents and grandparents of affected individuals who were living in the same household. Data included came from the REN survey domains of child and caregiver demographic information, seizure characteristics, child comorbid psychiatric and somatic conditions, and caregiver quality of life at baseline. Outcome variables (caregiver fatigue, sleep disturbance, and sleep impairment) were reported by the 742 eligible caregivers at baseline, which served as the basis of our analysis. This study was approved by the Institutional Review Boards of Columbia University and RTI International.

Patient-Reported Outcomes Measurement Information System

The Patient-Reported Outcomes Measurement Information System (PROMIS)[24,25] is a set of self- or proxy-completed measures that evaluates quality of life in adults and children. The REN assessed aspects of the caregiver's quality of life using PROMIS Short Forms v1.0–Anxiety 8a, Depression 8a, Companionship 8a, Fatigue 8a, Sleep Disturbance 8a, and Sleep Related Impairment 8a. Sleep disturbance evaluates the quality of sleep during the night. Sleep impairment evaluates the quality of sleep on daytime functioning. Raw PROMIS scores were converted into T-scores for standardization to the general US population using the PROMIS scoring guidelines. Specifically, PROMIS T-scores were designed with a mean of 50 and a SD of 10. Higher scores represent more of the concept being measured. Clinically actionable thresholds of greater than 60 for PROMIS measures for depression, anxiety, and sleep disturbance have been used by clinical providers.[26]

We evaluated caregiver sleep quality based on the PROMIS fatigue, sleep disturbance, and sleep-related impairment instruments.[27] These instruments have been validated.[27,28] The PROMIS sleep disturbance instruments were designed to measure self-reported perceptions of sleep quality, sleep depth, and restoration associated with sleep over the past seven days in adults.[29,30] The PROMIS sleep-related impairment instrument was designed to assess self-reported perceptions of alertness and tiredness during usual waking hours, and perceived functional impairment during wakefulness associated with sleep problems or impaired alertness over the past seven days in adults. The PROMIS fatigue instruments assess self-reported perceptions from mild feelings of tiredness to an overwhelming, debilitating sense of exhaustion decreasing one's ability to execute daily activities and normal function.[31]

Risk Factors

Three clusters of risk factors for caregiver fatigue, sleep disturbance, and sleep-related impairment were examined in this study. The first cluster included pediatric sleep disturbance (symptom or condition related to sleep, difficulty falling asleep, excess daytime sleepiness, frequent night-time awakenings, and very restless sleep), and nocturnal seizure. The second cluster consisted of nocturnal monitoring strategies used by caregivers, including sharing a bed or room with someone, audio monitor use, a seizure alert device use, a seizure response dog use, leaving the door open during sleep, watching or checking the child frequently during the night, and doing nothing to monitor for seizures. The third cluster included caregiver mental and social health conditions, including anxiety, depression, cognition, and companionship (ie, perceived availability of someone with whom to share delightful activities).

Statistical Analyses

Caregiver's characteristics and distributions of risk factors were presented as frequencies (percentages). Binary variables of caregiver's anxiety, depression, cognition, companionship, fatigue, sleep disturbance and sleep-related impairment were created using a cutoff PROMIS T-score of 60 (1 SD above the mean, with T-scores of >60 coded as yes and those ≤60 coded as no). Bivariate and multivariable logistic regressions were used to examine the associations between risk factors and caregiver fatigue, sleep disturbance and sleep-relation impairment. In multivariable logistic regression models, the child's age and caregiver's sex, ethnicity, marital status, educational level, and annual household income were included as covariates. Two-tailed P values of less than .05 were considered statistically significant for all tests. All analyses were performed using SAS 9.4 (SAS Institute, Cary, North Carolina).

Table I. Demographics of 742 caregivers at baseline

Demographic characteristics	N (%)
Age, years, median (range)	40 (22-79)
Sex	
Male	60 (8.1)
Female	682 (91.9)
Race	
American Indian or Alaskan Native	4 (0.5)
Asian	15 (2.0)
Black or African American	9 (1.2)
Native Hawaiian or Pacific Islander	0
White or Caucasian	675 (91.0)
Mixed/other	34 (4.6)
Missing	5 (0.7)
Ethnicity	
Hispanic	61 (8.2)
Non-Hispanic	677 (91.2)
Missing	4 (0.5)
Education	
High school/GED or below	55 (7.4)
Some college	200 (27.0)
Bachelor's degree	269 (36.3)
Post graduate school	214 (28.8)
Missing	4 (0.5)
Marital status	
Single, divorced, separated, widowed	105 (14.2)
Married, domestic partnership	634 (85.4)
Missing	3 (0.4)
Household income	
<$50 000	164 (22.1)
$50 000-$100 000	226 (30.5)
>$100 000	274 (36.9)
Missing	78 (10.5)
Employment	
Employed (full or part time)	447 (60.2)
Unemployed (including retired, disabled)	253 (34.1)
Paid caregiver	25 (3.4)
Student/other	15 (2.0)
Missing	2 (0.3)
Relationship to affected person	
Mother	675 (91.0)
Father	60 (8.1)
Grandmother	7 (0.9)

Table II. Demographics and epilepsy characteristics of 742 affected persons at baseline

Child characteristics	N (%)
Age, years, median (range)	8.6 (0.3-49.8)
Age group	
0-23 months	84 (11.3)
2-5 years	182 (24.5)
6-9 years	142 (19.1)
10-14 years	152 (20.5)
≥15 years	182 (24.5)
Primary epilepsy syndrome	
Aicardi syndrome	59 (8.0)
CDKL5 mutation	18 (2.4)
Doose syndrome	42 (5.7)
Dravet syndrome	100 (13.5)
Dup15q mutation	36 (4.9)
Hypothalamic hamartoma	40 (5.4)
West syndrome	38 (5.1)
Lennox Gastaut syndrome	103 (13.9)
Ohtahara syndrome	7 (0.9)
PCDH19 mutation	26 (3.5)
Phelan McDermid syndrome	26 (3.5)
SCN8A	17 (2.3)
SYNGAP mutation	11 (1.5)
Tuberous sclerosis complex	123 (16.6)
Other encephalopathy or genetic mutation	59 (8.0)
Other rare syndrome/diagnosis*	37 (5.0)
Total seizure in previous 6 months	
None	100 (13.5)
1-5	75 (10.1)
6-24	80 (10.8)
25-100	109 (14.7)
101-200	70 (9.4)
>200	245 (33.0)
Missing	63 (8.5)
Current seizure types (not mutually exclusive)	
Tonic-clonic, myoclonic, and/or tonic	497 (67.0)
Atonic (drop)	264 (35.6)
Infantile/juvenile spasms	257 (34.6)
Focal (complex or simple partial)	447 (60.2)
Gelastic (seizure with laughing or crying)	187 (25.2)
Missing	126 (17.0)
Rescue medication at home	
Yes	566 (76.3)
No	154 (20.8)
Missing	22 (3.0)
Nocturnal seizures	
Always or sometimes	514 (69.3)
Rarely, never, or don't know	228 (30.7)
Nocturnal seizure monitoring	
Audio monitor (with or without video)	214 (28.8)
Monitoring device with an alert	93 (12.5)
Share a bed with someone	121 (16.3)
Share a room with someone	62 (8.4)
Door left open	108 (14.6)
Frequent checks or watching at bedside	19 (2.6)
Seizure response dog	2 (0.3)
No monitoring	113 (15.2)
Missing	10 (1.3)

*Angelman (n = 2), congenital bilateral perisylvian syndrome (n = 2), electrical status epilepticus in slow wave sleep (n = 5), Jeavons (n = 3), KCNQ2 (n = 2), Landau Kleffner (n = 4), lissencephaly (n = 1), progressive or other myoclonic epilepsy (n = 4), Rasmussen's encephalopathy (n = 2), Ring 14 (n = 3), Ring 20 (n = 2), SCN2A (n = 3), SLC13A5 (n = 2), Unverricht Lundborg (n = 2).

Results

Our final analysis included 742 caregivers (median age, 40 years; range, 22-79 years). Thirty-two respondents were excluded because they did not live with the affected person (n = 28) or they were not a parent or grandparent of the affected person (2 spouses, 1 daughter, 1 niece). The majority of caregivers included were mothers (91.0%) and non-Hispanic white (85.3%). In terms of marital status, 85.4% of caregivers were married or had a domestic partner. Of note, more than one-third of caregivers were unemployed. Almost one-fourth of caregivers had an annual household income of less than $50 000, and 36.9% of caregivers had an annual household income of more than $100 000 (Table I).

The children with rare epilepsies had a mean age of 8.6 years, with 84 (11.3%) under 2 years of age at the time of enrollment and were diagnosed with more than 30 different epilepsy-related syndromes, disorders, or gene mutations (Table II). The most common syndromes were tuberous sclerosis complex (16.6%), Lennox Gastaut syndrome (13.9%), Dravet syndrome (13.5%), and Aicardi syndrome (8.0%). Seizure burden in the children was significant, with more than 42.4% having more than 100 seizures in the 6 months before enrollment. Tonic-clonic, myoclonic, and tonic were the primary seizure types in 497

(67.0%), and 566 (76.3%) had a rescue medication at home that parents could use to stop or attenuate prolonged seizures (Table II).

Risk Factors

It is notable that 69.3% of pediatric patients (n = 514) were affected by nocturnal seizures sometimes or always. Caregivers used a variety of methods to monitor for nocturnal seizures, the most common being using an audio monitor (28.8%), someone sharing a bed with the affected person (16.3%), leaving the door open to listen for seizures (14.6%), and using a monitoring device with an alert (12.5%) (Table II). Among the 84 children under the age of 2 years, the most common monitoring methods were using an audio monitor (32.1%) and sharing a room (22.6%). In addition to nocturnal seizures, there was a high prevalence of reported frequent night-time awakenings (48.8%), difficulties falling asleep (42.7%), and very restless sleep (37.9%) in the affected children (Tables III-V).

Caregiver Fatigue, Sleep Disturbance, and Sleep-Related Impairment

Factors of pediatric sleep disturbance, including symptoms or conditions related to sleep, difficulty falling asleep, excess daytime sleepiness, frequent night-time awakenings, and very restless sleep were significantly associated with caregiver fatigue after adjusting for covariates (Table III; aOR 1.5-2.2). There was no association between pediatric nocturnal seizures and caregiver fatigue. Sharing a room or bed or using a listening method was significantly associated with a 1.7- to 1.9-fold odds for increased caregiver fatigue compared with no night-time monitoring. Watching the child sleep or checking on them frequently was significantly associated with an aOR of 5.3 for increased caregiver fatigue compared with no monitoring. Caregiver anxiety and depression were positively associated with caregiver fatigue (aOR, 6.0; $P < .001$), and caregiver cognition and companionship were inversely associated with caregiver fatigue (aOR, 0.1-0.3; $P < .001$).

Very restless sleep among the children was significantly associated with a 2.6-fold odds (95% CI, 1.9-3.8) for caregiver sleep disturbance and a 2.4-fold odds (95% CI, 1.7-3.4) for caregiver sleep-related impairment after adjusting for covariates. Frequent night-time awakenings in the child were also significantly associated with caregiver sleep disturbance (aOR, 2.0; 95% CI, 1.4-2.9) and caregiver sleep-related impairment (aOR, 1.6; 95% CI, 1.2-2.3). Pediatric symptoms or conditions related to sleep, difficulty falling asleep, and excess daytime sleepiness were also significantly associated with increased risk for caregiver sleep disturbance (aOR, 1.7-1.9) as well as sleep-related impairment (aOR, 1.5-1.7) (Tables IV and V). The presence of pediatric nocturnal seizures was significantly associated with caregiver sleep disturbance (aOR, 1.7; 95% CI, 1.1-2.5) but not sleep-related impairment (Tables IV and V).

Among the methods for monitoring of nocturnal seizures, sharing a bed or room was significantly associated with a 2.8-fold odds (95% CI, 1.5-5.6) and using a method to listen for seizures (audio monitor, alert device or leaving the door open) was significantly associated with a 3.1-fold odds (95% CI, 1.7-5.8) for caregiver sleep disturbance compared with caregivers who did not monitor for nocturnal seizures. Watching the child sleep or checking on them frequently during the night had no association with sleep disturbance. None of the methods for monitoring of nocturnal seizures were

Table III. Logistic regression for risk factors by fatigue T-score

Risk factors	Fatigue T score ≤60, N (%)	Fatigue T score >60, N (%)	N in logistic model	aOR* (95% CI)	Adjusted *P* value
Characteristics of child					
Any sleep condition below	221 (55.4)	202 (67.1)	700	2.0 (1.4-2.7)	**<.001**
Difficulty falling asleep	156 (39.5)	141 (47)	695	1.5 (1.1-2.07)	**.01**
Excess daytime sleepiness	109 (28)	112 (37.8)	685	1.8 (1.3-2.5)	**.001**
Frequent night-time awakenings	173 (43.8)	165 (55.2)	694	1.8 (1.3-2.5)	**<.001**
Very restless sleep	121 (31.1)	138 (47.3)	681	2.2 (1.6-3.1)	**<.001**
Nocturnal seizures	282 (69.1)	222 (71.6)	718	1.3 (0.9-1.8)	.12
Methods for night-time monitoring					
Someone shares a room or bed with the person with epilepsy	91 (22.4)	87 (28.2)	715	1.9 (1.2-3.3)	**.01**
Audio monitor or seizure alert device or leave door open	231 (56.9)	174 (56.3)	715	1.7 (1.1-2.7)	**.03**
Watch or check frequently	5 (1.2)	12 (4.2)	715	5.3 (1.8-17.9)	**.04**
No night-time monitoring	79 (19.5)	35 (11.3)	715	ref	
Caregiver PROMIS scores					
Cognition T score >60	146 (35.4)	20 (6.4)	724	0.1 (0.1-0.2)	**<.001**
Companionship T score >60	133 (32.3)	44 (14.1)	724	0.3 (0.2-0.4)	**<.001**
Depression T score >60	34 (8.2)	101 (32.5)	724	6.0 (3.9-9.6)	**<.001**
Anxiety T score >60	75 (18.2)	176 (56.4)	724	6.0 (4.2-8.7)	**<.001**

P values <.05 are in bold.
*OR adjusted for caregiver sex, ethnicity, education, marital status, and household income, and child's age. Reference group for all OR includes those without the condition/risk factor except for methods for night-time monitoring.

Table IV. Logistic regression for risk factors by sleep disturbance T-score

Risk factors	Sleep disturbance T score ≤60, N (%)	Sleep disturbance T score >60, N (%)	No. in logistic model	aOR* (95% CI)	Adjusted *P* value
Characteristics of child					
Any sleep condition below	288 (56.4)	137 (70.6)	705	1.9 (1.3-2.8)	**<.001**
Difficulty falling asleep	199 (39.2)	100 (52.1)	700	1.7 (1.2-2.5)	**.002**
Excess daytime sleepiness	143 (28.5)	78 (41.5)	689	1.8 (1.3-2.5)	**.002**
Frequent night-time awakenings	224 (44.1)	116 (60.7)	699	2.0 (1.4-2.9)	**<.001**
Very restless sleep	157 (31.4)	103 (55.1)	686	2.6 (1.9-3.8)	**<.001**
Nocturnal seizures	351 (67.1)	156 (77.6)	724	1.7 (1.1-2.5)	**.009**
Methods for night-time monitoring					
Someone shares a room or bed with the person with epilepsy	126 (24.1)	54 (27.1)	721	2.8 (1.5-5.6)	**.002**
Audio monitor or seizure alert device or leave door open	282 (54.0)	126 (63.3)		3.1 (1.7-5.8)	**<.001**
Watch or check frequently	13 (2.5)	5 (2.5)		2.7 (0.7-8.7)	.1
No night-time monitoring	101 (19.4)	14 (7.1)		ref	
Caregiver PROMIS scores					
Cognition T score >60	150 (28.4)	17 (8.4)	730	0.2 (0.1-0.4)	**<.001**
Companionship T score >60	151 (28.6)	26 (12.9)	730	0.4 (0.2-0.6)	**<.001**
Depression T score >60	75 (14.2)	60 (29.7)	730	2.8 (1.9-4.2)	**<.001**
Anxiety T score >60	142 (27.9)	110 (54.5)	730	3.6 (2.5-5.1)	**<.001**

P values <.05 are in bold.
*OR adjusted for caregiver gender, ethnicity, education, marital status and household income, and child's age. Reference group for all OR includes those without the condition/risk factor except for methods for night-time monitoring.

associated with caregiver sleep impairment (Tables IV and V).

Caregiver self-reported anxiety was significantly associated with a 3.6-fold odds (95% CI, 2.5-5.1) and a 4.3-fold odds (95% CI, 3.1-6.1) for caregiver sleep disturbance and sleep-related impairment, respectively (Tables IV and V). Similarly, caregiver depression was significantly associated with a 2.8-fold odds (95% CI, 1.9-4.2) and a 4.5-fold odds (95% CI, 3.0-6.7) for caregiver sleep disturbance and sleep-related impairment, respectively. In contrast, caregiver perceived companionship and higher cognition were inversely associated with caregiver sleep disturbance (aOR, 0.2-0.4; $P < .001$) and caregiver sleep-related impairment (aOR, 0.1-0.3; $P < .001$).

Discussion

In this cross-sectional analysis of caregiver entered data in the REN, we identified a number of factors related to caring for children with rare epilepsy syndromes that were significantly associated with caregiver fatigue, sleep disturbance, and sleep-related impairment. These novel findings provide

Table V. Logistic regression for risk factors by sleep impairment T-score

Risk factors	Sleep impairment T score ≤60, N (%)	Sleep impairment T score >60, N (%)	No. in logistic model	aOR* (95% CI)	Adjusted *P* value
Characteristics of child					
Any sleep condition below	261 (56.9)	164 (66.7)	705	1.7 (1.2-2.4)	**.003**
Difficulty falling asleep	175 (38.4)	124 (50.8)	700	1.8 (1.3-2.5)	**<.001**
Excess daytime sleepiness	131 (29.3)	90 (37.2)	689	1.5 (1.1-2.2)	**.01**
Frequent night-time awakenings	205 (45.1)	136 (55.3)	699	1.6 (1.2-2.3)	**.004**
Very restless sleep	141 (31.4)	119 (50.2)	686	2.4 (1.7-3.4)	**<.001**
Nocturnal seizures	324 (68.7)	183 (72.6)	724	1.3 (0.9-1.9)	.1
Methods for night-time monitoring					
Someone shares a room or bed with the person with epilepsy	110 (23.5)	70 (27.8)	721	1.5 (0.9-2.6)	.1
Audio monitor or seizure alert device or leave door open	265 (56.5)	143 (56.8)		1.5 (0.9-2.3)	.1
Watch or check frequently	9 (1.9)	9 (3.6)		2.4 (0.9-6.9)	.1
No night-time monitoring	85 (18.1)	30 (11.9)		ref	
Caregiver PROMIS scores					
Cognition T score >60	154 (32.4)	13 (5.1)	730	0.1 (0.1-0.2)	**<.001**
Companionship T score >60	144 (30.3)	33 (12.9)	730	0.3 (0.2-0.4)	**<.001**
Depression T score >60	50 (10.5)	85 (33.5)	730	4.5 (3.0-6.7)	**<.001**
Anxiety T score >60	108 (22.7)	144 (56.5)	730	4.3 (3.1-6.1)	**<.001**

P values <0.05 are in bold.
*OR adjusted for caregiver gender, ethnicity, education, marital status and household income, and child's age. Reference group for all OR includes those without the condition/risk factor except for methods for night-time monitoring.

valuable information on health-related impacts of caregiving for children with rare epilepsies, and factors that can be targeted to improve sleep quality in those caregivers.

People with epilepsy who suffer with nocturnal seizures have increased risk for SUDEP compared with those without nocturnal seizures.[32,33] Although it has been suggested that nocturnal seizure involved a more severe SUDEP burden,[21] another study suggested that an unsupervised environment instead of severity of nocturnal seizure would better explain SUDEP during sleep time.[20] Limited by the current understanding of the pathogenesis of SUDEP and the lack of clinical trials studying preventive approaches, there are now guidelines for SUDEP prevention available to caregivers.[14] A case control study showed a protective effect of nocturnal supervision against SUDEP in the general epilepsy population[22]; however, a recent meta-analysis suggested that the proposed preventive effect of nocturnal supervision was of very low-quality evidence.[23] Caregivers of children with epilepsy generally fear nocturnal seizures and SUDEP in affected children,[34] which may drive them to pursue certain nocturnal monitoring strategies. The pediatric patients in this study had a surprisingly high prevalence of nocturnal seizures (69%), and more than 83% of our caregivers were reported to adopt at least 1 method of nocturnal monitoring.

Our findings showed that pediatric nocturnal seizures were highly associated with caregiver sleep disturbance, but not for caregiver fatigue or sleep-related impairment, suggesting that caregiver's sleep patterns are affected by the unpredictable nature and worry of nocturnal seizures and SUDEP. Larson et al showed that parents of children with epilepsy were much more likely to co-sleep or share a room with pediatric patients than the general population.[9] In this study, sharing a bed or room was practiced among a subset of caregivers (25%), which was significantly associated with a detrimental effect on caregiver sleep disturbance and fatigue. Other nocturnal monitoring approaches used by caregivers in this study, including an audio monitor (29%), a seizure alert device (13%), and door open (15%), were also associated with sleep disturbance and fatigue, but not for sleep-related impairment, suggesting that caregivers find ways to compensate during their waking hours for the impact of sleep disturbance and fatigue so that they can carry out daily responsibilities. A pilot study suggested that a seizure detection device may decrease parental fear for nocturnal seizure and co-sleeping arrangements, and improve quality of life in parents of people with epilepsy.[35] However, we failed to find a protective effect of the seizure alert device use on caregiver sleep quality and fatigue in this study. To date, seizure alert devices based on various mechanisms have been developed.[36-40] However, the efficacy of seizure alert devices is highly seizure type related,[41] and no study yet has compared efficacy and effectiveness among those devices in people with rare epilepsies.[42] One study suggested that patients and caregivers were generally interested in seizure detection devices, and the most valued feature of those devices was the ability to detect seizure.[43] The relatively low use of seizure detection devices in our caregivers may reflect their low confidence in those devices. Therefore, continuously upgrading seizure alert devices and further studies validating the efficacy and effectiveness of those devices in children with rare epilepsies are warranted.

Accumulated evidence has suggested that children with epilepsy are susceptible to sleep disorders, which may in turn exacerbate seizures.[44-47] Sleep disorders are common in typical children and more commonly reported in children with epilepsy.[48,49] In this study, difficulty falling asleep, frequent night-time awakenings, and very restless sleep of affected children were suggested to contribute to both caregiver sleep disturbance and sleep-related impairment. It is reasonable that pediatric sleep disturbance affects caregiver sleep quality, because caregivers usually closely monitor affected children during their sleep, using strategies such as co-sleeping and bed sharing. Therefore, caregivers might continuously check affected children who were having difficulty falling asleep, have frequent night-time awakenings or sleep very restlessly to comfort them or confirm that they are not having nocturnal seizures.

It has been suggested that caregivers of children with epilepsy are more likely to suffer from anxiety and depression.[50,51] In the present study, caregiver anxiety and depression were associated with substantial detrimental effects on caregiver sleep quality and fatigue; their perceived companionship and cognition, in contrast, seemed to be strongly protective for sleep quality and fatigue. Therefore, our findings might suggest that caregiver mental well-being could function as a mediator between pediatric epilepsy and caregiver sleep quality and fatigue. Nevertheless, owing to the cross-sectional nature of this study, temporality could not be set between caregiver mental health conditions and their sleep quality or fatigue. In addition, a bidirectional association between caregiver mental health and factors like sleep quality and fatigue could theoretically exist. Therefore, future prospective studies are needed to infer better the causality between perceived mental health burdens and sleep quality and fatigue in caregivers of children with epilepsy.

Several limitations should be noted in this work. First, the cross-sectional study design limits causal inference. Second, our data were not sufficient to allow us to determine whether affected individuals required overnight interventions, such as feeding or medical treatments that would affect sleep in the caregivers. We did not specifically assess the impact of discontinuous timescales of seizure activity (such as seizure clustering) on caregiver reports; some caregivers may have reported perceived impacts during very frequent seizure periods and others may have reported impacts during periods of fewer seizures. All data were entered by caregivers online and have not been validated through medical records. However, the misclassification of both exposure and outcome variables are reasonably considered as nondifferential, which likely drives their associations towards the null. Finally, this study was based on caregivers of children with rare epilepsies, and the respondent population was almost all white, non-Hispanic females who were highly educated and relatively

affluent. Therefore, our findings may not be generalizable to the full population of caregivers of people with epilepsy.

Overall our study demonstrates that most caregivers of children with rare epilepsies employ some kind of nocturnal seizure monitoring strategy during children's sleep. When children with rare epilepsies had any of the sleep conditions studied (difficulty falling asleep, excess daytime sleepiness, frequent night-time awakenings, or very restless sleep), caregivers reported significant impact on fatigue, sleep disturbance, and sleep-related impairment. However, nocturnal seizure monitoring approaches may also impose risk on caregiver's levels of fatigue and sleep disturbance. Caregiver perceived mental well-being is strongly associated with their sleep quality. These findings suggest that caring for a person with a rare epilepsy syndrome is associated with significant sleep disruption, fatigue, and sleep impairment in the caregiver. Sleep impairment has repercussions on caregiver mental health, as well as physical health. Sleep deprivation may also influence the daytime interactions with the affected child (eg, a fatigued parent may not be able to engage as fully during play time with the affected child, or to participate as meaningfully with siblings and other family members or to be more effective at work, as compared with a better-rested parent). Our study suggests that mental health problems should be actively evaluated and addressed in caregivers who suffer from fatigue, sleep disturbance and sleep related impairment. In addition, providers should be proactive about probing for sleep conditions in children with rare epilepsy, because treating these issues is likely to benefit both child and caregiver. Future prospective studies are warranted to confirm these findings, infer causality, and generalize these findings to a broader range of caregivers of people with epilepsy.[52] ■

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Data Statement

Data sharing statement available at www.jpeds.com.

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Appendix

List of organizations of the Rare Epilepsy Network (Steering Committee Representative)

Aaron's Ohtahara Foundation (Brianne McDonald, Omaha, NE)

Aicardi Syndrome Foundation

Alternating Hemiplegia of Childhood Foundation (Lynn Egan, Southfield, MI)

Brain Recovery Project: Childhood Epilepsy Surgery Foundation (Monika Jones, Los Angeles, CA)

Bridge the Gap SYNGAP (Monica Weldon, Cypress, TX)

Carson Harris Foundation (Michael Harris, Glen Arm, MD)

Chelsea's Hope (Kim Rice, Sacramento, CA)

CSWS Epilepsy & Landau Kleffner Syndrome (ESES) Foundation (Vinez Campbell, Williamsburg, VA)

The Cute Syndrome Foundation (Juliann Brandish, Troy, NY)

Doose Syndrome Epilepsy Alliance (Cindy Kercheval, Colorado Springs, CO)

Dravet Syndrome Foundation (Nichole Villas and Mary Ann Meskis, Cherry Hill, NJ)

Dup15q Alliance (Vanessa Vogel-Farley, Highland Park, IL)

Epilepsy Foundation

Hope for Hypothalamic Hamartoma (Ilene Miller, JD, Waddell, AZ)

Infantile Spasms Community (Mike Bartenhagen)

International Foundation for CDKL5 Research (Heidi Grabenstatter, PhD and Karen Utley, Wadsworth, OH)

International Rett Syndrome Foundation (Paige Nues, Cincinnati OH)

The Jack Pribaz Foundation (Angela Cherry and Gina Vozenilek, Winfield, IL)

KCNQ2 Cure Alliance (Scotty Sims, Denver, CO)

Lennox-Gastaut Syndrome Foundation (Tracy Dixon Salazar, PhD and Christina SanInocencio, MS, Bohemia, NY)

Liv4TheCure (Stephanie Forman, Latham, NY)

The NORSE Institute (Nora Wong, Boston, MA)

The Neurofibromatosis Network (Kim Bischoff, Wheaton, IL)

PCDH19 Alliance (Julie Walters, Novato, CA)

Phelan–McDermid Syndrome Foundation (Megan O'Boyle and Geraldine Bliss, Osprey, FL)

Pitt Hopkins Research Foundation (Audrey Davidow, Winston-Salem, NC)

RASopathies Network (Lisa Schoyer, Altadena, CA)

Ring 14 USA Outreach (Yssa DeWoody, PhD, Midland, TX)

Ring Chromosome 20 Alliance (Kira Wagner and Michael Arcieri, York, PA)

SLC6A1 Connect (Amber Freed, Denver, CO)

TESS foundation (Kim Nye, Menlo Park, CA)

Tuberous Sclerosis Alliance (Jo Anne Nakagawa, Silver Spring, MD)

Wishes for Elliott (JayEtta Hecker, Washington, DC)