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Original Article

Sleep disorders and associated factors in children with cerebral palsy

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Abstract

Background Sleep disorders are a condition affecting quality and quantity of sleep. Children with cerebral palsy (CP) have higher risk of sleep disorders than those with no chronic disease.

Objective To determine the prevalence and factors associated with sleep disorders in children with CP.

Methods We conducted an analytic, observational study with cross-sectional design in children aged 4-10 years with CP. Subjects were recruited consecutively; children with chronic diseases (cardiovascular, malignancy, chronic obstructive pulmonary disease, and diabetes mellitus) were excluded from the study. Primary data including sociodemographics, intensity of physiotherapy outside Sardjito General Hospital (SGH), sleep hygiene, and sleep disorders were collected from the *Children's Sleep Habit Questionnaire* (CSHQ). Secondary data were acquired from medical records, such as type of CP, severity of motor function impairment, presence of epilepsy, intensity of physiotherapy performed at SGH, as well as anti-epileptic, anti-spastic, and sleep-affecting medicines.

Results We found sleep disorders in 64 of 75 (85%) subjects, mostly bedtime resistance (66%). Spastic quadriplegia (OR 3.63; 95%CI 1.82 to15.94) and presence of epilepsy (OR 7.82; 95%CI 1.53 to 39.84) were significantly associated with sleep disorders in children with CP aged 4-10 years.

Conclusion Sleep disorders are common in children with CP, with the majority experiencing bedtime resistance. Sleep disorders are more prevalent in subjects with spastic quadriplegia and epilepsy. **[Paediatr Indones. 2021;61:179-85 ; DOI: 10.14238/pi61.4.2021.179-85**].

Keywords: *sleep disorders; children; cerebral palsy; CSHQ*

Sleep is defined as a state of reduced response to stimuli, characterized by reversibility, lack of movement, with diurnal timing and duration specific to the species.[1] Sleep disorders affect all age spectrums, including children. The prevalence of sleep disorders among children was estimated at 25%.[2] Children with chronic diseases, developmental delay, and severe neurological disorder such as cerebral palsy (CP) are especially at risk of sleep disorders.

Cerebral palsy is characterized as a nonprogressive, persistent motor disorder, present before the age of 2 years, and caused by brain damage. Cerebral palsy can affect perception, learning, sight, language, and musculoskeletal function.[3] The WHO estimated the CP prevalence to be 2-3 per 1,000 live births in undeveloped countries.[2] In developed countries, it was 1.5-2.5 per 1,000 live births.[4] Accurate data on the prevalence of CP in Indonesia is not available. Sleep disorders reportedly occur in 23-46% of children with CP,[5] potentially impacting their quality of life and that

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of their parents and family.

Sleep disorders in children with CP were correlated with respiratory problems, generalized muscle weakness, epilepsy, circadian rhythm disorders, chronic pain, and psychological problems.[6] As such, we aimed to determine the prevalence and factors associated with sleep disorders in children with CP.

Methods

We performed an analytic, observational study with a cross-sectional design to determine factors associated with sleep disorders in children with CP. Primary data were obtained from patients in the Outpatient Clinic of the Children's Health Department and Physical Medicine & Rehabilitation Department, SGH, Yogyakarta, using the *Children's Sleep Habit Questionnaire* (CSHQ).

Inclusion criteria were children with CP, 4-10 years of age, diagnosed with CP based on medical records, and parental consent to participate. Children with chronic diseases (conditions that lasted 1 year or more such as cardiovascular disease, malignancy, chronic obstructive pulmonary disease, and diabetes mellitus) were excluded from this study. Sleeping habits or sleep hygiene were behavioral practices that promote good sleep quality, adequate sleep duration, and full daytime alertness; namely feeding, physical touch (swinging or rocking, patting, holding), playing (grasping toys), none (no special routine before bed) or others (strolling, watching tv/video, sucking thumb, listening to music/lullaby, waiting until mother fall asleep, turning off lights, hugging bolster).[7] Sleep disorders were a collection of conditions characterized by disturbances in the amount, quality, or timing of sleep in an individual; such as bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night waking, parasomnias, sleep disordered breathing, daytime sleepiness.[8] Factors associated with sleep disorders can be divided into several categories, namely the type of cerebral palsy, GMfCS, epilepsy, physio intensity, antiepileptic drugs, anti-spastic.[2,9-12]

Children's Sleep Habit Questionnaire (CSHQ) was parent-rated questionnaire screening method for sleep behavior problems in school-aged children approximately 4 to 10 year-old based on the *International Classification of Sleep Pediatric Disorder Diagnostics*. The CSHQ consisted of 33 questions and 8 types of sleep disorder, namely (1) bedtime resistance, (2) sleep onset delay, (3) sleep duration, (4) sleep anxiety, (5) night waking, (6) parasomnias, (7) sleep disordered breathing, and (8) daytime sleepiness. The questionnaire were assessed with three-point scale ranging from 1 to 3. Number 1 for rarely (if it occurs 0-1 times a week), 2 for sometimes (if it happens 2-4 times a week), 3 for always (if it happens 5-7 times a week). There were 6 reversed items, which were scored in the opposite direction. A total score more than or equal 41 is classified as a sleep disorder, while total score below 41 classified as no sleep disorder. From each point of the CHSQ questionnaire, the percentage of the proportion of sleep disorders was calculated using the formula below:[13]

$$\text{Proportion of each sleep disorders} = \frac{\text{total score}}{\text{maximum score}} = \frac{\text{total score}}{\text{number of items x maximum points x number of sample}}$$

Primary data collected from the CSHQ filled by parents were demographics, physiotherapy intensity (if physiotherapy was performed outside SGH), presence of co-sleeping, and sleeping habits. Secondary data obtained from medical records were type of CP, severity of functional motor disorders based on the *Gross Motor Functional Classification System* (GMFCS), presence of epilepsy, intensity of physiotherapy performed at SGH, as well as anti-epileptic, anti-spastic, or other medications currently taken by the patient that potentially affect sleep. The independent variables were type of CP, GMFCS, and physiotherapy intensity. The GMFCS was the classification system to describes gross motor function for children with cerebral palsy on the basis of self-initiated movement abilities. There were five different levels of GMFCS; I) able to walks without any limitations ; II) walks with limitations; III) walks using a hand-held mobility device; IV) self-mobility with limitations (may use powered mobility); V) dependent mobility in a manual wheelchair.[14]

Data were analyzed using *Statistical Package for Social Science (SPSS) 20* software. Descriptive or univariate analyses were performed to measure frequency and distribution of subjects' characteristics. Bivariate analyses were Chi-square or Fischer's exact tests. Multivariate analysis with logistic regression was performed to analyze independent and dependent variables. This study was approved by the Ethics Committee for Medical Research at Universitas Gadjah Mada Medical School.

Results

This study on sleep disorders in 75 children with CP and influencing factors was conducted in SGH from April 2 to May 18, 2019. Male subjects comprised 52% and most subjects were 4-5 years old (49%). Subjects' main sleeping habits were feeding (31%) and co-sleeping (99%). The mean age of subjects was 77 (SD 25) months. Characteristics of study subjects are presented in **Table 1**.

The prevalence of sleep disorders in our subjects was 85%. Univariate analysis of the CSHQ findings noted 8 types of sleeping disorder **(Table 2)**. The most common sleep disorder found in this study was bedtime resistance (66%).

Bivariate analysis was done with Fisher's exact test because the requirements for Chi-square test were not fulfilled. Fisher's exact test revealed significant associations between sleep disorders and quadriplegic spastic type (OR 15.50; 95%CI 1.26 to 190.89), GMFCS level 5 (OR 13.13; 95%CI 1.48-116.27), and epilepsy (OR 8.00; 95%CI 1.89 to 33.85). Factors associated with sleep disorders are shown in **Table 3**.

All significant variables in the bivariate analysis were then analyzed by multivariate logistic regression. Quadriplegic spastic type of CP and epilepsy were significantly associated with sleep disorders, as shown in **Table 4**.

Table 1. Subjects' characteristics

Characteristics	(N=75)
Sex, n (%)	
Male	39 (52)
Female	36 (48)
Age, n (%)	
4-5 years	37 (49)
6-10 years	38 (51)
Anti-epileptic drug, n (%)	
Yes	51 (68)
No	24 (32)
Anti-spasticity drug, n (%)	
Yes	10 (13)
No	65 (87)
Co-sleeping, n (%)	
Yes	74 (99)
No	1 (1)
Sleeping habit, n (%)	
Feeding	23 (31)
Physical touch (swinging or rocking, patting, holding)	16 (21)
Playing (grasping toys)	7 (10)
None	13 (17)
Others	16 (21

Discussion

The CSHQ results revealed a sleep disorder prevalence of 85% in CP subjects, similar to a study from Semarang, Central Java (96%).[2] Our prevalence as in the referral hospital was considerably larger than those reported by studies in Ireland (23%), Uganda (32%), and Italy (13%).[9,10] This disparity might have been due to our setting, as SGH is a tertiary referral center that cares for the most severe patients. Mulago Hospital, the referral center in Uganda, also had higher rates of sleep disorders than the non-referral hospitals (32%).[9]

Multivariate logistic regression analysis showed that type of CP and epilepsy were significantly associated with sleep disorders. The quadriplegic spastic type increased the risk of sleep disorders by 3.63 (95%CI 1.82 to 15.94: P=0.040), similar to the Irish study results (OR 12.9; 95%CI 1.9 to 88.0).[10]

The spastic type of CP can cause posture abnormalities, growth retardation, muscle shortening, muscle tone abnormalities, joint subluxation or dislocation, contracture, involuntary movement, soft tissue rigidity, and muscle pain.[10,15,16] Spasticity leads to uncomfortable positioning, and reduces the child's ability to change positions during sleep, resulting in persistent and increased pain associated with sleep disorders.[5,16] Pain is transmitted from the peripheral to central nociceptors through several steps: sensory conduction, transmission, modulation, and perception. The nociceptive signal is actively modulated by excitatory factors and endogenic inhibition from the central nervous system that involves reticular formation. These processes activate the *Ascending Reticular Activating System* (ARAS) that controls the sleep-wake cycle.[17] Pain, mobility impairment, sensory

Table 2. Distribution of subjects according to type of sleep disorder

Type of sleep disorders	Total/max score	%
Bedtime resistance	763/1152	66
Sleep onset delay	125/192	65
Sleep duration	296/576	51
Sleep anxiety	471/768	61
Night waking	334/576	58
Parasomnias	663/1344	49
Sleep disordered breathing	364/576	46
Daytime sleepiness	802/1536	52

Table 3. Factors associated with sleep disorders in children with cerebral palsy (N=75)

Variables	Sleep disorder		OR (95%CI)	P value
	Yes	No		
CP type, n (%)				
Quadriplegic	62 (89)	8 (11)	15.50 (1.26 to 190.89)	0.048
Hemiplegic	1 (50)	1 (50)	2.00 (0.05 to 78.25)	1.000
Diplegic	1 (33)	2 (67)		
GMFCS, n (%)				
Level V	30 (97)	1 (3)	13.13 (1.48 to 116.27)	0.008
Level IV	4 (100)	0 (0)	-	0.545
Level III	6 (86)	1 (14)	2.63 (0.26 to 26.07)	0.638
Level II	8 (80)	2 (20)	1.75 (0.29 to 10.44)	
Level I	16 (70)	7 (30)		
Presence of epilepsy, n (%)				
Yes	48 (94)	3 (6)	8.00 (1.89 to 33.85)	0.003
No	16 (67)	8 (33)		
Intensity of physiotherapy, n (%)				
Not routine	50 (86)	8 (14)	1.05 (0.82 to 1.34)	0.704
Routine	14 (82)	3 (18)		
Anti-epileptic drug, n (%)				
Polytherapy	14 (100)	0	-	0.552
Monotherapy	34 (92)	3 (8)		
Anti-spasticity drug, n (%)				
Yes	10 (100)	0	-	-
No	54 (83)	11 (17)		

Table 4. Multivariate analysis of factors associated with sleep disorder in children with CP

Variables	OR (95%CI)	P value
Spastic quadriplegic type	3.63 (1.82 to 15.94)	0.040
GMFCS V	1.81 (0.93 to 3.19)	0.087
Presence of epilepsy	7.82 (1.53 to 39.84)	0.013

integration, and interpretation disorder can cause sleep disorders in children with CP.[18]

Epilepsy was also associated with sleep disorders (PR 7.82; 95%CI 1.53 to 39.84). Other studies reported a similar association, such as in Ireland (OR 17.1; 95%CI 92.5 to 115.3), Italy (OR 2.041; 95%CI 0.647 to 6.434), pre-schoolers in Italy (OR 14.04; 95%CI 1.255 to 157.078), and Uganda (OR 3.865; 95%CI 1.4 to 10.9).[9,10] While this association has not been clearly explained, the commonly accepted explanation is sleep fragmentation, a decrease in sleep efficacy and increase in wake frequency.[19] The non-rapid eye movement (NREM) and REM phases also play a role in seizures in epilepsy. Seizures reportedly occur more frequently in phase 2 of NREM (61-68%), phases 3 and 4 of NREM (9-14%), and the REM phase (0-5%).[20]

Circadian rhythm is also disorganized in children with epilepsy due to changes in the wake-sleep cycle controlled by the suprachiasmatic nucleus (SCN) in the anterior hypothalamus. Melatonin hormone secretion pattern is disturbed, with high concentrations at night or after a seizure. In normal conditions, melatonin peaks at 2 AM and 4 AM, and decreases in the morning, to the lowest concentration during the day. Disturbed melatonin secretion patterns change the wake-sleep cycle and wake-promoting signal of the SCN, thus causing sleep disorders.[20-21]

Epilepsy increases sleep onset latency or sleep onset delay, increases the number and duration of wakefulness episodes after sleep onset, decreases sleep efficiency, reduces spindle sleep, and increases REM phase abnormalities. A study in India showed that seizures in children with epilepsy had significant correlations with wake disorders and pathological sleep. Disturbed sleep microarchitecture due to no recognizable nocturnal seizure is one of the proposed hypotheses.[22] Sleep disorders in nocturnal seizures can cause decreased REM phase, increased NREM phase 1, and decreased sleep efficiency. Lack of sleep can cause seizures due to interictal epileptiform discharge.[23]

The most common anti-epileptic monotherapy drug used in our study was valproic acid (59%), while the most common polytherapy combination was valproic acid and phenobarbital (7%). Valproic acid can cause increased wake state, prolonged phase 1 NREM, and reduced long phase of REM.[11] Phenobarbital reduces REM phase, sleep latency, and the amount of sleep-wake, while it increases NREM phase 2 and sleep spindles. Other anti-epileptic drugs used can also affect sleep. The most common anti-spasticity agent used was diazepam, which can affect sleep by reducing sleep onset latency, increasing the duration of REM phase, reducing total duration of sleep, and reduce slow-wave sleep phase.[24-25] We found a non-significant relationship between mono or polytherapy anti-epileptic drugs with sleep disorders.

We found no association between GMFCS severity and sleep disorders (P=0.087). An Italian study on pre-school-aged children with CP also had similar results (P=0.146).[12,22] However, a cross-sectional study in Uganda found a significant association (OR 13.182; 95%CI 3.7 to 47.0).[9]

No association was found between sleep disorders and intensity of physiotherapy, perhaps because the physiotherapy techniques and methods were not uniform, as subjects used various physiotherapy providers.

The most common sleep disorders were bedtime resistance (66%), sleep onset delay (65%), and sleep anxiety (61%). Studies in Malaysia, Ireland, and Uganda using the *Sleep Disturbance Scale for Children* (SDSC) had higher proportions of sleep initiation,[9,10,24]6while a Semarang, Indonesia study using the CSHQ also found a predominance of sleep onset delay.[2]

Co-sleeping was practiced by nearly all of our subjects (99%), and is common in Asian culture. In normal population of healthy children, co-sleeping had a stronger correlation with sleep disorders in American children than in Japanese children.[27] Co-sleeping in Caucasians also had a correlation with sleep disorders.[28] A study reported that children with CP who did not co-sleep had more sleep disorders.[10] Studies in Malaysia and India reported that co-sleeping was not associated with sleep disorders in the patient, but reduced sleep duration of the carer.[10,22,26] Nevertheless, causality between co-sleeping and sleep disorders in CP is not clearly defined. In our study, an association between sleep disorders and co-sleeping could not be determined, as only one subject did not co-sleep.

In addition we found that on average, the duration of sleep for subjects aged 4-5 years was 10.30 (SD 2.23) hours per day, ranging from 6 to 18 hours per day. In 6 to10-year-olds, the average was 10.24 (SD 1.72) hours per day, ranging from 7 to 14 hours/day.

The most common sleeping habit was feeding (31%) and physical touch such as holding, patting, or rocking (21%). The patting and rocking habit was also found in a study in Malaysia, which has a culture similar to Indonesia.[26] In healthy children, the sleeping habit of rocking, feeding, and moving children could awaken them.[30] In contrast, another study noted that the habit of feeding, patting, and swinging were still advised as part of behavioral therapy in the normal child population to induce sleeping after awakening at night thereby reducing the incidence of insomnia in children.[31] A study stated that a short nap in a bed with slow swinging could induce sleep and slow wave activity, as well as increase the duration of phase 2 sleep.[32] In our study, food intake, and physical touch in the form of swinging, stroking, patting, and cuddling was not associated with sleep disorders. Further study is needed to incorporate and explore bedtime habits and sleep disorders in children with CP.

Limitations of our study were that data collection was based on parents' recall, which could lead to bias, as well as the lack of uniform physiotherapy methods. We recommend that physiotherapy be done in one place with a certified physiotherapist. In addition, this study only involved subjects aged 6-10 years, according to the valid age range of the CSHQ questionnaire. Future study should involve general early school age (6-12 years) with a validated, age-appropriate questionnaire. The advantage of our study compared to previous ones was the type of questionnaire used. The CSHQ was adapted to the condition of the child's physical limitations, including options for each of the questions. Another advantage was the existence of physiotherapy as one of the factors that influence sleep disorders, which had not been included in previous studies.

In conclusion, the prevalence of sleep disorders in children with CP is 85%, with bedtime resistance as the most common type. Spastic quadriplegia and epilepsy are associated with sleep disorders in children aged 4-10 years with CP.

The clinical application of this study can be used

for early detection of sleep disorders in children with CP, so that parental education and early treatment, both pharmacological and non-pharmacological (sleep hygiene and physiotherapy), can be carried out. Further study should include sleep hygiene, assessing for comorbid factors, and physiotherapy interventions to determine their effects on pain and sleep to improve the quality of life of children with CP.

Conflict of Interest

None declared.

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