ORIGINAL ARTICLE

Sleep Disturbances in Children with Mild to Moderate and Severe Chronic Kidney Disease

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ABSTRACT

Chronic kidney disease (CKD) is a common problem found in children. Generally, children with CKD may experience physical and psychological problems, such as sleep disturbances or sleep disorders. Sleep disturbance in pediatric CKD are correlated with decrease quality of life.

Objective: **Assessing sleep disturbances in pediatric patients with mild to moderate and severe CKD.**

Method: **Research subjects were 30 patients with mild-moderate CKD and 30 patients with severe CKD in Haji Adam Malik Hospital Medan from March May 2021. Samples were selected from consecutive sampling method. Direct and indirect interviews for data collection were conducted to the parents/guardians of CKD patients. Mann-Whitney comparative analysis test was carried out to assess the difference in sleep disorders between mild-moderate and severe pediatric CKD.**

Result: **From the total of 60 subjects, 41 (68.3%) of them had sleep disturbances, where 29 subjects (96.7%) were in severe CKD group. There was a significant relationship in sleep disturbances between mild-moderate and severe pediatric CKD. There were significant correlations between sleep disturbances and the following variables in CKD patients: nutritional status, disease management, parents' level of education, and CKD severity. Significant independent variables correlated to CKD in children were parents level of education and CKD severity, where the most dominant variable that affect sleep disturbances in children was CKD severity.**

Conclusion: **There were significant differences in sleep disturbances between mild-moderate and severe chronic kidney disease in children**

KEY WORDS

sleep disturbance, pediatric, chronic kidney disease

INTRODUCTION

Chronic kidney disease (CKD) is a common problem found in children. Advances in the management of patients with CKD have allowed the progression in the prognosis. Therefore, it is very important to understand the disease as early as possible. According to the guideline from National Kidney Foundation (NKF) on kidney disease outcomes quality initiative (KDQI), CKD is defined as kidney disease with minimum 3 months of renal failure with or without decreased glomerular filtration rate (GFR) to below 60 mL/min/1.73 m^2.[1)]

Pediatric CKD incidence rate is difficult to determine, so is the prevalence. CKD in the early stages of the disease is often asymptomatic and initially misdiagnosed[2)]. In year 2008, CKD average incidence rate worldwide was 9 per one million children, where the highest cases were in the United States, at 15.5 cases per one million children[3)]. The incidence rate in Indonesia alone cannot be ascertained yet as there has not been national data to assess the incidence of CKD in children[4)].

The causes of CKD in children are closely related to the age at the onset of the disease. The primary cause of CKD in children is as congenital abnormalities of the kidney and urinary tract (CAKUT), especially in < 5 years old age group. Whereas, in children over 5 years old, CKD usually occurs as inherited, acquired, or glomerular diseases[5)]. Problems that may be experienced by pediatric patients with CKD are generally physical and psychological problems that may affect their growth and development. Psychological problems experienced by CKD may be depression, delirium, panic disorder, anxiety, and sleeping disorders/disturbances[6)].

Sleep disorders or disturbances are conditions when the quality, time, and amount of sleep are disrupted and causing impaired functions in a person during the day. The study done by Darwish and Abdel-Nabi (2016) in Egypt to 95 pediatric CKD patients reported 75.9% of total subjects with sleep disorders, where 81.8% of them underwent dialysis and 71.8% of them did not[7)]. A systematic review done in year 2015 assessed sleep disturbances in children with CKD and found 77% 85% prevalence of sleep disorders in patients undergoing dialysis, 32% - 50% prevalence in transplant patients, and 40% - 50% prevalence in non-dialysis patients[8)].

Sleep disorders or disturbances in pediatric CKD are correlated to decreased quality of life of children. Davis *et al*., (2012) in their research reported a correlation of decreased PedsQl score by 10 points with the increasing sleep disorder risks to 86%. This concludes that sleep disorders in children with CKD are correlated with the decreased quality of life of children, which affects health[9)]. Roumeliti *et al*., (2010) stated higher CKD degree was related to increased sleep disturbance and later affected the quality of life of the patients[10)]. Beebe (2011) reported that sleep disorders impacted children's functions, such as causing drowsiness, lack of concentration, behavioral deficit, and cognitive disorder[11)]. Therefore, it is important for health workers taking care of children with CKD to recognize the disease early and anticipate sleep

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Table 1: Subject characteristic data

Demography Characteristic	Chronic Kidney Disease	
	Severe (n = 30)	Mild-moderate (n = 30)
Gender, n (%)		
Male	18 (60)	24 (80)
Female	12 (40)	6 (20)
Age, years old		
Average (SD)	8.9 (1.37)	8.4 (1.37)
Nutritional status, n (%)		
Malnutrition	10 (33.3)	0
Poor nutrition	20 (66.7)	8 (26.7)
Good nutrition	0	19 (63.3)
Overweight	0	3 (10)
Disease management, n (%)		
Kidney transplant therapy	29 (96.7)	0
Non kidney transplant therapy	1 (3.3)	30 (100)
Parents' level of education, n (%)		
Low	23 (76.7)	18 (60)
High	7 (23.3)	12 (40)
Parents' level of income, n (%)		
Above minimum wage	3 (10)	0
Below minimum wage	27 (90)	30 (100)
Sleep disturbance, n (%)		
Yes	29 (96.7)	12 (40)
No	1 (3.3)	18 (60)

disturbance.

There are several factors that affect the sleep pattern in children with CKD, such as disease factors, duration of hospital stay, treatment regimens, and state of emotional function[12]. Early recognition and management of sleep disorders can positively affect the growth and development of children living with CKD[7]. This research aimed to assess the differences in sleeping disturbances between mild to moderate CKD and severe CKD, especially in patients in Haji Adam Malik Hospital Medan.

METHODS

This was a cross-sectional research that assessed the differences in sleep disturbances between children with mild to moderate and severe chronic kidney disease (CKD). The research was conducted in pediatric nephrology unit Haji Adam Malik Hospital Medan between March and May 2021. The research subjects were children with CKD degree 1 to 5 meeting the inclusion and exclusion criteria. They were grouped based on GFR values, where mild-moderate CKD was patients with GFR > 45 mL/min/1.73 m^2 and severe CKD was patients with GFR < 45 mL/min /1.73 m^2. They were selected by consecutive sampling method. The inclusion criteria were children with CKD aged 4 — 10 years old whose parents agreed to be involved in the research by signing consent form. Exclusion criteria were children with CKD who consumed sedatives during the research, had mental organic disorders or any other chronic medical conditions.

The minimum sample size, calculated by using hypothesis testing for two-sample proportions formula in cross-sectional study with 95% confidence interval (CI) and 80% power, was 27 research subjects. There was a total of 60 research subjects in this research, where 30 subjects were in severe CKD group and 30 subjects in mild-moderate CKD group. Primary data was gathered by interviews, such as demographic data like age and gender, as well as parents' occupation, level of education, and income level. Anthropometric measurement (body weight and height) was performed ad plotted on 2000 CDC growth charts to determine growth status of the subjects. Secondary data was renal function data based on laboratory results from the medical record. CKD classification was done based on glomerular filtration rate (GFR) calculated by Schwatrz formula.[13] There was assessment on sleep disorders or disturbances by using The Children's Sleep Habits Questionnaire (CSHQ), where total score > 41 shows significant sleep disturbances in children[14].

Table 2: Sleep disturbance scale in severe and mil-moderate CKD group

Variable	Chronic Kidney Disease		p
	Severe	Mild-moderate	
Sleep disturbance scale			
Average (SD)	47.17 (4.3)	39.23 (4.17)	< 0.001*

*Mann Whitney test

Data Analysis

Collected data was processed and analyzed by using SPSS computer software system with 95% confidence interval (CI) and significance level of $P < 0.05$. Univariate analysis was conducted to subject characteristic data, by presenting frequency and percentage for categorical data. As for numerical data, average and standard deviation (SD) were used for normal distribution, otherwise median with minimum — maximum values was used. Bivariate analysis was used to assess whether there were differences in sleeping disorders between mild-moderate and severe CKD. For normal distribution data, independent t-test was used, otherwise Mann-Whitney test was used. Data distribution was assessed by using Saphiro-Wilk test.

Ethical Considerations

Parents of the research subjects were given explanations about the research and they were asked for consent to be involved in the study. This study was approved by Health Research Ethical Committee, Medical Faculty of Sumatera Utara (No. 194/KEP/USU/2020).

RESULTS

Characteristic Data of Research Subjects

There were 60 research subjects in this research, where there were 30 subjects each in mil-moderate and severe CKD groups. Both groups were dominated by male patients, where 18 subjects (60%) and 24 subjects (80%) in severe and mild-moderate CKD respectively. The average age for both groups was around 9 years old. Based on the nutritional status, most children in severe CKD groups experienced malnutrition (33.3%) and poor nutrition (66.7%). While over half (63.3%) children in mild-moderate group had good nutrition. Almost all children (96.7%) with severe CKD underwent kidney transplant therapy management, whereas all children with mild-moderate CKD had non kidney transplant therapy management.

Most parents of the research subjects had low education level, such as 23 parents (76.7%) in severe CKD group and 18 parents (60%) in mild-moderate CKD group. Moreover, most parents were earning below the minimum age.

Sleep disorders or disturbances were ascertained when the sleep quality scale is > 41. By grouping the scale, there were 41 subjects (68.3%) from the total subjects who suffered from sleep disturbances. Based on the severity of CKD, almost all subjects (96.7%) with severe CKD had sleep disturbance, while there were 12 subjects (40%) with sleep disturbances in mild-moderate CKD condition. Table 1 shows the demographic characteristic of research subjects.

Differences in Sleep Disturbance Score between Mild-moderate and Severe CKD

Table 2 shows the assessment of sleep disturbance in the two groups in the research. The average sleep disturbance score in severe CKD group was 47.17, with minimum value 38 and maximum value 54. Meanwhile, in mild-moderate group, the average was 39.23, with the lowest score being 30 and highest score 40. By Mann-Whitney test, there was a significant relationship between the severity of CKD and sleep disturbances ($p < 0.001$).

Table 3: Factors associated with sleep disturbances in children with CKD

Variable	Sleep Disturbance		P	Prevalence Ratio (CI 95%)
	Yes (n = 41)	No (n = 19)		
Gender, n (%)				
Male	27 (64.3)	15 (35.7)	0.303[a]	0.827
Female	14 (77.8)	4 (22.2)		(0.592-1.155)
Age, years old				
Average (SD)	8.8 (1.47)	8.32 (1.80)	0.345[b]	
Nutritional status, n (%)				
Malnutrition ─ poor nutrition	32 (84.2)	6 (15.8)	0.001[a]	2.058
Good nutrition - overweight	9 (40.9)	13 (59.1)		(1.223-3.465)
Disease management, n (%)				
Kidney transplant therapy	28 (96.6)	1 (3.4)	< 0.001[a]	2.302
Non kidney transplant therapy	13 (41.9)	18 (58.1)		(1.513-3.504)
Parents' level of education, n (%)				
Low	33 (80.5)	8 (19.5)	0.003[a]	1.912
High	8 (42.1)	11 (57.9)		(1.105-3.308)
Parents' level of income, n (%)				
Above minimum wage	2 (66.7)	1 (33.3)	1.000[d]	0.974
Below minimum wage	39 (68.4)	18 (31.6)		(0.429-2.211)
CKD severity, n (%)				
Severe CKD	29 (96.7)	1 (3.3)	< 0.001[a]	2.417
Mild-moderate CKD	12 (40)	18 (60)		(1.551-3.765)

[a]Chi Square, [b]Mann Whitney, [c]T Independent, [d]Fischer's Exact

Table 4: Multivariate analysis of factors associated with sleep disturbances in children with CKD

Variable	B	p	Exp(B)	95% CI for EXP(B)	
				Lower	Upper
Selection I					
Nutritional status	-0.599	0.599	0.549	0.059	5.123
Disease management type	-16.776	1.000	0.000	0.000	
Parents' level of education	2.234	0.015	9.333	1.539	56.581
CKD severity	21.093	1.000	1.451	0.000	
Constant	-1.791	0.345	0.167		
Selection II					
Nutritional status	-0.600	0.599	0.549	0.059	5.125
Parents' level of education	2.240	0.015	9.397	1.550	56.959
CKD severity	4.332	0.004	76.075	4.124	1403.483
Constant	-1.796	0.344	0.166		
Selection III					
Nutritional status	-0.589	0.532	0.555	0.087	3.520
Parents' level of education	2.238	0.014	9.377	1.574	55.857
CKD severity	4.329	0.003	75.849	4.205	1368.254
Constant	-1.824	0.038	0.161		
Selection IV					
Parents' level of education	2.204	0.014	9.063	1.551	52.966
CKD severity	4.497	0.001	89.751	5.710	1410.708
Constant	-1.706	0.031	0.182		

Factors Associated with Sleep Disturbances in Children with CKD

Table 3 shows the analysis of factors from all independent variables in this study that were associated with sleep disturbances. There was no significant relationships in variables, such as gender, age, and parents' level of income ($p > 0.05$). On the other hand, variables like nutritional status, therapy management type, parents' level of education, and severity of CKD were significantly correlated.

Based on the nutritional status, there were 38 children with malnutrition and poor nutrition, where 32 (84.2%) of them experienced sleep disturbance. Meanwhile, there were 9 children (40.9%) from the total of 22 children in good nutritional status and overweight classification that suffered from sleep disturbance. The analysis by Chi-square test showed a significant relationship between nutritional status and sleep disturbance ($p = 0.001$) with prevalence ration (PR) 2.058 (95% CI 1.223 ─ 3.465), which means children with CKD with malnutrition and poor nutrition were 2.058 more likely to experience sleep disturbance than children with good nutritional status and overweight.

From the aspect of disease management therapy, 29 children under-

went renal replacement therapy (RRT), where 28 (96.6%) of them had sleep disturbance. Meanwhile, only 13 children (41.9%) from 31 children without RRT who suffered from sleep disturbance. Chi-square test analysis showed a significant relationship between disease therapy management and sleep disturbance (p = 0.001) with PR of 2.302 (95% CI 1.513 — 3.504), which means that hemodialysis in children with CKD increased sleep disturbance by 2.302 times more than children with CKD without hemodialysis.

Based on parents' level of education, there were 33 children (80.5%) from 41 children whose parents had low level of education. Whereas, 8 children (42.1%) from 19 children whose parents had high level of education suffering from sleep disturbances. Chi-square analysis tests showed a significant relationship between parents' level of education and sleep disturbances (p = 0.003) with PR of 1.912 (95% CI 1.223 — 3.465), which means children with CKD whose parents had low level of education were 1.912 more likely to experienced sleep disturbances than children with CKD with parents of higher level of education.

Based on the severity of CKD, almost all children (96.7%) in the severe CKD group had sleep disturbances. Meanwhile, in 30 children with mild-moderate CKD, only 12 children (40%) suffered from sleep disturbances. The analysis by using Chi-square test showed that there was a significant relationship between the severity of CKD and sleep disturbances (p < 0.001) with PR 2.417 995% CI 1.551 3.765), which means that children with severe CKD were 2.417 times more likely to had sleep disturbances than children with mild-moderate CKD.

Multivariate Analysis of Factors Associated with Sleep Disturbances in Children with CKD

Multivariate analysis with a multiple logistic regression was carried out in this study to assess independent variables with dominant effect to predict sleep disturbances in children with CKD. Besides that, we could predict the probability of sleep disturbances from the significant independent variables from multivariate analysis.

The data in this study was categorical. The variables in the multivariate analysis were independent variables from bivariate analysis with p < 0.25, such as nutritional status, disease management therapy, parents' level of education, and CKD diagnosis. The result of the multivariate analysis is shown in Table 4.

By using the method of entry (enter method), which was taking out one independent variable at a time starting from the highest p value > 0.05, there were only two significant independent variables to sleep disturbances in this study, such as parents' level of education (p = 0.017) and CKD severity (p = 0.001). The most dominant variable that affects sleep quality was the severity of CKD itself with Exp (B) value of 55.314 (95% CI = 5.491 — 557.215), that means children with severe CKD were at 55.314 higher risk of sleep disturbances than children with mild-moderate CKD.

DISCUSSION

From 60 research subjects, there were 41 children (68.3%) with sleep disturbances. Based on the severity of chronic kidney disease (CKD), almost all (96.7%) of children in severe group had sleep disturbances, while there were only 40% of research subjects in the mild-moderate group experiencing sleep disturbances. Davis *et al*., (2013) reported higher number of patients (68.6%) experiencing sleep disturbances in GFR group < 30 mL/min/1.73 m^2, while only 48.3% subjects had sleep disturbances in GFR group ≥ 60 mL/min/1.73 m^2.[9] In the study done by Roumelioti *et al*., (2020) showed that patients with severe CKD with GFR < 30 mL/min/1.73 m^2 were four time at higher risk of sleep disturbances than mild CKD patients with GFR ≥ 60 mL/min/1.73 m^2.[10]

Sleep disturbance scale in this study showed the average scale of 47.17 and 39.23 in severe CKD and mild-moderate CKD cases respectively. Using Mann-Whitney test, there was a significant difference in sleep quality scale between severe and mild-moderate CKD groups (p < 0.001). Darwish and Abdel-Nabi (2016) reported no significant difference in sleep disturbance scale between children with CKD who received kidney transplant therapy and who did not[7]. This result was obtained because they did not classify the stage of disease other than therapy classification. Children who did not receive kidney transplant therapy may be children with severe CKD classification.

There was a few factors in this research that significantly correlated with sleep disturbances, such as nutritional status, disease management therapy, parents' level of education, and severity of CKD. Based on the nutritional status (p = 0.001, PR = 2.058), the majority of research subjects in this study had poor nutritional status. Darwish and Abdel-Nabi (2016) stated that there was no relationship between nutritional status and The Children's Sleep Habits Questionnaire (CSHQ) with p = 0.125, where most of the research samples in their study had good nutritional status[7]. From the disease management therapy, Davis *et al*., (2013) reported more frequent cases of sleep disturbances in patient group with kidney transplant therapy than the group that did not (p = 0.05). Generally, patients who did not receive kidney transplant therapy would have had the tendency to have more sleeping problems than the other groups[9]. This study also reported a significant difference between disease management therapy and sleep disturbances, where p = 0.001 and PR = 2.302. From the severity of disease, there was a significant relationship between CKD severity classification and sleep disturbances (p < 0.001, PR = 2.417). Darwish and Abdel-Nabi (2016) reported negative correlation between CSHQ score and GFR values, where the increase in CSHQ level indicated lower GFR values (r — 0.28, p = 0.04). This showed that lower GFR values were a risk factor of sleep disturbance in children with CKD, where every decrease in 10 mL/min/1.73 m^2 was correlated with the increase in CSHQ score by 0.65[7]. Finally, there was also a significant relationship between parents' education level and sleep disturbances in children with CKD (p = 0.003, PR = 1.912).

Multivariate analysis in this study showed two significant independent variables associated with sleep disturbances in children with CKD, such as parents' level of education (p = 0.017) and CKD severity (p = 0.001). The most dominant variables that affect the quality of sleep was the severity of CKD with Exp (B) value of 55.314 (95% CI = 5.491 — 557.215). Roumelioti *et al*., (2020) stated that patients with GFR < 30 mL/min/1.73 m^2 had four time more risk of sleep disturbances than patients with GFR ≥ 50 mL/min/1.73 m^2. Meanwhile, patients with GFR between 40 — 50 mL/min/1.73 m^2 were at three times highest risk of sleep disturbances than GFR ≥ 50 mL/min/1.73 m^2. This showed that the more severe the CKD was, the bigger the sleep problems experienced by the patients[10].

CONCLUSION

There was a significant difference in sleep disturbance score between severe and mild-moderate CKD group. There were significant relationships of sleep disturbances in children with CKD with nutritional status, disease management therapy, parents' level of education, and severity of CKD variables. However, no significant relationship were observed with gender, age, and parents level of income variables. Independent variables with significant correlation to sleep disturbances in children with CKD were parents' level of education and CKD severity, where the most dominant variable that disturbs sleep was CKD severity.

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