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Brief communication (Original)

Prevalence of attention deficit hyperactivity disorder in children with epilepsy in a Thai Hospital

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Background: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental and behavioral disorder commonly prevalent in school-aged children. ADHD can be a comorbid diagnosis in those with epilepsy. However, the relationship between ADHD and epilepsy is complex and not entirely known.
Objectives: To compare the prevalence of ADHD between children with epilepsy at Prapokklao Hospital and healthy children in Chantaburi province, Thailand.
Methods: We recruited 73 children with epilepsy at Prapokklao Hospital and 73 age- and sex-matched healthy children at a local school in Chantaburi. The parents of all children rated their child's behavior using ADHD rating scales. In those with higher scores, a child psychiatrist at Prapokklao Hospital then diagnosed ADHD based on the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5).
Results: Children with epilepsy appeared to be from families with a lower socioeconomic status than their counterparts. Furthermore, those with epilepsy tended to have a greater probability of diagnosis with ADHD than healthy controls (19% versus 3%, $P < 0.001$). However, this finding was not significant after data were controlled for the socioeconomic status of the children.
Conclusions: There was an interesting trend towards a greater probability of ADHD diagnosis in those children with epilepsy than in healthy children. As such, epilepsy may increase the risk of these children developing ADHD. To document the prevalence of ADHD in children with epilepsy and healthy controls, both groups of children should be matched not only based on age and sex, but also socioeconomic status.

Keywords: ADHD, attention deficit hyperactivity disorder, epilepsy, prevalence, seizures

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental and behavioral disorder commonly prevalent in school-aged children with a rate of approximately 5%–10% [1-3]. According to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), children with ADHD must have at least 6 symptoms of inattention and/or hyperactivity and impulsivity for 6 months in 2 or more settings of these individuals and such symptoms should be present before 12 years of age and not better accounted for by other mental disorders [4]. ADHD and epilepsy are both common childhood disorders that can have significant negative consequences on behaviors, learning, and social functioning of affected children. Moreover, ADHD could be a comorbid diagnosis in children with epilepsy [5, 6] with a prevalence of approximately 8%–77% [7-13]. This particularly wide range of the prevalence of ADHD in those with epilepsy was thought to be the result of differences in studied populations and measures used for the diagnosis of ADHD between studies. However, there were very few studies thus far investigating the prevalence of ADHD in children with epilepsy in Southeast Asian countries, including Thailand [14, 15]. Furthermore, the relationship between ADHD and epilepsy is complex and not entirely known, particularly in Southeast Asian populations, where different ethnicity might contribute

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to the varying prevalence observed in previous studies. We therefore compared the prevalence of ADHD between children with epilepsy at Prapokklao Hospital, a secondary health care center located in Chantaburi province, east of Thailand and healthy controls from the same province.

Materials and methods

There were 110 children with epilepsy aged 4 to 18 years who were seen by a pediatric neurologist at the pediatric epilepsy clinic at Prapokklao Hospital during 2006 to 2013. Those who were born prematurely (gestational age < 37 weeks), having a birth weight <2,500 g, documented to have known syndromes, visual, and hearing impairment were excluded from this study. As such, 73 children with epilepsy were finally enrolled in this present study. We also recruited 73 healthy children who were matched to those with epilepsy based on age and sex from a local school in Chantaburi province. Those children with epilepsy and healthy controls were initially screened for ADHD by their parents using ADHD rating scales following the Clinical Practice Guidelines for management of Thai children with ADHD in 2010 [16]. In those with higher scores on the rating scales, an ADHD diagnosis was then confirmed based on the DSM-5 criteria by a child psychiatrist who was blinded to the seizures status. This study was approved by the Ethics Committee at Prapokklao Hospital (CTIREC 028/57). The parents or guardians of all children provided written informed consent for their child to participate in the study and those children who were capable provided documented assent for their participation.

Statistical analysis

Continuous and categorical variables between children with epilepsy and healthy controls were compared by using a paired *t* test and chi-square test respectively. To analyze the association between epilepsy and ADHD, the data are presented as odds ratios and 95% confidence interval in both unadjusted and adjusted analyses, where the adjustment included all variables listed in **Table 1**. $P < 0.05$ was defined as significant. All statistical analyses were performed using the Stata statistical software package (StataCorp, College Station, Texas, USA).

Results

Although the age of the children's parents was not significantly different between the groups of study children, socioeconomic status of the parents including education, occupation, and income in the epilepsy group were significantly lower than that of the control group. In the epilepsy group, most parents studied until high school level and then became temporary workers. Demographic characteristics of children with epilepsy and healthy controls are displayed in **Table 1**.

With regard to the ADHD diagnosis, 14 of 73 (19%) children in the group with epilepsy and 2 of 73 (3%) children in the control group were diagnosed as ADHD. However, the odds of having an ADHD diagnosis in those with epilepsy was decreased from 8.4 to 5.2 (95% confidence interval 0.8 to 32.6, $P = 0.08$) after adjusting for demographic characteristics as documented in **Table 1** by using logistic regression analysis.

We further investigated whether there were any differences in baseline and seizure characteristics, particularly age of onset of seizures, duration of seizure-free status, and number of antiepileptic drugs between those with epilepsy who were finally diagnosed as ADHD and those without (**Table 2**).

Table 1. Demographic characteristics of children with epilepsy and healthy controls

	Children with epilepsy (n = 73)	**Healthy controls (n = 73)**	***P***
Age (year, mean ± SD)	8.9 ± 3.6	8.9 ± 3.6	0.99
Male, n (%)	42 (56%)	42 (56%)	0.99
Father's age (year, mean ± SD)	41.3 ± 8.5	41.9 ± 6.4	0.61
Mother's age (year, mean ± SD)	36.6 ± 8.4	39.1 ± 6.6	0.055
Father's education: bachelor's degree, n (%)	6 (8%)	40 (56%)	<0.001
Mother's education: bachelor's degree, n (%)	6 (8%)	47 (65%)	<0.001
Father's occupation: government officer, n (%)	4 (5%)	22 (31%)	<0.001
Mother's occupation: government officer, n (%)	3 (4%)	25 (35%)	<0.001
Family income (baht/month)	18,123 ± 13,895	57,232 ± 32,710	<0.001

Table 2. Comparison of baseline and seizure characteristics between children with attention deficit hyperactivity disorder (ADHD) and without ADHD in the epilepsy group

	ADHD (n = 14)	Non-ADHD (n = 59)	*P*
Baseline characteristics			
Age (year, mean ± SD)	7.7 ± 1.5	9.1 ± 3.9	0.18
Male, n (%)	7 (50%)	35 (59%)	0.53
Seizure characteristics			
Age of onset of seizures (y, mean ± SD)	4.5 ± 2.4	5.7 ± 3.5	0.24
Duration of seizure-free (mo, mean ± SD)	13.2 ± 10.3	17.6 ± 8.6	0.10
Number of antiepileptic drugs (mean ± SD)	1 ± 0.7	1 ± 0.7	0.75
Father's age (y, mean ± SD)	40.5 ± 7.4	41.5 ± 8.7	0.72
Mother's age (y, mean ± SD)	35.5 ± 8.5	36.9 ± 8.4	0.57
Father's education: grade 6, n (%)	4 (29%)	23 (39%)	0.93
Mother's education: grade 6, n (%)	1 (7%)	16 (27%)	0.34
Father's occupation: temporary workers, n (%)	6 (43%)	26 (44%)	0.90
Mother's occupation: temporary workers, n (%)	6 (43%)	23 (39%)	0.61
Family income (Baht/month)	17,357 ± 9,755	18,305 ± 14,770	0.82

Although there were no significant differences in such variables between those with epilepsy who were finally diagnosed as ADHD and those without, there was an interesting trend towards a shorter duration of seizure-free status in those who were later confirmed to have ADHD.

Discussion

Children with epilepsy appeared to have a greater probability of comorbid diagnosis of ADHD than their counterparts (19% vs 3%), but the level of significance was diminished after adjusting for the socioeconomic status of their parents including education, occupation, and income. The prevalence of ADHD in those with epilepsy observed in our present study was somewhat lower than that of previous studies (24.6%–59%) [13,17-22]. Differences in the rate of ADHD reported in children with epilepsy between these studies were possibly because of at least one of the following explanations: (1) varying onset, patterns, and severity of seizures, (2) subtypes and severity of ADHD, (3) comorbid conditions also diagnosed in children with epilepsy, (4) study designs, (5) studied population (both cases and controls), and (6) sociodemographic characteristics of enrolled subjects [13, 17-22]. There were several factors including the age of onset of seizures, types of seizures or epileptic syndromes, multifocal epileptiform discharges, and duration of medical treatment with antiepileptic drugs that were considered to be associated with the increased risk of having the ADHD diagnosis [21]. Although there were no significant differences in characteristics of seizures between those with epilepsy who were later diagnosed with ADHD and those without, there was an interesting trend towards a shorter duration of seizure-free status in those with ADHD, than in those without a diagnosis of ADHD. This finding may reflect the possibility of more severe symptoms of seizures, particularly in those who were uncontrolled with antiepileptic medications, or in subjects who were poorly compliant with the treatment related to ineffective parental monitoring that could potentially put these individuals at risk of developing ADHD. However, we could not draw this conclusion based on our case–control study. As such, performing behavioral surveillance longitudinally in children with epilepsy at health supervision visits is needed.

The increased prevalence of ADHD in those with epilepsy may be plausibly because of neurological insults caused by epilepsy and different patterns of brain development, particularly decreased cortical pruning in the frontal lobe and reduced activation in the functional network involved in working memory observed in children with epilepsy and a comorbid ADHD that results in executive dysfunction, a core deficit in individuals with ADHD [19, 20, 23, 24]. Moreover, the increased prevalence of ADHD in our study may be a consequence of lower socioeconomic status in those with epilepsy compared with controls. Therefore, there were possible cumulative risk

factors for ADHD related to such sociodemographic background, including lower parental intelligence, poverty, underdiscipline, and parental psychopathology, which leads to ADHD in their children with epilepsy.

To our knowledge, this is the first case–control study examining the risk of children with epilepsy developing ADHD compared with healthy controls in Thailand. However, there were several limitations in that the case–control nature of this study may limit the reliability of data ascertainment and the direction of the relationship between ADHD and epilepsy remains inconclusive. Differences in sociodemographic backgrounds, especially parental education, occupation, and income between those with epilepsy and controls may contribute to a weaker association between ADHD and epilepsy, as observed here in the results of the logistic regression analysis. Furthermore, the prevalence of ADHD documented in healthy children in our study was relatively lower than that found in previous studies, perhaps reflecting an under diagnosis of ADHD in the control group where only parents completed the ADHD rating scales, and this may contribute to underdetection. However, the child psychiatrist who ultimately made the diagnosis of ADHD in both groups of children was blinded to the seizure status of these children. As such, this method of documenting the ADHD diagnosis could somewhat lessen this limitation for both groups of participants.

Conclusion

There was an interesting trend towards a greater probability of ADHD diagnosis in those with epilepsy than healthy controls. As such, epilepsy may increase the risk of developing ADHD in these children. To document the exact prevalence of ADHD in those with epilepsy and healthy controls, both groups of subjects should be matched not only based on age and sex, but also on socioeconomic status. Moreover, children with epilepsy should be initially screened for ADHD so that any comorbidity of ADHD will be early detected, leading to appropriate management and better outcomes for these individuals with epilepsy.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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