HK J Paediatr (new series) 2019;**24**:65-69

Original Article

Prevalence, Risk Factors and Impact of ADHD on Children with Recent Onset Epilepsy

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Abstract ***Introduction:*** Attention deficit hyperactivity disorder (ADHD) is the most common psychiatric comorbidity amongst children with epilepsy. We identified the prevalence, risk factors associated with ADHD and the impact of ADHD on seizure outcome in Hong Kong children with recent onset epilepsy. ***Methods:*** Children aged 6-18 years old with recent onset epilepsy with follow up in a regional hospital were recruited. Chinese Strengths and Weaknesses of ADHD-Symptoms and Normal-Behaviours Questionnaire was administered. Children with ADHD scores above cut-off were compared to those below cut-off for identification of demographic and seizure related variables. ***Results:*** Forty-eight children with recent onset epilepsy were recruited. Ten (20.8%) had ADHD scores above cut-off. Younger age at seizure onset (OR 1.41, 95% CI 1.05-1.88, p=0.009) and younger age at time of study (OR 1.32, 95% CI 1.01-1.73, p=0.009) were significant risk factors for ADHD. ADHD was not associated with seizure outcome, discontinuation of anticonvulsant or need of polytherapy. ***Conclusions:*** There is an increased prevalence of ADHD amongst children with recent onset epilepsy compared with the general population. Screening for ADHD in children with recent onset epilepsy is recommended.

Key words Attention deficit hyperactivity disorder; Child; Epilepsy

Introduction

Children with epilepsy are at higher risk for psychiatric comorbidities with attention deficit hyperactivity disorder (ADHD) being the most common co-morbid psychiatric disorder.[1] The reported prevalence of ADHD in children with epilepsy is around 30-40% in the western population. A recent study in Taiwan also showed an increased risk of ADHD in Asian children with epilepsy with ADHD symptoms seen in 24.6% of children with epilepsy.[2]

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Received May 15, 2017

Two epidemiological studies carried out in the UK showed that children with epilepsy had a significantly higher rate of mental health disorders than the general population and children with non-neurological chronic disorders.[3] The risk of mental health disorder was further increased in children with complicated epilepsy. In the Isle of Wight Study carried out in 1970, mental health disorders were present in 29% and 58% of children with uncomplicated and complicated epilepsy, compared with 7% of children in the general population and 12% of children with non-neurological chronic medical disorders.[4] Thirty years later, Davies et al showed similar findings with a higher percentage of children with epilepsy having psychiatric disorders; 9.3% in the general population, 10.6% in non-neurological chronic medical disorder, 26% in uncomplicated epilepsy and 56% in complicated epilepsy had psychiatric disorders.[5]

Although it is well known that children with epilepsy have comorbid psychiatric diseases, the onset of these comorbid diseases in relation to the onset of epilepsy has not been well studied. Accumulating evidence suggests that

some comorbid diseases including ADHD may antedate the onset of epilepsy.[6] Underlying neurobiological abnormalities, genetic predisposition and effect of environmental factors that underlie both epilepsy and ADHD remain to be clarified.

Literature concerning the impact of ADHD on seizure outcome is scarce. This study aims to identify the prevalence, risk factors associated with ADHD and the impact of ADHD on seizure outcome in Hong Kong children with recent onset epilepsy.

Methods

This is a prospective cohort study. Children aged 6-18 years old with recent onset epilepsy (≤2 years duration) with follow up in a regional hospital were recruited between January to July 2010. Children attending special schools were excluded. Chinese Strengths and Weaknesses of ADHD-Symptoms and Normal-Behaviours Questionnaire (Chinese SWAN) was administered to all participants on follow up. It was completed by their parents and returned to our neurology nurse.

The Chinese SWAN rating scale has previously been validated and applied in the local population.[7] This is a 19-item questionnaire with a 7-point response for each item, ranging from +3 (far below average) to -3 (far above average). The cut-off score for the Chinese SWAN rating scale was 1.65SD above the mean scores calculated from local community data.[7] Community data was obtained from the validation study of the Chinese SWAN[7] and included randomly selected children aged 6-12 years from government funded primary schools across Hong Kong. Schools for children with mental or physical disabilities were excluded.

To evaluate socio-demographic and seizure-related variables, children with scores above the cut-off were included as ADHD cases and compared to controls, children with scores below the cut-off.

Seizure aetiology was classified according to the International League Against Epilepsy (ILAE) classification as genetic, structural/metabolic and unknown origin.[8] All patients received neuroimaging including CT brain or MRI brain. Genetic tests were carried out by the Clinical Genetics Service of the Department of Health in selected patients (e.g. a positive family history of epilepsy, dysmorphic features or developmental delay). Metabolic tests were performed for individual cases according to clinical indication. Good seizure outcome was defined as seizure free on medication for 1 year or more.

Demographic data including parents' education level, parents' employment status, type of housing and whether family is on comprehensive social security assistance (CSSA) were obtained through interview. Seizure characteristics including age of seizure onset, type of seizure (generalised, focal, unknown), aetiology and epilepsy syndrome classification, history of status epilepticus, EEG finding, neuroimaging finding, antiepileptic drugs used and seizure outcome were obtained through medical records. We analysed seizure outcome at the last follow up before July 2013.

Approval from regional hospital ethics committee was obtained prior to the study.

Statistical Analysis

Data processing and analysis was performed using SPSS version 11.0. Student's t-test was used for continuous variables and chi-square test or Fisher's exact test was used for categorical variables. Logistic regression was used for multivariate analysis. P-value ≤0.05 was considered significant.

Results

Forty-eight children (28 females and 20 males) with recent onset epilepsy were recruited. Their mean age at the time of recruitment was 12.1±3.4 years. The mean duration of follow up was 4.3±0.7 years.

Socio-demographic data is depicted in Table 1. Seizure type according to the ILAE 2017 classification[9] was generalised onset motor in 17 (35%), generalised onset non-motor in 8 (17%), focal onset with impaired awareness motor in 19 (40%), focal onset with impaired awareness non-motor in 2 (4%) and unknown onset motor in 2 (4%). Seizure aetiology was genetic in 13 (27%), structural/metabolic in 9 (19%) and unknown in 26 (54%). Nine patients had medical comorbidities: asthma (1), cataract (1), scoliosis (1), pervasive developmental disorder (1), obesity (1), ovarian tumour (1), hearing loss (1), obstructive sleep apnoea syndrome (1) and limited intelligence (1).

Ten (20.8%) children, 5 girls and 5 boys had ADHD scores above cut-off, of which 7 had scores above cut-off in the hyperactive-impulsivity domain and 3 in combined scores. Four patients had psychiatric assessment according to clinical needs and two were put on stimulant medication.

One patient had ADHD diagnosed prior to recruitment into this study but did not require medication. Combined, inattentive and hyperactive-impulsive scores in girls was -2.12 (SD 3.32), -0.63 (SD 0.94), -1.1 (SD 1.34) and in boys -1.19 (SD 2.99), -0.43 (SD 0.98), -0.31 (SD 1.00) respectively. Hyperactive-impulsive subtype scores were significantly higher in boys than girls (p=0.037).

Table 2 depicts the socio-demographic and seizure related variables of cases and controls.

Age at time of study was younger in cases than controls, 10.1±2.2 years versus 12.6±3.5 years (OR 1.32, 95% CI 1.01-1.73, p=0.009). More children with ADHD lived in rented housing (80% vs. 46.9%), were on comprehensive social security assistance (CSSA) (25% vs. 18.9%) and had medical co-morbidities (30% vs. 16.2%) although the difference did not reach statistical significance.

Regarding seizure related variables, children with ADHD had a younger age of seizure onset than controls, 7.5±3.1 years and 11.1±3.6 years respectively (OR 1.41, 95% CI 1.05-1.88, p=0.009). Frequent seizures (seizures occurring weekly or more frequently) were more common in children with ADHD (55% vs. 26%) but the difference was not of statistical significance. Other clinical variables were not of statistical significance.

The impact of ADHD on seizure outcome assessed by seizure control and anticonvulsant requirement is shown in Table 3. Thirty-five children (72.9%) in the entire cohort had good seizure outcome (seizure free on medication for 1 or more years) and there was no statistical difference between ADHD group and control group in achieving good seizure control. There was also no statistical difference between the ADHD and control groups in whether anticonvulsants could be stopped and the need for multiple anticonvulsants for seizure control.

Table 1 Social demographic features of sample

Social demographic feature (n=48)	
Sex	
Male (no.)	20
Female (no.)	28
Mean age	
Years ± SD	12.1±3.4
Father's educational level	
University or above (%)	9.8
Mother's education level	
University or above (%)	4.5
Father's employment status	
Economically inactive (%)	22
Mother's employment status	
Economically inactive (%)	47.7
Housing	
Rented accommodation (%)	47.9
Comprehensive social security assistance scheme (%)	18.9

Discussion

Children with epilepsy are at a higher risk of developing ADHD. An increased prevalence of ADHD ranging from 29.1 to 38% has been reported in children with chronic

Table 2 Socio-demographic and seizure related variables of cases and controls

	Case N=10	**Control N=38**	**P-value**
Age			
Mean (SD) years	10.1 (2.2)	12.6 (3.48)	0.009
Father's educational level			
University or above (%)	0	12.5	0.355
Mother's educational level			
University or above (%)	0	5.9	0.593
Father's employment status			
Economically inactive (%)	22.2	21.9	0.650
Mother's employment status			
Economically inactive (%)	30	52.9	0.285
Rented accommodation (%)	80	46.9	0.068
CSSA (%)	25	18.9	0.511
Co-morbidity (%)	30	16.2	0.285
Age at seizure onset			
Mean (SD)	7.46 (3.1)	11.1 (3.58)	0.009
Frequent seizures at onset (%)	55	26	0.100
Seizure type			
Generalised (%)	66.6	51.4	0.478
Seizure aetiology			
Genetic (%)	30	26	0.551
Structural metabolic (%)	20	18	0.611
Unknown (%)	50	55	0.521
Status epilepticus (%)	0	2.6	0.809
Febrile convulsion (%)	22.2	10.5	0.322
EEG abnormalities (%)	88.9	89.5	0.673
MRI abnormalities (%)	37.5	43.5	0.552

epilepsy[10-12] which is not seen in children with other long term medical illnesses.[5] Children with newly diagnosed epilepsy have also been reported to have an increased prevalence of ADHD,[4] and ADHD symptoms may even antedate the onset of the first seizure.[11] Chou et al reported a bidirectional association between epilepsy and ADHD.[13] Possible common neurobiological processes which may be responsible for the development of both ADHD and epilepsy are still to be identified.

The prevalence of ADHD in our cohort of children with recently diagnosed epilepsy is 20.8%. This figure is higher when compared to the general childhood population. ADHD had been reported in 6.1% of Chinese schoolboys.[14] Hermann et al reported a significantly higher rate of ADHD (31.5%) in children with epilepsy compared to controls (6.4%).[11] The discrepancy in frequency can be partly explained by variability in methodology, socioeconomic and geographic factors.

ADHD in children with epilepsy show different characteristics to ADHD seen in the general population. Within our cohort of children with epilepsy, there was an equal sex distribution amongst cases with ADHD which differs from the general population where there is a male predominance. This phenomenon is similar to that reported by Dunn et al.[10] This suggests that there are other factors predisposing to ADHD in children with epilepsy which is common to both sexes.

In the general population, ADHD-combined subtype is the most common type. In children with epilepsy some studies have reported a higher proportion of the inattentive subtype,[3,10] while an equal proportion of inattentive and hyperactive-impulsive subtype has also been reported.[15] In our study the most common subtype was hyperactive/impulsive type. Seven out of ten had hyperactive-impulsive type and three out of ten had combined type of ADHD. However, the above observation is limited by the relatively small sample size.

Early age of seizure onset was a significant risk factor for ADHD in this study. This can be explained by the adverse effect of epileptiform discharges on the developing brain. Attention control involves a complex interaction of networks located in multiple areas of the brain including the frontal, parietal, midbrain and thalamic areas.[16] Cortical pruning and increase in myelination occurs throughout the brain during childhood with large changes happening in the frontal and parietal regions during late childhood and early adolescence.[11] Disruption to these neurodevelopmental processes may affect the normal formation and function of the attention networks.

Although certain areas of the brain such as the frontal lobes are associated with control of attention, seizure localisation was not a significant risk factor for ADHD in this study. This is probably related to the global impact of epilepsy on the brain. This is consistent with findings from other studies which showed no significant difference between localisation related and generalised epilepsies.[11]

Comorbid ADHD did not have a significant negative impact on seizure outcome in our cohort. There was no increase in the need for multiple drugs for seizure control. There was also no significant difference in achieving good seizure outcome (seizure free for 1 or more years) or the ability to stop anticonvulsants between cases and controls. However the duration of follow up was short and long term seizure outcome could not be assessed.

Chinese Strengths and Weaknesses of ADHD-Symptoms and Normal-Behaviours Questionnaire (Chinese SWAN) was used. This has been validated in a Hong Kong Chinese population.[7] The advantage of using this questionnaire is that the normative score compares well with that of western counterparts unlike other scales which produced a higher questionnaire-rated hyperactivity in the Hong Kong population. The Chinese SWAN questionnaire is phrased in a neutral manner and compares a child's behaviour to that of their peers instead of focusing on the presence of problematic behaviour. It also uses a 7 point response scale allowing for neutral responses. Other questionnaires phrased questions with an emphasis on the presence or frequency of problematic behaviour. In Chinese culture, non-conforming behaviours are less well tolerated and often regarded as problematic thus giving rise to a higher score.[7]

This study is unique in that the prevalence of ADHD in children with epilepsy in our local population has not been reported before. Most data in the literature report ADHD in children with chronic epilepsy. There is limited literature on ADHD in children with recent onset epilepsy. This study adds to the literature on the increased prevalence of ADHD in children with recent onset epilepsy. The impact of ADHD on seizure outcome has also not been reported in the literature before.

Table 3 Seizure outcome of cases and controls

	Case	Control	P-value
Seizure outcome Good (%)	90	68.4	0.052
Off anticonvulsant (%)	60	34.2	0.081
Polytherapy (%)	10	15.8	0.596

Limitations of this study is that there is a relatively small sample size. Despite a modest sample size we were able to identify age of seizure onset as a significant risk factor for development of ADHD. However no independent risk factor could be retained on multivariate analysis suggesting a multi-factorial cause for ADHD. Future studies with a larger sample size may be beneficial in identifying further risk factors for the development of ADHD in children with recent onset epilepsy. Extending the study period over a longer duration may also give more information on seizure outcome.

ADHD has a negative impact on a child's academic[17] and social performance. Children with epilepsy and ADHD have poorer health related quality of life scores and decreased adaptive abilities.[18] It also poses a significant psychological burden on the family members of children with ADHD.[19] Proactive screening for ADHD is recommended not only for chronic epilepsy but also for those with recent onset epilepsy.

Conclusion

There is a higher prevalence of ADHD amongst children with epilepsy than the general population. This increase in prevalence is demonstrated early in the course of disease. Earlier age of onset of epilepsy is a risk factor for ADHD symptoms. As ADHD has a negative impact on children's academic and social performance, it is important to screen for presence of ADHD symptoms in this group of patients and offer appropriate intervention.

Acknowledgement

I would like to acknowledge Dr TS Lai and Dr SM Lam from the Department of Child Psychiatry, Castle Peak Hospital, Hong Kong, for their support in ADHD assessment tools. I would also like to acknowledge Ms Lai-Han Yip, our paediatric neurology nurse, for her help in coordinating the questionnaire returns.

Declaration of Interest

There are no conflicts of interest.

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