ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH IDIOPATHIC GENERALIZED EPILEPSY

By

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ABSTRACT

Background: *About 5.8% of school-aged children worldwide suffer from Attention deficit hyperactivity disorder (ADHD), which is a complex neurodevelopmental illness. Many researchers reported an increased prevalence of ADHD among the epileptic paediatric population.*

Aim of the Work: *To evaluate the prevalence rate and characteristics of ADHD in children diagnosed with idiopathic generalized epilepsy (IGE).*

Patients and Methods: *This cross-sectional comparative study was carried out in AlAzhar University Hospital (Assiut branch) during the period from 1 May 2020 to 30 April 2021 on 40 children (aged from 4 to 12 years), full clinical history was obtained this includes (Medical history of epilepsy, age of onset, type, and severity, Past history including: prenatal, natal, and postnatal, Social and family history, Nutritional history and developmental milestone, Antiepileptic medications if present: name of the drugs, doses, duration of treatment, and its response. Lastly screening by DSM IV for detection of ADHD. The children divided into two groups. Group 1 included 20 children with IGE before starting anti-epileptic drugs; group 2 included 20 children with IGE after 6 months of anti-epileptic drugs.*

Results: *our results indicated that, there was a statistically significant difference ($p<0.05$) between studied groups regarding ADHD in Group I and Group II. The mean ADHD index values were 7.70 ±5.41 and 4.70 ±1.69 among group I, group II, respectively. Also, the results indicated, statistically significant difference between the studied groups regarding to ADHD index ($p=0.038$), before treatment and after treatment. The incidence of ADHD in our study cases was about 42% (17 from 40 among group I: 12 cases - among group II: 5 cases).*

Conclusion: *our results concluded that, there is a decrease of incidences of ADHD among Group II than Group I. So these results indicated that, the treatment of IGE is beneficial as it decreased the incidences of ADHD.*

Recommendation: *Screening of epileptic children for early detection of ADHD. Rapid diagnosis of epilepsy and treatment is required for decreasing the incidences of ADHD.*

Keywords: *Generalized epilepsy, ADHD, children, pediatric.*

INTRODUCTION

Epilepsy is a neurological condition characterized by abrupt repeated episodes of sensory disturbance, consciousness loss, or convulsions linked with irregular brain electrical activity. The definition and terms of epilepsy have significantly changed during recent years. Classification of epilepsies was revised by International League against Epilepsy (ILAE) classification depends upon **(Scheffer et al.,)**[(1)].

According to a recent systemic review and meta-analysis, the point and lifetime prevalence of active epilepsy were reported to be 6.38 and 7.6 per 1000 persons, respectively. There was no difference in the epilepsy prevalence between both genders or age groups. The most common types of epilepsy were generalized seizures as well as epilepsy of unknown etiology[(2)].

Attention deficit hyperactivity disorder (ADHD) is a developmental neurological disorder characterized by lack of attention and distractibility, either with or without hyperactivity. The American Psychiatric Association's Diagnostic and Statistical Manual, Fifth Edition (DSM-5) describes three types of ADHD: inattentive, hyperactive-impulsive, as well as a combination of both[(3)].

Patients with ADHD have a chronic history of lack of attention, either with or without hyperactivity, which interferes with a child's functioning or growth. The problems usually manifest themselves in two or more aspects of a child's life: home, work, education, and social connections[(4)].

Globally, the ADHD prevalence rate is 7%–9% among the general children population; of them, some cases tend to experience symptoms into adolescence, with boys being diagnosed to have ADHD twice as often as girls. ADHD has a significant genetic factor, with first-degree relatives of those with ADHD being at increased risk (5). ADHD can be a hardship for family members, friends, and teachers, and it is often associated with substantial financial strain on families and public health services[(6)].

A recently published population-based survey of the pediatric population diagnosed with active epilepsy showed that a number of neurobehavioral co-morbidities were noted in the majority of epileptic children (80%). Besides, ADHD was noted in about one-third of patients. Intellectual disability and autism spectrum disorders were noted in 40% and 21% of patients, respectively[7].

Previous literature suggests that the severity of epilepsy increases the risk of ADHD since co-morbidity has been noted in benign and refractory epilepsy in children. The aetiology of epilepsy, disease duration, frequency of seizures, seizure management, as well as utilization of anti-epileptic drugs (AEDs) are all essential factors linked with both neuropsychological as well as neurobehavioral issues among children patients with epilepsy and ADHD[8].

Aim of the Work

The aim of this study is to evaluate the prevalence rate and characteristics of ADHD in children diagnosed with idiopathic generalized epilepsy (IGE) and the effect of treatment on the incidences of ADHD.

1. A written informed consent was obtained from parents/legal guardians of the included patients.
2. An approval by the local ethical committee was obtained before the study.
3. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
4. All the data of the patients and results of the study are confidential, and the parents/legal guardians have the right to keep it.
5. The authors received no financial support for the research, authorship, and/or publication of this article.

PATIENTS AND METHODS

This cross-sectional comparative study was carried out in AlAzhar University Hospital (Assiut branch) during the period from 1 May 2020 to 30 April 2021 on 40 children (aged 4 to 12 years) selected by simple random method, the children divided into two groups. Group 1 included 20 children with IGE before starting anti-epileptic drugs; group 2 included 20 children with IGE after 6 months of anti-epileptic drugs.

Ethical consideration:

Inclusion criteria: We included children meeting the following criteria:

a. Children with manifested idiopathic generalized epilepsy.
b. Age group between 4 and 12 years of either gender.
c. Children with no neurologic disabilities, or other underlying health issues.

Exclusion criteria: We excluded:

a. Children with any type of epilepsy other than idiopathic generalized epilepsy.
b. Children with any other identifiable childhood physical disorder (protein-energy malnutrition, nephrotic syndrome, etc.).
c. Children with impaired cognition, perinatal asphyxia, history of less than1.5 kg birth weight, severe head trauma, lesions of the brain, or other significant risk factors for neurologic disorders that may lead to the emergence of ADHD.

All children were subjected to:

Full clinical history: History of epilepsy, including: age of onset, type, and severity, past history including prenatal, natal, and postnatal, social and family history, nutritional history and developmental milestone, AEDs if present: name of the drugs, doses, duration of treatment, and its response and manifestations of attention deficit and hyperactivity and the time of its appearance.

Clinical examination: The general examination includes, anthropometric measurements, complexion, and any visible anomalies. Systematic physical examination, complete neurological examination to assess the neurological condition.

The psychometric study, including: The DSM-4 text revision (DSM-IV-predominantly inattention type was used.

Operational design: The principal investigator introduced him to all included participants' parents. After explaining the study's objectives and potential benefits, he invited them to participate in this study.

Statistical Analysis:

We used the Statistical Package for the Social Sciences (IBM SPSS) software, version 20.0 (Armonk, NY: IBM Corp), for statistical analysis. We described the qualitative data as frequencies and percentages. To assess the data normality, the Kolmogorov-Smirnov test was used. We presented the continuous data as mean and standard deviation (SD) in case of normally distributed

data or median and interquartile range (IQR) in case of not normally distributed data. We assessed the significance of findings at the 5% level.

RESULTS

Table (1): Comparison between the studied two groups according to demographic data

Demographic data	Group I (n = 20)		Group II (n = 20)		Test of Sig.	P
Age						
Min. – Max.	3.0 – 12.0		3.0 – 11.0		F=	0.082
Mean ± SD.	7.0 ± 2.75		7.20 ± 2.57		2.609	
Median (IQR)	7.0 (4.5 – 9.0)		8.0 (5.0 – 9.0)			
Sex	No.	%	No.	%		
Male	11	55	6	30		0.272
Female	9	45	14	70	2.606	
Birth order among siblings						
Min. – Max.	1.0 – 4.0		1.0 – 4.0		H=	0.662
Mean ± SD.	2.45 ± 1.23		2.50 ± 1.10		0.824	
Median (IQR)	3.0 (1.0 – 3.5)		3.0 (1.5 – 3.0)			

X^2: Chi-square test; F: F for ANOVA test; H: H for Kruskal Wallis test; IQR: Inter Quartile Range; SD: Standard deviation; p: p-value for comparing between the studied groups

This table shows insignificant differences regarding to demographic data between both groups.

Table (2): Comparison between the studied two group according to the medical history of epilepsy

Medical history of epilepsy	Group I (n = 20)		Group II (n = 20)		Test of Sig.	p
	No.	%	No.	%		
Age of onset						
Min. – Max.	3.0 – 12.0		2.0 – 10.0		U=	0.114
Mean ± SD.	7.0 ± 2.75		5.90 ± 2.57		140	
Median (IQR)	7.0 (4.5 – 9.0)		7.0 (4.0 – 8.0)			
Severity according to National Hospital Scale						
Mild	7	35	7	35		0.53
Moderate	8	40	6	30	0.619	
Severe	5	25	7	35		
Use of anti-epileptic drugs						
Polytherapy	13	65	15	75		0.39
Monotherapy	7	35	5	25	0.476	

X^2: Chi-square test; t: Student t-test; U: Mann Whitney test; IQR: Inter Quartile Range; SD: Standard deviation; p: p-value for comparing between the studied groups; *: Statistically significant at $p \leq 0.05$

This table shows insignificant differences regarding to medical history of epilepsy between both groups.

Table (3): Comparison of EEG changes in both group.

	Group I		**Group II**		Chi^2	**p**
EEG findings						
Normal	17	85	10	50	**15.22****	**>0.001****
Abnormal	3	15	10	50		
Total	20	100	20	100		
Type of abnormality						
Focal	2	10	7	35	**5.17****	**0.53**
Generalized	1	5	3	15		
Total	3	15	10	50		
Site of focal abnormality						
Frontal	0	0	0		**11.22****	**0.114**
Occipital	1	5	5	25		
Parietal	0	0	1	5		
Temporal	2	10	4	20		
Total	3	15	10	50		

** = Significant at (P < 0.001)

This table shows highly significant differences regarding to EEG changes between both groups.

Table (4): Comparison between the studied two group according to ADHD index

ADHD index	Group I (n = 20)	Group II (n = 20)	P
Min. – Max.	1.0 – 19.0	1.0 – 7.0	0.01**
Mean ± SD.	7.70 ± 5.41	4.70 ± 1.69	
Median (IQR)	6.0 (3.5 – 12.0)	5.0 (4.0 – 6.0)	
Sig. bet. Groups	p_1=0.095, p_2=0.402, p_3=0.012*		
Number of affected cases	12	5	

Cut point for ADHD index: (6).

Total number of affected cases in our study 17 from 40 – 12 among group I and 5 among group II about 42%.

This table shows highly significant differences regarding to ADHD index between both groups.

DISCUSSION

The main aim of this study was to assess the prevalence and characteristics of Attention Deficit Hyperactivity Disorder (ADHD) in children with idiopathic generalized epilepsy and effect of treatment of IGE on ADHD symptoms.

Epilepsy is the most common neurological disorder characterized by sudden, temporary, and recurrent epileptic seizures, with an incidence rate of 0.5–1% in children and adolescents. Epilepsy is a major public health concern, which may cause disability, interfering with the ability to learn, and negative impact on social and psychological function. The situation is even worse when attention deficit hyperactivity disorder (ADHD) occurs, a common comorbidity of childhood epilepsy[17]

Idiopathic generalized epilepsy (IGE) is a group of epileptic disorders that are believed to have a strong underlying genetic basis. IGE refers explicitly to the epilepsy syndromes: juvenile myoclonic epilepsy (JME), juvenile absence epilepsy (JAE), childhood absence epilepsy (CAE), and generalized tonic-clonic seizures alone. Patients with idiopathic generalized epilepsy, by definition, have no evidence of structural brain lesions on MRI, as well as a lack of symptoms and signs interictally, eliminating most of the etiological groups[18].

ADHD is a common developmental disorder in childhood with three subtypes, including inattentive (ADHD-I), hyperactive/impulsive (ADHD-HI), and combined type (ADHD-C). The incidence of ADHD is 3–7% in general school–aged children. However, the prevalence of ADHD ranges from 8 to 77% in children with epilepsy, based on different samples and diagnostic criteria. As compared with epileptic children, the quality of life is dramatically decreased in children with epilepsy and comorbid ADHD. Early recognition and diagnosis of coexisting ADHD, and timely intervention and treatment measures are necessary for the improvement of the prognosis in this group of children[19].

As regard demographic data, among group I the mean of ages was 7.0 (± 2.75 SD) with range (3.0 – 12.0), there were 11(55%) males, 9(45%) females, the mean of order among siblings was 2.45(± 1.23 SD) with range (1.0 – 4.0) Among group II the mean of ages was 7.20 (±2.57 SD) with range (3.0 – 11.0), there were 6(30%) males, 14(70%) females, the mean of order among siblings was 2.50(±1.10 SD) with range (1.0 – 4.0). There was no statistically significant difference between studied groups.

As regard demographic data our result cleared that the group II is the group of higher age followed by group I respectively the result cleared also the female more suspected than male.

The present study showed that there was high statistically significant difference between studied groups as regarded Current EEG changes.

Our results clear that treatment of children with IGE and ADHD cause significant results in curing. ADHD co-morbidity was more remarkable in children who not received AEDs than children treated with AEDs. There was a consider association between the frequency of AEDs used to manage cases and lower risk of ADHD. Also the result indicate that EEG finding after change from abnormal EEG to normal EEG and the treatment of children with IGE and ADHD is very benficial in reducing the symptoms of ADHD (findings, abnormality type and site of focal abnormalities this results may be attributed to the treatment affected by many factors as genetic predispositions, dysregulation of the noradrenergic system, subclinical epileptiform discharges, epileptic seizures, the consequences of AEDs, as well as psychosocial influences[10, 12, 13].

The current study showed that there were 20(100%) of groups I and II had good prenatal, natal and post-natal history. There was no statistically significant difference between studied groups as regard social history, family history and nutritional history. There was no statistically significant difference between studied groups as regard weight and Height.

Our results were in line with study of **[Breen, D. P., Högl, B., Fasano, A., Trenkwalder, C., & Lang, A. E. (2018)]**, as they reported that there was no statistically significant difference between their studied groups regarding family history.

A multitude of studies done in both community and hospital settings has demonstrated that ADHD has a greater prevalence in CWE (children with idiopathic epilepsy) when compared to the general population. In the study of **[Brikell, I. et al. (2017)]**, which was hospital based, 22 out of the calculated sample size of 94 were found to have features of ADHD, representing 23.4% of the total sample. This figure was found to be statistically significant, closely approximating the prevalence of 26.4% propounded, in their study in epilepsy clinics. The high prevalence of ADHD in CWE thus advocates the need to sensitize physicians and pediatricians to aggressively look for ADHD in CWE.

CONCLUSION

Patient with IEG were liable to be affected with ADHD more than normal population.

AEDs decrease the incidence of ADHD in children with IGE.

RECOMMENDATIONS

Screening of epileptic children for early detection of ADHD. Rapid diagnosis of epilepsy and treatment is required for decreasing the incidences of ADHD.

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دراسة اضطراب نقص الانتباه وفرط الحركة لدى الأطفال الذين يعانون من الصرع المعمم مجهول السبب

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يعرف الصرع بأنه اضطراب عصبي يتميز بنوبات متكررة مفاجئة من الاضطراب الحسي، وفقدان الوعي، أو التشنجات، المرتبطة بالنشاط الكهربائي غير الطبيعي في الدماغ. وجدت مراجعة منهجية أن معدل انتشار الصرع عالميا 6.38 لكل 1000 شخص ولم يختلف انتشاره بين الجنسين أو حسب الفئة العمرية وكان للصرع المعمم مجهول السبب أعلى معدل انتشار. الصرع المعمم مجهول السبب هو مجموعة من اضطرابات الصرع التي يعتقد أن لها أساس وراثي قوي. المرضى الذين يعانون من الصرع المعمم مجهول السبب لا يوجد دليل على وجود آفات دماغية هيكلية بهم بإستخدام التصوير بالرنين المغناطيسي، بالإضافة إلى عدم وجود أعراض وعلامات بين العظام. أبلغ الباحثون عن أمراض نفسية كبيرة مرتبطة بصرع الأطفال وأن المرضى الذين يعانون من الصرع مجهول السبب الذي قد يكون لديهم تواتر منخفض من المشاكل العصبية والنفسية والسلوكية. اضطراب نقص الانتباه وفرط الحركة هو اضطراب نمائي عصبي شائع في مرحلة الطفولة وبعضهم قد يستمر في ظهور أعراضه في مرحلة البلوغ. طبقا للدليل التشخيصي والإحصائي لجمعية

الطب النفسي الأمريكية، يعاني هؤلاء المرضي من نمط دائم من عدم الانتباه مع أو بدون فرط النشاط الذي يتعارض مع عمل أو نمو الطفل. يبلغ معدل انتشار اضطراب فرط الحركة ونقص الانتباه من 7٪ إلى 9٪ في عموم الأطفال و يمكن أن يضع تأثير هذا المرض عبئًا على أفراد الأسرة والمعارف والمعلمين. وجدت دراسة حديثة أن اضطراب فرط الحركة ونقص الانتباه كان موجودًا في 33٪ من مرضى الصرع النشط و يعتقد الباحثون أن مرض الصرع يزيد من الاستعداد لهذا الاضطراب حيث أن مرضى الصرع كان لديهم معدلات أعلى مرتين إلى ثلاث مرات للإصابة باضطراب فرط الحركة ونقص الانتباه. مؤخرا وجدت العديد من الدراسات السكانية أن معدلات انتشار اضطراب فرط الحركة ونقص الانتباه بين 23٪ و 40٪ لدى مرضى الصرع مقارنة بانتشار 6٪ -12٪ في الشواهد. كان الهدف الرئيسي من هذه الدراسة هو تقييم انتشار وخصائص اضطراب فرط الحركة ونقص الانتباه لدى الأطفال المصابين بالصرع المعمم مجهول السبب.

كانت هذه دراسة مقطعية أجريت في مستشفى جامعة الأزهر بأسيوط. تم تضمين أربعين طفلاً (تتراوح أعمارهم من 4 إلى 12 عامًا) في الفترة من مايو 2020 حتى أبريل 2021 ، وتم تقسيمهم إلى مجموعتين: المجموعة 1: تضمنت 20 طفلًا يعانون من الصرع المعمم مجهول السبب قبل البدء في تناول الأدوية المضادة للصرع. المجموعة الثانية: تضمنت 20 طفلاً يعانون من الصرع المعمم مجهول السبب بعد 6 أشهر من تناول الأدوية المضادة للصرع. تراوحت مدة الدراسة من

6 إلى 12 شهرًا. وقد كشف النتائج الرئيسية للدراسة ما يلي: توجد فروق ذات دلالة إحصائية بين المجموعات المدروسة فيما يتعلق بالمشاكل المعرفية والمعارضة/ قلة الانتباه وفرط النشاط والكمالية والمشاكل الاجتماعية.

بناءً على النتائج التي توصلنا إليها، نوصي بإجراء مزيد من الدراسات حول حجم العينة الأكبر وعلى نطاق جغرافي كبير للتأكيد على استنتاجنا.