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Comparison of cognitive function, socioeconomic level, and the health-related quality of life between epileptic patients with attention deficit hyperactivity disorder and without

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Abstract

Background: Epilepsy is one of the most common neurological conditions. Attention deficit hyperactivity disorder (ADHD) in children with epilepsy proves to be very common. Both epilepsy and ADHD impair quality of life. We aimed to evaluate cognitive function, socioeconomic level, and quality of life (QOL) among children with ADHD and epilepsy. A total of 100 children were divided into 5 groups (20 children/group) as (I) epilepsy, (II) ADHD with epilepsy, (III) ADHD with EEG changes, (IV) ADHD without EEG changes, and (V) control. Children aged between 6 and 11 years were recruited for this study. Early Childhood Epilepsy Severity Scale (E-Chess), Conners' Parent Rating Scale (CPRS), Wechsler Intelligence Scale for Children-3rd edition (WISC-III), socioeconomic scale for assessment of social burden and socioeconomic classes, and PedsQL (quality of life measure) assessed.

Results: Children with ADHD and epilepsy had the lowest PedsQL total scores and lower scores than other groups especially in performance IQ score. The highest percentage of low socioeconomic class (25%) was observed in the group of ADHD with epilepsy and the group of epilepsy.

Conclusion: ADHD with epilepsy is associated with low performance IQ, poor socioeconomic level, and quality of life. Pediatric Quality of Life Inventory scores show significant correlation with total IQ score in the group of ADHD with epilepsy.

Keywords: Epilepsy, ADHD, Quality of life, Socioeconomic, Intelligence

Background

Epilepsy is the most common neurological condition affecting approximately 65 million people worldwide [1], and it also affects nearly 3.2–5.5/1000 children in the developed world [2].

Epilepsy in children is associated with marked impairment of cognitive functioning [3], increasing the risk of attention deficits and impairing executive functioning [4].

Executive functions are various high-level skills, which allow for flexibility in goal-directed behavior [5], such as response inhibition, working memory, and set-shifting [6]. Additionally, AEDs have been affirmed to increase the risk of cognitive impairment and executive dysfunction in young people with epilepsy [7–9].

Children with epilepsy (CWE) suffer from epileptic seizures and from executive, behavioral, and emotional issues [10]. Deficits in executive functioning are associated with poor health-related quality of life (HRQOL) in these children [11, 12].

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Moreover, the lives of CWE are constantly threatened by physical injuries, such as falls and burns, caused by epilepsy. The fear of acquiring these injuries prevents them from engaging in outdoor activities [13]. They may also need to isolate themselves from society because of the stigma associated with epilepsy [14].

Attention-deficit/hyperactivity disorder (ADHD) is one of the most widespread disorders in CWE [15, 16]. ADHD is generally characterized by persistent inattention, hyperactivity, and impulsivity [17]. Furthermore, several studies found that ADHD children may have electroencephalogram (EEG) abnormalities such as interictal epileptiform discharges (IEDs) or localization of IEDs foci [18, 19]. Lee et al. evaluated the effect of epileptiform discharges in ADHD by comparison between group of ADHD patients with EEG changes and group of ADHD patients with normal EEG. It was found that interictal epileptiform discharges were associated with seizures in children with ADHD [20]. Moreover, a study showed that valproate decreased EEG paroxysm abnormality as well as ADHD scores [21]. This represents pathophysiology overlapping between ADHD and epilepsy [20].

Patients with ADHD suffer from many cognitive deficits because they lack attention and strategic flexibility, struggle to control and inhibit behavior, and have poor planning and working memory capabilities [22–26].

Similar to epilepsy, ADHD is associated with impairment in many aspects of the lives of children who have it, including academic performance, social functioning, and subsequently impaired overall quality of life (QOL) [27–29]. Additionally, ADHD may have a significant economic consequence for children who have it, their families, and society [30].

Hence, epilepsy and ADHD affect the QOL [31]. In the medical researches, "quality of life has become an important measure of outcomes in both research and clinical settings" [32].There is positive association between QOL impairment and severity of disorder [33]. So, many studies are examining the QOL of patients with epilepsy or ADHD worldwide, particularly in developed countries. However, due to the influence of various variables, such as demographic features and socioeconomic and clinical presentations, the QOL of these patients differs from country to country [30].

Method

Aim of study

We aim to compare the cognitive function, socioeconomic level, and QOL among epileptic children with ADHD and without.

Study design

This is a case-control study.

Site of the study and selection of participants

One hundred children were between 6 and 11 years of age in the period between September 2018 and October 2019. The sample size was calculated with statistical power of 95% by using Epi info 7. Participants were recruited from the Child Psychiatry Clinic of Neurology and Psychiatric Hospital, Assiut University. The children were divided into five groups, namely, as group (1) children with epilepsy alone, group (2) children with ADHD with epilepsy, group (3) children with ADHD with EEG changes, group (4) children with ADHD without EEG changes, and group (5) healthy controls, and each group included 20 children.

We consider using EEG as tool for differing ADHD group as there was evidence that ADHD with EEG changes can be transferred to ADHD with epilepsy after few years [20]. Also, categorizing children with epilepsy by time of seizure onset showed that 15.8% of them were ADHD in early onset of seizures compared to 8.1% in those with newly diagnosed seizures. These results suggested that seizures or subclinical epileptiform bursts play an important role in the development of attention disorders [34]. So, there is bidirectional relationship between both diseases. Our classification to ADHD groups by EEG will help in clarifying this relationship and also, clarify if there is difference between ADHD with EEG changes and without regarding cognitive function and quality of life.

The caregivers of the children and adolescents with epilepsy were interviewed for informed consent and medical information concerning epilepsy and ADHD. ADHD was diagnosed according to DSM-5 [35], and the seizure types were classified according to the International League Against Epilepsy (ILAE) criteria.

Inclusion criteria

(i) Diagnosis of ADHD and/or epilepsy was verified and confirmed on a clinical basis.
(ii) Idiopathic type of epilepsy that was confirmed on clinical basis, neurological assessment, and imaging investigations.

Exclusion criteria

(i) Children with significant intellectual disability (Wechsler Intelligence Scale IQ < 70);
(ii) Children with history or current substance use
(iii) Children with comorbid medical or other neurological conditions.
(iv) Children with other psychiatric disorders,

Patients received their medication, as ADHD children received non-stimulant medication (atomoxetine), while epileptic children received their antiepileptic drugs.

Ethical considerations
This study obtained ethical approval from the Institutional Review Board (IRB) of the Faculty of Medicine, Assiut University, with an approval number of 17200196. This study was also registered on a clinical trial with the following registration number NCT03806946. The parents signed informed consent on behalf of their children to take part in the study.

Tools
The included children were firstly assessed by semi-structured interview by using the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI KID) Arabic version [36] for psychiatric evaluation then all subjects had the following:

Electroencephalography
Conventional EEGs were obtained with eight channels and scalp electrodes placed with the international 10–20 system with bipolar and referential montages; it is a Nihon Kohen equipment model. Chloral hydrate was used to induce sleep if needed. Data analysis for EEG was done by determined location and side of none provoked paroxysmal activities, and focal activities if present.

Early Childhood Epilepsy Severity Scale (applied only for the epileptic group) [37]
The Early Childhood Epilepsy Severity Scale (E-Chess) was developed for use in the Tuberous Sclerosis 2000 Cohort Study to quantify the severity of epilepsy. The scale assesses the severity of seizures by scores on five variables. The variables are frequency of seizures, the time period over which seizures occur, the number of seizure types, the number of antiepileptic drugs used, and response to treatment. Each of these variables was given a score, with a higher score indicating greater severity. Thereafter, the scores were added up to give a total severity score that was used to indicate seizure severity in the current study. E-Chess total score ≤ 9 is associated with favorable epilepsy outcomes, while E-Chess total score > 10 is associated with drug-resistant epilepsy with poor responses.

Conners' Parent Rating Scale [38]
The Conners' Parent Rating Scale (CPRS) is a 110-item parent-rated scale that diagnoses ADHD with other behavioral disorders in children aged 6–18 years. These behavioral disorders are oppositional defiant and conduct disorders.

Wechsler Intelligence Scale for Children-3rd edition (Arabic version by [39])
Each participant was assessed using the Wechsler Intelligence Scale for Children-3rd edition (WISC-III), which is composed of 13 subtests to test the cognitive abilities of children of different dimensions. The subtest of the WISC includes questions about general knowledge, traditional arithmetic problems, vocabulary, the completion of mazes, and the arrangement of blocks and pictures. WISC-III provides scores for verbal, performance, and full-scale IQs.

Socioeconomic scale [40]
The socioeconomic scale is a tool used to assess the social burden and socioeconomic classes. It also contains four main variables: the educational level of the father and the mother, the occupation of the father and the mother, the total family income, and the lifestyle of the family.

Pediatric Quality of Life Inventory, parent–proxy report formats [41]
The Pediatric Quality of Life Inventory (PedsQL) is a questionnaire assessment tool used to evaluate the QOL of children. It is composed of 23 items that assess functions in the following four areas: physical, emotional, social, and school. The psychosocial health summary score is a computed mean of the emotional, social, and school functioning subscales of the PedsQL. The physical functioning scale is the same as the physical summary score. In addition, the computed mean of the emotional, social, school functioning, and physical scales are used to generate a total summary score. The parents of children reported their response using a 5-point Likert scale ranging from 0 = never to 4 = always, and these responses were associated with a higher score indicating a higher QOL.

Statistical analysis
The analysis was conducted using SPSS version 26. The frequency and proportion analyses were performed for qualitative variables, while quantitative variables were presented as mean ± SD. We used three different statistical tests: the chi-square test was used for analysis between categorical groups, the ANOVA test was employed to detect the presence of significant differences in the mean values for more than two groups, and the Student's t test was utilized to test the mean values between two independent groups. Furthermore, the Spearman correlation test was applied for testing correlations between quantitative variables. All the tests were two-tailed, and p values of < 0.05 were considered statistically significant.

Results
Demographic data
No statistical significance was observed regarding the age of studied groups. Males were significantly higher in all groups (p = 0.001), while the group of ADHD with epilepsy comprised 45% of males and 55% of females (see Table 1).

Table 1 Demographic features of studied group

	Epilepsy (*N* = 20) *N* (%)	ADHD with EEG changes (*N* = 20) *N* (%)	ADHD without EEG changes (*N* = 20) *N* (%)	ADHD with epilepsy (*N* = 20) *N* (%)	Control (*N* = 20) *N* (%)	*P* value
Age mean ± SD	**8.20 ± 2.462**	**7.25 ± 1.410**	**7.33 ± 1.958**	**7.65 ± 1.348**	**7.80 ± 1.436**	**0.448**
Sex						**0.002***
Male	**18 (90%)**	**18 (90%)**	**14 (70%)**	**9 (45%)**	**12 (60%)**	
Female	**2 (10%)**	**2 (10%)**	**6 (30%)**	**11 (55%)**	**8 (40%)**	

**P* value is significant

Clinical features among epilepsy groups

The clinical features among the group of epilepsy and the group of ADHD with epilepsy validate that a significant difference was observed regarding the types of seizure (*p* value = 0.035) as most of the cases were of generalized type (80% and 100%, respectively). Conversely, no significant differences were detected between the group of epilepsy and the group of ADHD with epilepsy as regards age at the onset of seizure, the duration of epilepsy, or time since the last seizure. However, it was observed that the time since the last seizure between the group of epilepsy and the group of ADHD with epilepsy was less than 1 year (65% and 50%, respectively) (Table 2).

The comparison of the EEG changes among the group of epilepsy, the group of ADHD with epilepsy, and the group of ADHD with EEG changes shows the significant predominance of unprovoked generalized paroxysmal changes in the measured EEG changes (*p* value < 0.000).

Table 3 exhibits that a significant difference exists between the group of epilepsy and the group of ADHD with epilepsy regarding the number of anticonvulsants used and the total E-Chess severity score.

Children who received one or two anticonvulsants showed the highest percentage in the group of epilepsy and the group of ADHD with epilepsy (70%, 80%, respectively).

As regards total E-Chess severity score, children with favorable outcomes (≤ 9) had the highest percentage in the group of epilepsy and the group of ADHD with epilepsy (70% and 100%, respectively).

Conners 3rd Edition Scale

All the subscales of the CPRS were significantly different in all groups. The combined type of ADHD represented the highest percentages (70% and 50%, respectively) in the group of ADHD with EEG changes and the group of ADHD with epilepsy. However, the group of ADHD without EEG changes had the highest frequency of hyperactivity type (45%).

Table 4 shows that significant differences among the studied groups in all the CPRS subscales include: inattention, hyperactivity/impulsivity, learning problems, executive functioning, defiance/aggression, and peer/family relation.

The group of ADHD with EEG changes had the worst responses in all the CPRS subscales, where highly elevated clinical ratings represented the highest proportion of all the responses followed by the group of ADHD with epilepsy and ADHD without EEG changes. In contrast, the group of epilepsy had the lowest proportion of clinical ratings in all its subscales, except for the defiance/aggression subscale (55%).

Wechsler Intelligence Scale for Children-3rd edition

No significant difference was observed between the studied groups in the IQ classification measured by the WISC-III (*p* value = 0.233).

Moreover, no statistically significant difference emerged among the studied groups in the mean values of verbal and total IQ scores ($p > 0.05$). With regard to performance IQ scores, the group of ADHD with epilepsy had the lowest mean value among all the studied groups (82.28 ± 5.78), while the control group had a significantly high mean value (91.85 ± 6.03) (*p* value = 0.017) (Fig. 1).

The group of ADHD without EEG changes had low performance IQ and total IQ than ADHD with EEG

Table 2 Clinical features among epilepsy groups

Clinical variables		Epilepsy (*N* = 20) *N* (%)	ADHD with epilepsy (*N* = 20) *N* (%)	*P* value
Age of onset of seizure (years)	**(means ± SD)**	**2.35 ± 1.348**	**2.75 ± 1.209**	**0.648**
Duration of epilepsy (years)	**(means ± SD)**	**5.80 ± 2.142**	**4.90 ± 1.209**	**0.084**
Time since the last seizure	**< 1 year**	**13 (65%)**	**10 (50%)**	**0.107**
	1–2 years	**7 (35%)**	**6 (30%)**	
	> 2 years	**0 (0%)**	**4 (20%)**	
Types of seizure	**Partial**	**4(20%)**	**0 (0%)**	***0.035****
	Generalized	**16 (80%)**	**20 (100%)**	

**P* value is significant

Table 3 Early Childhood Epilepsy Severity Scale (E-Chess) among the studied epilepsy groups

Items variables	Epilepsy (*N* = 20)	ADHD with epilepsy (*N* = 20)	*P* value
Frequency of seizures			-
Weekly	**20 (100%)**	**20 (100%)**	
Daily	**0 (0%)**	**0 (0%)**	
More than daily	**0 (0%)**	**0 (0%)**	
Time period over which seizures occurred (months)			-
Less than 1 month	**0 (0%)**	**0 (0%)**	
1–6 months	**0 (0%)**	**0 (0%)**	
More than 6 months	**20 (100%)**	**20 (100%)**	
Number of seizure types			**0.244**
One seizure type	**18 (90%)**	**20 (100%)**	
Two seizure types	**2 (10%)**	**0 (0%)**	
Three seizure types	**0 (0%)**	**0 (0%)**	
Number of anticonvulsants used			***0.006****
None	**0 (0%)**	**4 (20%)**	
One or two anticonvulsants	**14 (70%)**	**16 (80%)**	
More than two anticonvulsants	**6 (30%)**	**0 (0%)**	
Response to treatment			**0.052**
Complete cessation of seizures	**7 (35%)**	**12 (60%)**	
Partial cessation of seizures	**13 (65%)**	**6 (30%)**	
No improvement of seizures	**0 (0%)**	**2 (10%)**	
Total severity score			
≤ 9	**14 (70%)**	**20 (100%)**	**0.010***
10–13	**6 (30%)**	**0 (0%)**	
13–15	**0 (0%)**	**0 (0%)**	
Total severity score (mean ± SD)	**9.05 ± 0.759**	**8.10 ± 0.852**	**0.001***

*P value is significant

changes (59.01 ± 16.03 vs 61.24 ± 11.03 and 61.64 ± 16.91 vs 63.08 ± 10.71, respectively).

Socioeconomic scale

A statistically significant difference emerged between socioeconomic classes among groups. The highest percentage of low socioeconomic class (25%) was observed in the group of ADHD with epilepsy and the group of epilepsy.

Furthermore, a significant difference was observed between the mean values of social class among the studied groups. The control group had a significantly higher mean value of social class scores compared with the studied cases (227 ± 26.350) (Table 5).

The group of ADHD without EEG changes had high socioeconomic scale score relative to the group of ADHD with EEG changes (177.72 ± 64.696 vs 148.16 ± 56.155).

Pediatric Quality of Life Inventory

No significant difference was detected between the mean values of the physical summary scores among the studied groups. The group of ADHD with epilepsy had significantly the worst score of the psychological summary score (56.91 ± 12.98) and the total QOL (61.13 ± 15.96) among all the studied groups (Fig. 2).

The group of ADHD without EEG changes had low psychological summary score and total quality of life score than the group of ADHD with EEG changes (59.01 ± 16.03 vs 61.24 ± 11.03 and 61.64 ± 16.91 vs 63.08 ± 10.71, respectively). Meanwhile, the group of ADHD with EEG changes had lower physical summary score than ADHD without EEG changes (66.73 ± 19.05 vs 71.08 ± 21.27).

Correlation results

Correlation between the total IQ score with socioeconomic scale score and the subscales of PedsQL scores among the studied groups

The socioeconomic score had no significant correlation with the total IQ score in all the studied groups. The physical summary score of PedsQL shows a significant moderate positive correlation with a total IQ score in the group of ADHD with epilepsy. The psychological summary and total QOL scores had a significantly

Table 4 The Conners' Parent Rating Scale (CPRS) score subscales among the studied groups

Conners' Parent Rating Scale subscales			Epilepsy (*N* = 20) *N* (%)	ADHD with EEG changes (*N* = 20) *N* (%)	ADHD without EEG changes (*N* = 20) *N* (%)	ADHD with epilepsy (*N* = 20) *N* (%)	Control (*N* = 20) N (%)	*P* value
Inattention	**Clinical rating**	**Very elevated**	**0 (0%)**	**15 (75%)**	**8 (40%)**	**9 (45%)**	**0 (0%)**	< ***0.000****
		Elevated	**0 (0%)**	**0 (0%)**	**0 (0%)**	**2 (10%)**	**0 (0%)**	
	Borderline	High average	6 (30%)	4 (20%)	5 (25%)	9 (45%)	0 (0%)	
		Average	14 (70%)	1 (5%)	7 (35%)	0 (0%)	20 (100%)	
Hyperactivity/ impulsivity	**Clinical rating**	**Very elevated**	**0 (0%)**	**14 (70%)**	**12 (60%)**	**18 (90%)**	**0 (0%)**	< ***0.000****
		Elevated	**2 (10%)**	**3 (15%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	
	Borderline	High average	2 (10%)	1 (5%)	5 (25%)	2 (10%)	8 (40%)	
		Average	16 (80%)	2 (10%)	3 (15%)	0 (0%)	12 (60%)	
Learning problems	**Clinical rating**	**Very elevated**	**6 (30%)**	**17 (85%)**	**13 (65%)**	**17 (85%)**	**1 (5%)**	
		Elevated	**4 (20%)**	**0 (0%)**	**3 (15%)**	**1 (5%)**	**0 (0%)**	
	Borderline	High average	0 (0%)	1 (5%)	1 (5%)	2 (10%)	3 (15%)	
		Average	10 (50%)	2 (10%)	3 (15%)	0 (0%)	16 (80%)	
Executive functioning	**Clinical rating**	**Very elevated**	**0 (0%)**	**15 (75%)**	**9 (45%)**	**12 (60%)**	**2 (10%)**	< ***0.000****
		Elevated	**0 (0%)**	**3 (15%)**	**1 (5%)**	**4 (20%)**	**0 (0%)**	
	Borderline	High average	18 (90%)	0 (0%)	5 (25%)	0 (0%)	0 (0%)	
		Average	2 (10%)	2 (10%)	5 (25%)	4 (20%)	18 (90%)	
Defiance/aggression	**Clinical rating**	**Very elevated**	**11 (55%)**	**19 (95%)**	**16 (80%)**	**18 (90%)**	**1 (5%)**	***0.002****
		Elevated	**0 (0%)**	**1 (5%)**	**2 (10%)**	**0 (0%)**	**2 (10%)**	
	Borderline	High average	3 (15%)	0 (0%)	1 (5%)	0 (0%)	5 (25%)	
		Average	6 (30%)	0 (0%)	1 (5%)	2 (10%)	11 (55%)	
Peer/Family relation	**Clinical rating**	**Very elevated**	**8 (40%)**	**18 (90%)**	**16 (80%)**	**18 (90%)**	**2 (10%)**	< ***0.000****
		Elevated	**0 (0%)**	**1 (5%)**	**3 (15%)**	**2 (10%)**	**2 (10%)**	
	Borderline	High average	6 (30)	1 (5%)	1 (5%)	0 (0%)	1 (5%)	
		Average	6 (30)	0 (0%)	0 (0%)	0 (0%)	15 (75%)	

**P* value is significant

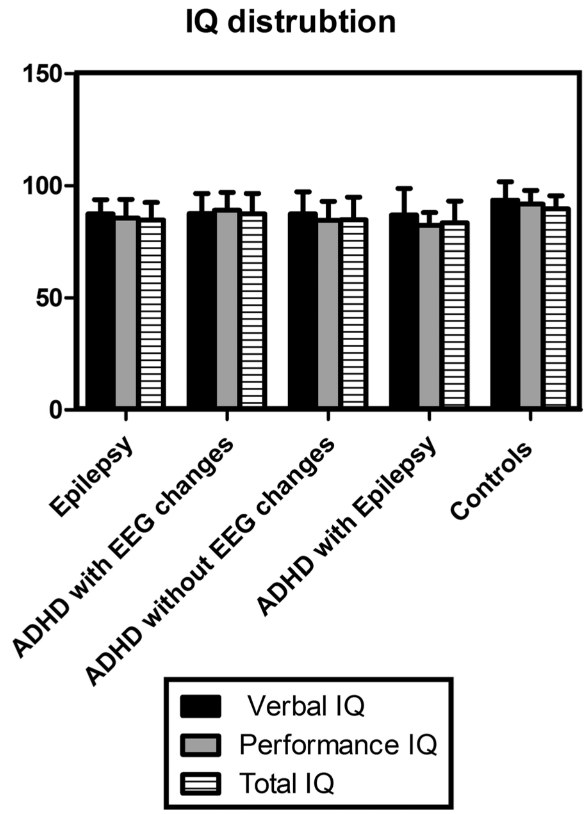

Fig. 1 Wechsler Intelligence Scale for Children-3 (WISC-III) score among the studied groups

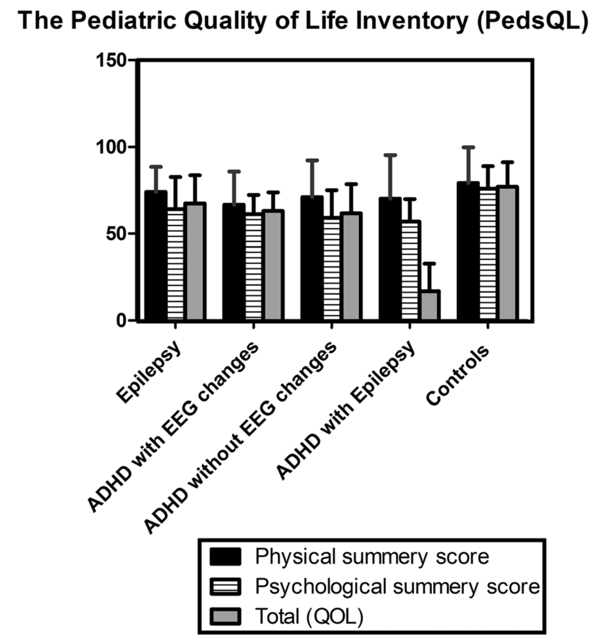

Fig. 2 The Pediatric Quality of Life Inventory (PedsQL) scores among the studied groups

strong positive correlation with the total IQ score in the group of ADHD with epilepsy, whereas no significant correlations were detected in other groups (see Table 6a and table 6b in supplement data).

Correlation among socioeconomic score, total IQ score, subscales of PedsQL scores with the clinical variables of epilepsy, and E-Chess total severity score in the group of epilepsy and the group of ADHD with epilepsy

There was a significantly moderate correlation existed between the age at the onset of seizure and the total IQ score in the group of epilepsy. Meanwhile, other scores did not show a significant correlation (see Table 7 in supplement data).

Discussion

Epilepsy, as a chronic disorder, involves patients in different ways, i.e., physically and socially [42]. Psychiatric–behavioral problems are common in CWE and can have a major influence on their QOL and families. In many cases, these problems are more challenging than epilepsy itself [43]. This study examined cognitive functions, socio-economic levels, and the QOL of ADHD and epilepsy patients.

Although the proportion of males was higher in all groups, except for the group of ADHD with epilepsy, they were almost equal when compared with the controls. Similarly, other studies have reported a prevalence of males with ADHD up to 3–7 times greater than females. Meanwhile, ADHD and epilepsy children often have the same gender ratios [44–46].

In the present study, the relation among epilepsy-related variables showed no significant difference regarding age at the onset of seizure, the duration of epilepsy, and time since the last seizure in CWE-ADHD and

Table 5 Socioeconomic class scores among the studied groups

Socioeconomic classes	Epilepsy (*N* = 20) *N* (%)	ADHD with EEG changes (*N* = 20) *N* (%)	ADHD without EEG changes (*N* = 20) *N* (%)	ADHD with Epilepsy (*N* = 20) *N* (%)	Control (*N* = 20) *N* (%)	*P* value
High classes	0 (0%)	4 (20%)	5 (25%)	0 (0%)	7 (35%)	< *0.000**
Middle classes	15 (75%)	14 (70%)	13 (65%)	15 (75%)	10 (50%)	
Low classes	5 (25%)	2 (10%)	2 (10%)	5 (25%)	3 (15%)	
Total socioeconomic scale score	106.24 ± 30.836	148.16 ± 56.155	177.72 ± 64.696	112.50 ± 35.464	227 ± 26.350	< *0.000**

**P* value is significant

those with epilepsy, while the type of seizure was significantly different between the two groups.

Hermann et al. observed no correlation between younger age at the onset of seizure and the presence of ADHD in the cohort study with a newly diagnosed epilepsy [44], and the same result was found by [47] in a retrospective cohort study on CWE. Contrarily, some studies have demonstrated a significantly high prevalence of ADHD in patients with an earlier epilepsy onset as confirmed by [48]. Moreover, [49] observed that earlier epilepsy onset in younger children was associated with more attention deficit, especially in childhood epilepsy with centrotemporal spikes. ILAE has concluded that the relationship between early seizure onset and ADHD development is still uncertain [50].

Regarding the type of seizures, the higher proportion had a generalized type of epilepsy in both groups. Considerable research has examined whether distinct seizure types were associated with a higher risk of ADHD and epilepsy and has found no association [31, 51, 52]. ILAE has also concluded that specific seizure types are not anticipated higher risk of ADHD in epilepsy [44, 45, 50, 53].

In the current study, the comparison of EEG changes among the three groups, namely, the group of epilepsy, the group of ADHD with epilepsy, and the group of ADHD with EEG changes, showed significant differences for unprovoked generalized paroxysmal changes, which could be attributed to the generalized type of seizures observed in most of the cases.

Additionally, the E-Chess scores in the group of ADHD with epilepsy and the group of epilepsy were significantly different in the number of the anticonvulsants used and the total E-Chess severity score. Regarding the number of the anticonvulsant drugs used, multiple studies have been conducted to clarify the effect of antiepileptic drugs (AEDs) on ADHD comorbidity, but the variety of the anticonvulsant drugs involved restricted the comparison among studies due to their poor consistency. Polytherapy was typically associated with a higher level of behavioral issues according to ILAE [50, 54].

In contrast, several studies from divergent settings have found no correlation between the numbers of anticonvulsant drugs and psychiatric problems [50, 55]. Furthermore, Hermann et al. found no differences between the group of epilepsy and the group of ADHD with epilepsy in terms of the number of anticonvulsant drugs [44]. Regarding seizure frequency, many previous studies have found no correlation of seizure frequency in the studied groups [31, 51, 52].

Regarding the CPRS, a combined subtype of ADHD predominated in the group of ADHD with EEG changes and the group of ADHD with epilepsy, while the hyperactivity subtype predominated in the group of ADHD without EEG changes. Other studies have presented similar results, in which the combined subtype of ADHD was more prevalent than the inattentiveness subtype in ADHD with epilepsy patients [31, 56–58].

Some studies have corroborated that the combined subtype was more common in patients with ADHD [31, 59]. Meanwhile, other studies have asserted that hyperactivity and impulsivity subtypes were more common [60, 61].

According to EEG, our study categorized ADHD into two subgroups. The group of ADHD with EEG changes showed a predominance of the combined subtype of ADHD similar to ADHD with epilepsy, while the group of ADHD without EEG changes was different from other groups. That was further confirmed by the CPRS subscales, as the group of ADHD with EEG changes similar to the group of ADHD with epilepsy had a highly elevated clinical rating response in all subscales relative to the group of ADHD without EEG changes. These variations in ADHD subtypes could be attributed to the characteristics of the methodology of different studies [51].

In our study, the assessment of cognitive functions by WISC-III questionnaires showed no significant difference in IQ classification among all groups. This is similar to studies that have validated that ADHD patients with and without epilepsy did not vary with respect to IQ (p = 0.48), thereby promoting a correlation between epilepsy and ADHD, irrespective of lower IQ scores [57]. Nevertheless, the ADHD and epilepsy groups had lower scores on the measurement of the IQ subscales (verbal, output, and overall IQs) than other groups including the controls with a significant difference in performance IQ.

This was explained by Hermann et al., who argued that motor/psychomotor speed and executive functioning tended to severely affect epilepsy-ADHD children with neuropsychological problems. This was marked by response inhibition impairment, concept formation, mental flexibility/working memory, and passive inattention [44, 56, 62, 63].

According to the socioeconomic scale score, most of the children in the group of ADHD with epilepsy and the group of epilepsy were in low socioeconomic classes with low mean values of social scores in comparison with the other studied groups. This could be explained as epilepsy might be responsible for the decrease of socioeconomic levels.

In a systematic review, there has been growing evidence of the correlation between socio-economic disadvantages and ADHD, indicating that socio-economic disadvantages may lie on the causal pathway between, or may be triggered by, ADHD genotype and phenotype [64].

Several studies reported that low socioeconomic status is a risk factor for the development of epilepsy [65, 66], as low socioeconomic status is associated with social and economic deprivation, unemployment, and low income, which in turn are associated with risk factors as birth defects, trauma, infection, and poor nutrition that may cause epilepsy [67–69].

Another study has revealed that epilepsy prevalence is closely linked to specific socio-economic deprivation measures. When epilepsy is found in areas of greater socioeconomic deprivation, the existing major consequence of epilepsy on employment and higher education may be substantial [70].

Regarding PedsQL, significant differences were detected between groups, while the group of ADHD with epilepsy had the poorest PedsQL scores. The total score and certain subscores of PedsQL (psychological summary score) were the lowest in the group of ADHD with epilepsy. Our findings indicate that the relationship between ADHD and epilepsy co-occurrence with poor PedsQL is greater than that between isolated ADHD or epilepsy and poor PedsQL.

A poor PedsQL may be related to epilepsy, chronic course, social stigma, learning challenges, and seizure fear [71]. Additionally, persistent inattentiveness, hyperactivity, and impulsive ADHD symptoms usually have severe adverse effects on the academic, family, and social life of the children affected [72]. The co-existence of these two conditions may increase the risk of psychosocial and cognitive difficulties and impairment in the QOL.

In the present study, the correlation between the total IQ score with the total socioeconomic scale score and the subscales of PedsQL scores among the studied groups showed that physical summary, psychological summary, and total QOL scores had a significant positive correlation with the total IQ score in the group of ADHD with epilepsy, whereas no significant correlations were detected in other groups.

Similarly, Abd El Naby et al. verified that there was a strong significant correlation between PedsQL scores with IQs (p value = 0.001) [17]. Other studies have confirmed that ADHD with epilepsy is inversely correlated with the QOL and that treating ADHD significantly improves the QOL of CWE [73, 74].

In our study, the correlation between the total socioeconomic scale, total IQ, subscales of PedsQL scores with the clinical variables of epilepsy and the E-Chess total severity score in the group of epilepsy and the group of ADHD with epilepsy showed a significant correlation between the age at the onset of seizure and the total IQ score in the group of epilepsy. Meanwhile, other scores have not affirmed a significant correlation. In a similar study, young age at the onset of seizure was strongly associated with cognitive impairment in most childhood epilepsies [75].

In contrast, some research has suggested that cognitive dysfunction at the onset of epilepsy does not lead to the increase of intensity over time but keeps on a trajectory [76, 77].

Several factors may have a severe effect on cognitive function in epilepsy, such as underlying structural lesions and epilepsy-related disorders, alternation in neurogenesis and synaptogenesis and change of excitatory/inhibitory balance, and network connectivity. Other factors such as epileptic activity severity, psychosocial aspects, and surgical or pharmacological treatment of seizures may contribute to increased cognitive impairment in epilepsy [78, 79].

Moreover, no significant correlation emerged between the total E-Chess severity scores with PedsQL, which can be explained as the majority of patients in epilepsy groups had low severity of epilepsy.

Some studies have revealed a positive correlation between higher severity of epilepsy and lower QOL. This could be attributed to the stigma of epilepsy, worries about having seizures in school, cognitive impairment, impaired memory, and inability to pay attention which may be associated with some epilepsy syndromes [80, 81].

Additionally, we found that no significant correlation exists between PedsQL and socioeconomic scale scores with the age at the onset of seizure and the duration of epilepsy. This may be suggested by the prolonged duration of illness that is associated with the adaptation of the child and parents to illness, the acceptance of its stigma with decreased anxiety and depression, and the risk of psychiatric comorbidities that cause the impairment of the QOL.

This study has some limitations. First, our sample size was sufficient for the present study but not large, potentially raising the risk of sample-specific findings and potentially restricting their generalizability to more diverse populations. Second, most of the participants were on medications that had several side effects that should be investigated.

We recommend that all CWE be evaluated for ADHD and given appropriate treatment for them to improve their QOL and protect them against cognitive impairments. Also, further research on a larger group of patients will help support our results.

Conclusion

Our study demonstrated that ADHD with epilepsy is associated with low performance IQ, poor socioeconomic level, and the QOL. PedsQL shows a significant correlation with the total IQ score.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s43045-020-00054-9.

Additional file 1:. Supplemental Data.

Abbreviations

PedsQL: The Pediatric Quality of Life Inventory; CPRS: Conners' Parent Rating Scale; WISC-III: Wechsler Intelligence Scale for Children-3rd edition; E-Chess: Early Childhood Epilepsy Severity Scale; EEG: Electroencephalography; CWE: Children with epilepsy; ILAE: The International League Against Epilepsy

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Authors' contributions
GA recruited patients, interpreted the patients' data, and was the contributor in writing the manuscript. AD and HK revised data interpretation, read, and approved the final manuscript. MK helped in data entry, analyzed, and generated result sheets. The author(s) read and approved the final manuscript.

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Availability of data and materials
All data generated or analyzed during this study are available from corresponding author on request.

Ethics approval and consent to participate
This study had ethical approval from Institutional Review Board (IRB) of Faculty of Medicine, Assiut University, with approval number 17200196. This study was registered on clinical trial with registration number NCT03806946. The parents signed an informed consent on behalf of their children to take part in the study.

Consent for publication
Not applicable

Competing interests
The authors declare no conflicts of interests.

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