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RESEARCH

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Neuropsychiatric comorbidities in adult patients with new-onset epilepsy

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Abstract

Background Neuropsychiatric comorbidities in adult patients with new-onset epilepsy in our university hospitals has not been assessed, so the purpose of this study was to identify the neuropsychiatric comorbidities in adult patients with new onset epilepsy in our university hospitals. We recruited one hundred patients, assessed them clinically, radiologically, electrophysiologically, and we performed Wechsler Adult Intelligence Scale Fourth Edition (WAIS-IV), Liverpool Seizure Severity Scale (LSSS), Generalized Anxiety Disorder 7-item (GAD-7) scale, Beck's Depression Inventory II (BDI II) and Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10) to assess cognitive function, seizure severity, anxiety, depression, and quality of life of the patients, respectively.

Results Older adult age group had higher LSSS than other groups. Middle-aged adults' group had higher WAIS-IV full scale Intelligence Quotient (IQ) score and lower GAD-7 scale scores than other age groups. Patients regularly on more than one anti-seizure medication had lower IQ results, more seizure severity, depression, anxiety and worse quality of life than those on monotherapy. Males had slightly higher IQ scores. Patients with moderate and severe BDI-II score had significantly higher rate of uncontrolled seizures, higher seizures' frequency, more abnormal EEG and were regularly on valproate at significantly higher rates as compared to those with minimal BDI-II score. Patients with moderate anxiety were significantly older than those with normal and severe anxiety. Patients with severe anxiety had higher rate of family history of epilepsy, higher rates of uncontrolled seizures and higher seizures' frequency as compared to those with mild and moderate anxiety. Patients with mild, moderate, and severe score on GAD-7 had more abnormal EEG as compared to those with normal GAD-7 score. Patients with severe and very severe seizures had significantly higher levels of anxiety, depression and impaired quality of life than those with mild and moderate seizure severity.

Conclusions Most patients with epilepsy had psychiatric comorbidities such as depression and anxiety which strongly reduce their quality of life and interfere with their compliance to anti-seizure medication. Males had slightly higher Intelligence Quotient (IQ) scores on WAIS-IV. Moreover, patients regularly taking more than one anti-seizure medication had a statistically significantly lower IQ score, more seizure severity, higher Beck's depression inventory II score, higher generalized anxiety disorder 7-item scale score, and worse quality of life than those on monotherapy.

Keywords Epilepsy, Anti-seizure medication, Cognitive function, Depression, Anxiety and quality of life

Background

Epilepsy is one of the most common serious brain conditions, affecting over seventy million people worldwide. A complete clinical history taking, and a reliable eyewitness account of a seizure are the cornerstones of the diagnosis. Ancillary investigations can help to confirm diagnosis, and determine cause and prognosis. Advances in brain

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imaging are helping to find out the structural and functional causes and consequences of the epilepsies [1].

Up to ten percent of general population experience at least one seizure in their lifetime with the highest incidence occurring in early childhood and late adulthood. Adult onset seizures are most prevalent in the young and middle-aged adults (after the age of 18 years). Seizures beginning in the adult life require special attention regarding their etiology because these are likely to be due to an identifiable etiology. These are mainly due to trauma, central nervous system infections, space-occupying lesions, cerebrovascular accidents, metabolic disorders, and drugs [2].

No single drug is ideal for new-onset epilepsy in adults, and the choice depends on the type of seizure and the comorbidities present, and age and sex considerations [3].

Epilepsy in later life aggravates isolation, low mood, cognitive decline, reduced independence, depression and anxiety. Those with poor anti-seizure medications adherence and uncontrolled seizures may be particularly prone to mood disorders. Preexisting psychiatric comorbidities should also help guide the choice of anti-seizure medications in older people, as some anti-seizure medications may have a beneficial/stabilizing impact on mood (for example valproate, carbamazepine, lamotrigine, pregabalin, gabapentin), while others should be used with caution in those with relevant psychiatric history (for example levetiracetam, topiramate, zonisamide) [4].

Data on the neuropsychiatric comorbidities of adult patients with new onset epilepsy in our university hospitals are inconclusive or are not known for the majority of patients; this is especially true for Egyptian aged population admitted to our university hospitals where no specific study addressed this issue before to the best of our knowledge. Therefore, the aim of this work was to identify the neuropsychiatric comorbidities of adult patients with new onset epilepsy in our university hospitals.

Methods

This prospective, cross-sectional, tertiary hospital-based study was conducted in our university hospitals (in outpatient clinics, and inpatient Departments of Neurology, Neurosurgery and Internal medicine, including intensive care units) during the period from August 2020 to May 2022. Our university hospital is a tertiary hospital including about 1751 beds, and it is the main medical service provider of our government. Our University hospitals support investigations and treatment of patients at reduced prices. Also, it provides medical consultation and inpatient services almost free of charge.

Written informed consents were obtained from all recruited patients or written assents from relatives, and the ethics of research as put by institutional research board of faculty of medicine of our university were followed thoroughly with institutional research board number 6115 at 2019.

One hundred patients with new onset epilepsy who fulfilled criteria for epilepsy diagnosis after the age of 18 years were included in this study. We excluded from the study patients with history of epileptic seizures before 18 years, or use of antiepileptic drugs before 18 years, or patients with unclear time of onset of epileptic seizures or epilepsy and patients presented with acute symptomatic seizures.

All the patients were subjected to clinical assessment with detailed medical history with seizures history with special stress on age of onset, frequency per month, type and duration. Then, patients were arranged into three groups according to seizure frequency: the first group had from 1 to 4 seizures per month, the second group had from 5 to 8 seizures per month, and the third group had from 9 to 15 seizures per month. Thorough general and neurological examination was done for all participants with focus on seizures time, onset, level of consciousness, limbs tone and movement during the seizures, up rolling of eyes, frothy secretions from the mouth, frequency and duration of seizures, presence of eyewitness, admission to hospital, occurrence of complications, status epilepticus, comorbid diseases, investigations done, treatment and compliance to treatment.

Diagnosis of Epilepsy was done according to International league against Epilepsy Commission on Classification and Terminology [5]. Studied patients were subjected to electroencephalography (EEG), and/or video_EEG monitoring when needed via interictal scalp digital EEG that was performed to all participants using EBNeuro machine (Italy) in quiet room while participants were relaxed under normal standard conditions. The electrodes were placed according to 10–20 international system of electrode placement, and bipolar as well as referential montages were applied. For every participant, a 30-min awake record was obtained, using hyperventilation and photic stimulation as provocative methods. We analyzed carefully the EEG tracings as regards; background activity, presence of epileptiform activity, which were then classified into focal, primary generalized or focal with second generalization.

All patients were subjected to plain computed tomography (CT) brain scan by using Philips (Tomoscan 350) with 4.8 scanning time and 512×512 matrix size. Axial scans were obtained with the patients supine, the slice thickness was nine mm. Contrast brain CT scan or magnetic resonance imaging (MRI) of the brain was carried out when needed by using 1.5 Tesla Philips (Achieva, Philips Medical Systems) with a standard head coil with

the following sequences: sagittal, axial and coronal T1 weighted images (500–600\12) time of repetition TR/time of echo TE at 2mm slice thickness. T2 weighted images in coronal and axial plan with 2800TR/80TE and T2W Fluid attenuated inversion recovery (FLAIR) images with 3500 TR/20TE.

The following scales were used to assess the seizure severity, cognitive function, psychiatric comorbidities and quality of life of the participants. Seizure severity was assessed using Liverpool seizure severity scale [6]. Authors used the 20 questions scale translated into Arabic, each had one to four scores, and the scores were calculated and arranged as follows [7]: mild seizures from one to 20, moderate seizures from 21 to 40, severe seizures from 41 to 60, and very severe seizures from 61 to 80.

Assessment of cognitive function was done using the Wechsler Adult Intelligence Scale Fourth Edition (WAIS-IV): Full-Scale Intelligence Quotient (FSIQ) is the sum of the scores derived from the Verbal IQ (VIQ) and the Performance IQ (PIQ). The VIQ was based on the total combined performance of the Verbal Comprehension Index (VCI) and Working Memory Index (WMI). The PIQ was based on the total combined performance of the Perceptual Reasoning Index (PRI) and Processing Speed Index (PSI). In our study we used the version for Arabic speakers of WAIS-IV adapted and validated by Abdelhamid and colleagues [8, 9]. Scores from 90 to 109 were average, scores from 80 to 89 were low average, and scores from 70 to 79 were borderline.

We used Beck Depression Inventory II (BDI II) for assessment of associated depression. The scores from 0 to 13 = minimal range, from 14 to 19 = mild depression, from 20 to 28 = moderate depression, and from 29 to 63 = severe depression [10]. Generalized Anxiety Disorder 7-item (GAD-7) scale was done for assessment of associated anxiety by asking patients to evaluate their level of symptoms over the last 2 weeks. Scores from 0 to 4 are normal, from 5 to 9 are mild anxiety, from 10 to 14 are moderate anxiety and from 15 to 21 are severe anxiety [11].

Quality of life of the studied patients was assessed using the Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10) [12]. This scale consists of ten questions designed to assess the patients' subjective rating of their memory, level of physical and mental well-being, energy, depression, worries about seizures and work, social limitations, and overall quality of life. Each item in the questionnaire is ranked on a scale of one to five except first two questions ranked from one to six and ninth question ranked from one to four, and the patient receives a total QOLIE-10 scale score of 10 to 51 by answering all the questions. Scores of 25 or more were considered as indicator for impaired quality of life [13]. QOLIE-10 scale was used in Arabic language and was shown to be reliable in our study.

Statistical analysis

Data were recorded, and data entry was done using the Excel program. We used in the current study IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative variables were described utilizing number and percent. We used the Kolmogorov–Smirnov test to verify the normality of distribution. Quantitative variables were described using range (minimum and maximum), mean, standard deviation (SD), median and interquartile range (IQR). Significance of the obtained results in this study was judged at the 5%. We used Chi-square test for categorical variables, to compare between different groups. Monte Carlo correction for chi-square was used when more than 20% of the cells have expected count less than five. Student t-test was utilized for normally distributed quantitative variables, to compare between two studied groups.

Results

One hundred adult patients with new onset epilepsy were studied, and the following results were obtained, 57.0% of the studied patients were males, mean age (± SD) of the studied patients was 52.83 (± 17.33). In this study, 47.0% of the studied cases had controlled seizure, and 53.0% had uncontrolled seizure (61.0% of cases had one to four seizures per month, 30.0% of cases had 5 to 8 seizures per month, and 9.0% had 9 to 15 seizures per month). As regard severity of seizures among our patients, 47% had mild seizure severity, 26% had moderate, 17% had severe, 10% had very severe seizures.

Thirty-one percent of the studied cases had epilepsy due to cerebrovascular stroke, 22% had epilepsy due to intracranial neoplasms, 15% had epilepsy due to previous central nervous system infection, 15% had epilepsy due to previous cranial trauma, two percent had epilepsy due to arteriovenous malformations, one percent had epilepsy due to mesial temporal sclerosis, one percent had epilepsy due to focal cortical dysplasia, and 13% had epilepsy with undetermined etiology (Table 1).

There were 88% had abnormal CT/MRI brain, and 12% of the studied cases had normal CT/MRI brain. Global brain atrophy was found in 34%, focal encephalomalacia was found in 30%, space occupying lesion was found in 22%, mesial temporal sclerosis was detected in 1%, and focal cortical dysplasia was detected in 1%.

Thirty-two percent of the studied cases had focal epilepsy, and sixty-eight percent presented with generalized epilepsy. There were 43% of the studied cases had abnormal EEG, and 57% had normal EEG. Generalized

Table 1 Distribution of the studied cases according to etiology of epilepsy

Etiology	No. of patients	%
Post-stroke epilepsy	31	31.0
Ischemic	11	11.0
Hemorrhagic	20	20.0
Intracranial neoplasms	22	22.0
Post-traumatic epilepsy	15	15.0
Post-central nervous system infection	15	15.0
Arteriovenous malformations	2	2.0
Focal cortical dysplasia	1	1.0
Mesial temporal sclerosis	1	1.0
Undetermined	13	13.0

(No): number, (%): percent

epileptiform activity was found in 19%, while focal epileptiform activity was found in 11%, and focal epileptiform activity with secondary generalization was found in one percent of cases. Generalized non-epileptiform activity (diffuse slowing) was found in 10%, and focal non-epileptiform activity (localized slow activity) was found in two percent of cases.

Patients in middle-age adults group had lower anxiety score and higher Wechsler Adult Intelligence-IV full scale Intelligence Quotient (IQ) score than other age groups. We found that older adults group had higher scores in Liverpool seizure severity scale than other age groups. But, no statistically significant difference was found in Beck's depression inventory II score or quality of life in epilepsy-10 questionnaire score among different age groups.

The mean (± SD) for verbal comprehensive index was 88.68 (± 8.52), for working memory index was 87.55 (± 7.91), for perceptual reasoning index was 88.87 (± 8.89), and for processing speed index was 87.89 (± 8.67). Also, in our study the mean (± SD) of Wechsler Adult Intelligence Scale-IV (WAIS-IV) Full Scale Intelligence Quotient (FSIQ) score was 88.22 (± 8.49), and 52% of the studied patients had average FSIQ score, 44% had low average FSIQ score, and 4% had borderline FSIQ score. Middle-age adults group had higher FSIQ score than other groups [mean (± SD): 91.05 (± 8.65)].

Table 2 shows that patients regularly taking more than one antiepileptic drug had a statistically significantly lower IQ score than those regularly taking a single anti-seizure medication. Also, according to scores on Liverpool seizure severity scale, patients on polytherapy had a statistically significantly more seizure severity than those on monotherapy. Besides, in this table, Beck's depression inventory II score shows that patients on polytherapy had a highly statistically significantly higher score than those on monotherapy. Moreover, according to generalized anxiety disorder 7-item score patients on polytherapy had highly statistically significant more score than those on monotherapy. Furthermore, in this table, score of quality of life in epilepsy-10 questionnaire shows that patients on polytherapy had a statistically significantly worse quality of life than those on monotherapy.

Table 2 Relation between the number of anti-seizure medication and different scales Scores

	Number of ASM		*P* value
	Monotherapy (*n* = 49)	Polytherapy (*n* = 51)	
Wechsler Adult Intelligence- IV Scale: Full Scale IQ Score			
Mean (± SD)	92.0 (± 7.37)	84.59 (± 7.94)	< 0.001*
Median (Min.–Max.)	92.0 (74.0–102.0)	80.0 (70.0–102.0)	
Liverpool seizure severity scale score			
Mean (± SD)	19.57 (± 18.14)	36.0 (± 20.52)	< 0.001*
Median (Min.–Max.)	11.0 (3.0–76.0)	30.0 (5.0 –78.0)	
Beck's depression inventory II score			
Mean (± SD)	14.4 (± 14.60)	27.09 (± 16.76)	< 0.001*
Median (Min.–Max.)	7.0 (3.0–60.0)	25.0 (3.0–61.0)	
Generalized anxiety disorder 7-item score			
Mean (± SD)	8.24 (± 6.67)	12.58 (± 6.84)	< 0.001*
Median (Min.–Max.)	5.0 (2.0–20.0)	12.0 (2.0–29.0)	
Quality of life in epilepsy-10 questionnaire score			
Mean (± SD)	15.41 (± 8.52)	19.15 (± 7.82	0.01
Median (Min.–Max.)	10.0 (10.0–35.0)	19.0 (10.0–33.0)	

ASM anti-seizure medication, *SD* standard deviation, *n* number of patients, *IQ* Intelligence Quotient, *p* p value for comparing between monotherapy and polytherapy

* statistically significant at $P \leq 0.05$

There was a statistically significant relation between WAIS-IV Full Scale IQ score and sex distribution as males had slightly higher scores. Likewise, there was a statistically significant relation between WAIS-IV Full Scale IQ score and seizure' control, and seizure' frequency ($P<0.001$), as patients with average IQ scores had less seizure' frequency, and more seizure' control when compared to those with borderline IQ scores (Table 3).

Table 4 shows that there was a statistically significant relation between Wechsler adult intelligence scale (WAIS-IV) full scale IQ score and presence of EEG abnormalities, number of ASM taken regularly by patients ($P<0.001$), as patients with average WAIS-IV full scale IQ score had more normal EEG, and higher rate of monotherapy as compared to those with borderline, and low average WAIS-IV full scale IQ score.

Table 5 shows that there was a statistically significant relation between Beck's Depression Inventory II (BDI II) score and seizure' control ($P<0.001$), as patients with moderate, and severe BDI II score had significantly higher rate of uncontrolled seizures as compared to those with minimal, and mild BDI II score. Similarly, there was a statistically significant relation between BDI II score and seizure' frequency ($P<0.001$), as patients with mild, moderate, severe BDI II score had higher seizures' frequency when compared to those with minimal BDI II score.

There was a statistically significant relation of BDI II score with presence of EEG abnormalities, number of ASM regularly used by the patients, and valproate administration ($P<0.001$), as patients with mild, moderate, and severe BDI II score had more abnormal EEG with higher rates of polytherapy as compared to those with minimal BDI II score. Patients with moderate and severe BDI-II score had valproate regular intake

Table 3 Relation between Wechsler Adult Intelligence Scale (WAIS) Score and different patients' characteristics

Patients' characteristics	Wechsler adult intelligence scale score			*P* value
	Borderline ($n=4$)	Low average ($n=44$)	Average ($n=52$)	
Age (years)				
Min–Max	33–65	19–81	19–82	0.733
Mean (± SD)	49 (± 16.83)	54.25 (± 19.39)	51.92 (± 15.67)	
Sex				
Male	4 (100%)	20 (45.5%)	33 (63.5%)	0.021*
Female	0 (0%)	24 (54.5%)	19 (36.5%)	
Family history				
Absent	4 (100%)	37 (84.1%)	46 (88.5%)	0.466
Present	0 (0%)	7 (15.9%)	6 (11.5%)	
Epilepsy type				
Focal	3 (75%)	14 (31.8%)	15 (28.8%)	0.187
Generalized	1 (25%)	30 (68.2%)	37 (71.2%)	
Seizure' control				
Controlled	0 (0%)	5 (11.4%)	42 (80.8%)	< 0.001*
Uncontrolled	4 (100%)	39 (88.6%)	10 (19.2%)	
Seizure' frequency/month				
Min.–Max	3–15	1–15	1–9	< 0.001*
Mean (± SD)	7.25 (± 5.32)	5.7 (± 2.88)	2.31 (± 2.09)	
Comorbidities				
Hypertension	2 (50%)	13 (29.5%)	17 (32.7%)	0.708
Diabetes mellitus	1 (25%)	6 (13.6%)	7 (13.5%)	0.837
Dyslipidemia	1 (25%)	5 (11.4%)	3 (5.8%)	0.384
Coronary heart disease	0 (0%)	1 (2.3%)	4 (7.7%)	0.376
Atrial fibrillation	0 (0%)	11 (25%)	5 (9.6%)	0.063
Chronic kidney disease	0 (0%)	1 (2.3%)	2 (3.8%)	0.799
Chronic liver disease	0 (0%)	0 (0%)	1 (1.9%)	0.518
Migraine	1 (25%)	7 (15.9%)	10 (19.2%)	0.857

SD standard deviation, *n* number of patients, *p* p value for comparing between WAIS and different patients' characteristics

* statistically significant at $P \leq 0.05$

Table 4 Relation of Wechsler adult intelligence scale score with cerebral imaging and EEG findings, and anti-seizure medication profile

	Wechsler Adult Intelligence Scale (WAIS-IV) score			*P* value
	Borderline (*n* = 4)	Low average (*n* = 44)	Average (*n* = 52)	
CT/MRI findings				
Normal	0 (0%)	6 (13.6%)	6 (11.5%)	0.565
Abnormal	4 (100%)	38 (86.4%)	46 (88.5%)	
EEG				
Normal	0 (0%)	12 (27.3%)	45 (86.5%)	< 0.001*
Abnormal	4 (100%)	32 (72.7% %)	7 (13.5%)	
Number of ASM				
Monotherapy	1 (25%)	10 (22.7%)	38 (73.1%)	< 0.001*
Polytherapy	3 (75%)	34 (77.3%)	14 (26.9%)	
2	0	31	9	
3	1	3	5	
4	2	0	0	
Type of ASM				
Valproate	1 (25%)	17 (38.6%)	16 (30.8%)	0.667
Phenytoin	0 (0%)	12 (27.3%)	8 (15.4%)	0.145
Carbamazepine	1 (25%)	20 (45.5%)	11 (21.2%)	0.037*
Oxcarbazepine	2 (50%)	1 (2.3%)	4 (7.7%)	0.024*
Levetiracetam	2 (50%)	18 (40.9%)	20 (38.5%)	0.891
Lacosamide	1 (25%)	1 (2.3%)	1 (1.9%)	0.221
Topiramate	1 (25%)	9 (20.5%)	6 (11.5%)	0.437
Zonisamide	0 (0%)	2 (4.5%)	3 (5.8%)	0.782

ASM anti-seizure medication, *EEG* electroencephalogram, *CT* computed tomography, *MRI* magnetic resonance imaging, *n* number of patients, p p value for comparing between WAIS and different examinations and ASM

* statistically significant at $P \leq 0.05$

at significantly higher rates as compared to those with minimal and mild BDI-II score (Table 6).

Family history of epilepsy was significantly associated with GAD-7 score ($P = 0.005$), as patients with severe anxiety had higher rate of family history of epilepsy as compared to those with mild and moderate anxiety. There was a statistically significant relation between anxiety and seizure' control, as patients with severe anxiety had significantly higher rates of uncontrolled seizures as compared to those with normal level of anxiety. Likewise, higher seizures' frequency was significantly associated with more severe anxiety ($P < 0.001$) (Table 7).

There was a statistically significant relation between GAD-7 score and presence of EEG abnormalities, number of ASM regularly taken by patients, and oxcarbazepine and lacosamide administration ($P < 0.001$), as patients with mild, moderate, and severe GAD-7 score had more abnormal EEG, with higher rates of polytherapy as compared to those with normal GAD-7 score. Patients having moderate GAD-7 score are found to be regularly taking oxcarbazepine and lacosamide at significantly higher rates as compared to those with normal, mild and severe GAD-7 score (Table 8).

There was a positive correlation between seizure severity measured by LSSS and anxiety level measured by GAD-7 (Fig. 1).

There was a positive correlation between severity of seizure measured by Liverpool Seizure Severity Scale (LSSS) and depression measured by Beck's Depression Inventory II (Fig. 2).

Discussion

In the current study, 57% of the studied patients were males, and 43% were females, with male to female ratio of 1.3 to 1.

This met with the finding of Zydan and colleagues [14] who found that their participants were divided into 56% males and 44% females. This low proportion of females among the studied sample might be attributed to underdiagnosis due to cultural and social issues that gain the social isolation and diminish social support, and preventing females from accessing healthcare facilities. Also, several reports have recommended reduction of the rate of marriages among participants with epilepsy. The social sign that companioned with the epilepsy can significantly

Table 5 Relation between Beck's depression inventory II score and different patients' characteristics

	Beck's depression inventory II score				*P* value
	Minimal (*n* = 41)	Mild (*n* = 14)	Moderate (*n* = 22)	Severe (*n* = 23)	
Age (years)					
Min–Max	19–82 50.71 (± 14.93)	28–77	22–72	19–81	0.587
Mean (± SD)	19–82 50.71 (± 14.93)	56.07 (± 16.04)	51.5 (± 18.88)	55.91 (± 20.67)	
Sex					
Male	26 (63.4%)	11 (78.6%)	11 (50%)	9 (39.1%)	0.079
Female	15 (36.6%)	3 (21.4%)	11 (50%)	4 (60.9%)	
Family history					
Absent	36 (87.8%)	14 (100%)	18 (81.8%)	19 (82.6%)	0.191
Present	5 (12.2%)	0 (0%)	4 (18.2%)	4 (17.4%)	
Epilepsy type					
Focal	12 (29.3%)	8 (57.1%)	7 (31.8%)	5 (21.7%)	0.15
Generalized	29 (70.7%)	6 (42.9%)	15 (68.2%)	18 (78.3%)	
Seizure' control					
Controlled	36 (87.8%)	7 (50%)	3 (13.6%)	1 (4.3%)	< 0.001*
Uncontrolled	5 (12.2%)	7 (50%)	19 (86.4%)	22 (95.7%)	
Seizure' frequency/month					
Min–Max	1–7	1–15	2–15	1–15	< 0.001*
Mean (± SD)	1.73 (± 1.32)	3.79 (± 2.42)	5.55 (± 3.23)	6.7 (± 2.91)	
Comorbidities					
Hypertension	13 (31.7%)	1 (7.1%)	9 (40.9%)	9 (39.1%)	0.15
Diabetes mellitus	8 (19.5%)	2 (14.3%)	0 (0%)	4 (17.4%)	0.051
Dyslipidemia	3 (7.3%)	4 (28.6%)	1 (4.5%)	1 (4.3%)	0.115
Coronary heart disease	4 (9.8%)	1 (7.1%)	0 (0%)	0 (0%)	0.099
Atrial fibrillation	6 (14.6%)	2 (14.3%)	3 (13.6%)	5 (21.7%)	0.873
Chronic kidney disease	1 (2.4%)	1 (7.1%)	0 (0%)	1 (4.3%)	0.549
Chronic liver disease	0 (0%)	0 (0%)	1 (4.5%)	0 (0%)	0.382
Migraine	9 (22%)	2 (14.3%)	3 (13.6%)	4 (17.4%)	0.835

SD standard deviation, *n* number of patients, p p value for comparing between BDI II and different patients' characteristics

* Statistically significant at $P \leq 0.05$

impede marital prospects immensely, especially among young ladies [14].

Thirty-one percent of the studied cases had epilepsy due to cerebrovascular stroke, 22% had epilepsy due to intracranial neoplasms, 15% had epilepsy due to previous central nervous system infection, 15% had epilepsy due to previous cranial trauma, two percent had epilepsy due to arteriovenous malformations, one percent had epilepsy due to mesial temporal sclerosis, one percent had epilepsy due to focal cortical dysplasia, and 13% had epilepsy with undetermined etiology.

Similar to our results, Mahmoud and colleagues [15] found that cerebrovascular diseases are the most commonly identified etiology of adult new-onset seizure across males and females, followed by idiopathic epilepsy syndrome by 18.33% of patients, other symptomatic etiologies by 10.83% of patients, 8.33% patients with metabolic, 0.83%patient with vasculitis, 0.83%patient with posterior reversible encephalopathy syndrome, and 0.83% patient with drug-induced seizures, 9.17% patients with brain tumors, 6.67% patients with post-traumatic seizure/epilepsy (post-traumatic concussion and traumatic hemorrhage), 5.83% patients with encephalitis, and 5%patients with cryptogenic seizures. Zydan and colleagues [14] found that Structural causes of epilepsy were recorded in only 20.5%.

We found that 88% had abnormal CT / MRI brain, and 12% of the studied cases had normal CT/MRI brain. Parallel to the results of our study, Mahmoud and colleagues [15] mentioned that abnormal findings in neuroimaging were detected among 75% of adult-onset epilepsy patients. Also, Bhatia and colleagues [16] showed that almost 72% had abnormal brain imaging. Sheikh and colleagues [17] reported that MRI findings presented abnormal findings in 59.7% of the patients. This can be going with the expected relatively higher percentage of organic

Table 6 Relation of Beck's depression inventory II score with cerebral imaging and EEG findings, and anti-seizure medication profile

	Beck's depression inventory II score				*P* value
	Minimal (*n* = 41)	Mild (*n* = 14)	Moderate (*n* = 22)	Severe (*n* = 23)	
CT/MRI findings					
Normal	4 (9.8%)	1 (7.1%)	2 (9.1%)	5 (21.7%)	0.48
Abnormal	37 (90.2%)	13 (92.9%)	20 (90.9%)	18 (78.3%)	
EEG					
Normal	35 (85.4%)	7 (50%)	9 (40.9%)	6 (26.1%)	< 0.001*
Abnormal	6 (14.6%)	7 (50%)	13 (59.1%)	17 (73.9%)	
Number of ASM					
Monotherapy	32 (78%)	5 (35.7%)	4 (18.2%)	8 (34.8%)	< 0.001*
Polytherapy	9 (22%)	9 (64.3%)	18 (81.8%)	15 (65.2%)	
2	8	8	16	8	
3	1	1	2	5	
4	0	0	0	2	
Type of ASM					
Valproate	9 (22%)	3 (21.4%)	12 (54.5%	10 (43.5%)	0.034*
Phenytoin	7 (17.1%)	2 (14.3%)	6 (27.3%)	5 (21.7%)	0.74
Carbamazepine	10 (24.4%)	6 (42.9%)	7 (31.8%)	9 (39.1%)	0.496
Oxcarbazepine	2 (4.9%)	1 (7.1%)	2 (9.1%)	2(8.7%)	0.909
Levetiracetam	17 (41.5%)	6 (42.9%)	8 (36.4%)	9 (39.1%)	0.976
Lacosamide	0 (0%)	0 (0%)	2 (9.1%)	1 (4.3%)	0.15
Topiramate	6 (14.6%)	3 (21.4%)	4 (18.2%)	3 (13%)	0.898
Zonisamide	1 (2.4%)	2 (14.3%)	1 (4.5%)	1 (4.3%)	0.484

ASM anti-seizure medication, *EEG* electroencephalogram, *CT* computed tomography, *MRI* magnetic resonance imaging, *n* number of patients, *p* p value for comparing between BDI II and different examinations and ASM

* Statistically significant at $P \leq 0.05$

cerebral pathology in adult-onset epilepsy as in our study inclusion criteria.

Thirty-two percent of the studied cases had focal epilepsy, and sixty-eight percent presented with generalized epilepsy. There were 43% of the studied cases had abnormal EEG, and 57% had normal EEG. As regard the study of Zydan and colleagues [14], they found that generalized onset seizures were 73.5%, focal-onset seizures reported 20.5% and 6% was unknown type. Abnormal EEG occurred in 77.5% of patients. In agreement with our study, Mahmoud and colleagues [15] found that electroencephalographic data were useful; where it detected abnormality in 37.5%, and Sheikh and colleagues [17] reported that EEG findings were abnormal in 52.8% of their patients.

Fifty two percent of the studied patients had average FSIQ score, 44% had low average Full Scale Intelligence Quotient (FSIQ) score, and 4% had borderline FSIQ score**.** Middle-age adults group had higher FSIQ score than other groups. Our study showed a highly statistically significant relation between Wechsler Adult Intelligence Scale (WAIS-IV) full scale IQ score and presence of EEG abnormalities, number of ASM taken regularly by patients, as patients with average WAIS-IV full scale IQ score had more normal EEG, and higher rate of monotherapy as compared to those with borderline, and low average WAIS-IV full scale IQ score. There was a statistically significant relation between WAIS-IV Full Scale IQ score with sex distribution (as males had slightly higher scores), seizure' control, and seizure' frequency (as patients with average IQ scores had less seizure' frequency, and more seizure' control when compared to those with borderline IQ scores).

Similar to our results, a study done in Sudan by Mohamed and colleagues [18] showed that 47.1% of patients had an average score on FSIQ, 23.5% had low average, whereas 19.6% had borderline score. The FSIQ score was negatively affected by polytherapy, and uncontrolled seizures. Another recent study done by Kishk and colleagues [19] on 118 patients with focal drug resistant epilepsy showed that 67.3% of patients had less than average FSIQ scores, that significantly correlated with the number of anti-seizure medications.

Among the studied patients, 47% had mild seizure severity, 26% had moderate, 17% had severe, 10% had very severe seizures, and older adults group had higher

Table 7 Relation between Generalized Anxiety Disorder 7-item (GAD-7) score and different patients' characteristics

	Generalized anxiety disorder 7-item score				*P* value
	Normal ($n=31$)	Mild ($n=26$)	Moderate ($n=9$)	Severe ($n=34$)	
Age (years)					
Min–Max	19–71	42–82	33–72	19–81	0.002*
Mean (± SD)	47.13 (± 13.92)	63.23 (± 11.31)	53.78 (± 15.55)	49.82 (± 21.07)	
Sex					
Male	19 (61.3%)	15 (57.7%)	7 (77.8%)	16 (47.1%)	0.363
Female	12 (38.7%)	11 (42.3%)	2 (22.2%)	18 (52.9%)	
Family history					
Absent	26 (83.9%)	26 (100%)	9 (100%)	26 (76.5%)	0.005*
Present	5 (16.1%)	0 (0%)	0 (0%)	8 (23.5%)	
Epilepsy type					
Focal	9 (29%)	8 (30.8%)	5 (55.6%)	10 (29.4%)	0.468
Generalized	22 (71%)	18 (69.2%)	4 (44.4%)	24 (70.6%)	
Seizure' control					
Controlled	28 (90.3%)	13 (50%)	3 (33.3%)	3 (8.8%)	< 0.001*
Uncontrolled	3 (9.7%)	13 (50%)	6 (66.7%)	31 (91.2%)	
Seizure' frequency/month					
Min–Max	1–7	1–9	1–15	2–15	< 0.001*
Mean (± SD)	1.68 (± 1.35)	3.65 (± 2.58)	5.11 (± 4.34)	6.09 (± 2.93)	
Comorbidities					
Hypertension	10 (32.3%)	6 (23.1%)	4 (44.4%)	12 (35.3%)	0.623
Diabetes mellitus	6 (19.4%)	3 (11.5%)	0 (0%)	5 (14.7%)	0.316
Dyslipidemia	2 (6.5%)	4 (15.4%)	1 (11.1%)	2 (5.9%)	0.602
Coronary heart disease	1 (3.2%)	3 (11.5%)	1 (11.1%)	0 (0%)	0.112
Atrial fibrillation	4 (12.9%)	7 (26.9%)	0 (0%)	5 (14.7%)	0.144
Chronic kidney disease	0 (0%)	1 (3.8%)	1 (11.1%)	1 (2.9%)	0.366
Chronic liver disease	0 (0%)	1 (3.8%)	0 (0%)	0 (0%)	0.436
Migraine	8 (25.8%)	1 (3.8%)	1 (11.1%)	8 (23.5%)	0.071

SD standard deviation, *n* number of patients, *p* p value for comparing between GAD-7 and different patients' characteristics

* statistically significant at $P \leq 0.05$

scores in Liverpool seizure severity scale than other age groups. Another important finding in the current study was that patients regularly on ASM polytherapy had significantly more score on LSSS than those on monotherapy.

Viteva [6] done a study on 70 adult patients with refractory epilepsy, and 70 patients with pharmaco-sensitive epilepsy, and evaluated the seizure severity using the Liverpool seizure severity scale. Severe seizures were found in 18 (30.51%) participants, moderate in 32 (54.24%), and mild in 8 (13.56%) participants.

In our study, concerning Beck's depression inventory II (BDI II) score, 41% had minimal depression, 14% had mild, 22% had moderate, and 23% had severe depression. There was a statistically significant relation between BDI II score and seizure' control, seizure' frequency the presence of EEG abnormalities, number of ASM regularly used by the patients, and valproate administration.

Similar to the results of our study, a study in Sri Lanka by De Silva and colleagues [20] demonstrated that 22% of studied patients screened positive for depression with BDI II. Where 4.6% ($n=7$) had mild depression, 8% ($n=12$) had moderate depression, and 8.6% ($n=13$) were severely depressed. Depression was strongly associated with the use of more than one anti-seizure medication, and the greater the number of medications the higher the risk of depression.

Regarding Generalized Anxiety Disorder 7-item (GAD-7) score in our study, 34% had severe anxiety, 9% had moderate anxiety, 26% had mild anxiety, and 31% were normal, and also the middle-age adults group had the lowest scores. In our study, patients with severe anxiety were regularly on ASM polytherapy (and oxcarbazepine and lacosamide administration), with higher seizure frequency per month, having less seizure control, and had abnormal EEG findings all at significantly higher

Table 8 Relation between Generalized Anxiety Disorder 7-item (GAD-7) score with cerebral imaging and EEG findings, and anti-seizure medication profile

	Generalized anxiety disorder 7-item score				*P* value
	Normal (*n* = 31)	Mild (*n* = 26)	Moderate (*n* = 9)	Severe (*n* = 34)	
CT/MRI findings					
Normal	2 (6.5%)	2 (7.7%)	2 (22.2%)	6 (17.6%)	0.358
Abnormal	29 (93.5%)	24 (92.3%)	7 (77.8%)	28 (82.4%)	
EEG					
Normal	27 (87.1%)	15 (57.7%)	4 (44.4%)	11 (32.4%)	< 0.001*
Abnormal	4(12.9%)	11 (42.3%)	5 (55.6%)	23 (67.6%)	
Number of ASM					
Monotherapy	24 (77.4%)	12 (46.2%)	1 (11.1%)	12 (35.3%)	< 0.001*
Polytherapy	7 (22.6%)	14 (53.8%)	8 (88.9%)	22 (64.7%)	
2	6	12	6	16	
3	1	2	2	4	
4	0	0	0	2	
Type of ASM					
Valproate	7 (22.6%)	9 (34.6%)	4 (44.4%	14 (41.2%)	0.388
Phenytoin	5 (16.1%)	7 (26.9%)	2 (22.2%)	6 (17.6%)	0.75
Carbamazepine	8 (25.8%)	11 (42.3%)	2 (22.2%)	11 (32.4%)	0.529
Oxcarbazepine	2 (6.5%)	0 (0%)	3 (33.3%)	2 (5.9%)	0.026*
Levetiracetam	11 (35.5%)	12 (46.2%)	3 (33.3%)	14 (41.2%)	0.835
Lacosamide	0 (0%)	0 (0%)	2 (22.2%)	1 (2.9%)	0.039*
Topiramate	6 (19.4%)	2 (7.7%)	1 (11.1%)	7 (20.6%)	0.472
Zonisamide	1 (3.2%)	0 (0%)	1 (11.1%)	3 (8.8%)	0.231

ASM anti-seizure medication, *EEG* electroencephalogram, *CT* computed tomography, *MRI* magnetic resonance imaging, *n* number of patients, *P* p value for comparing between (GAD-7) and different patients' characteristics

* Statistically significant at $P \leq 0.05$

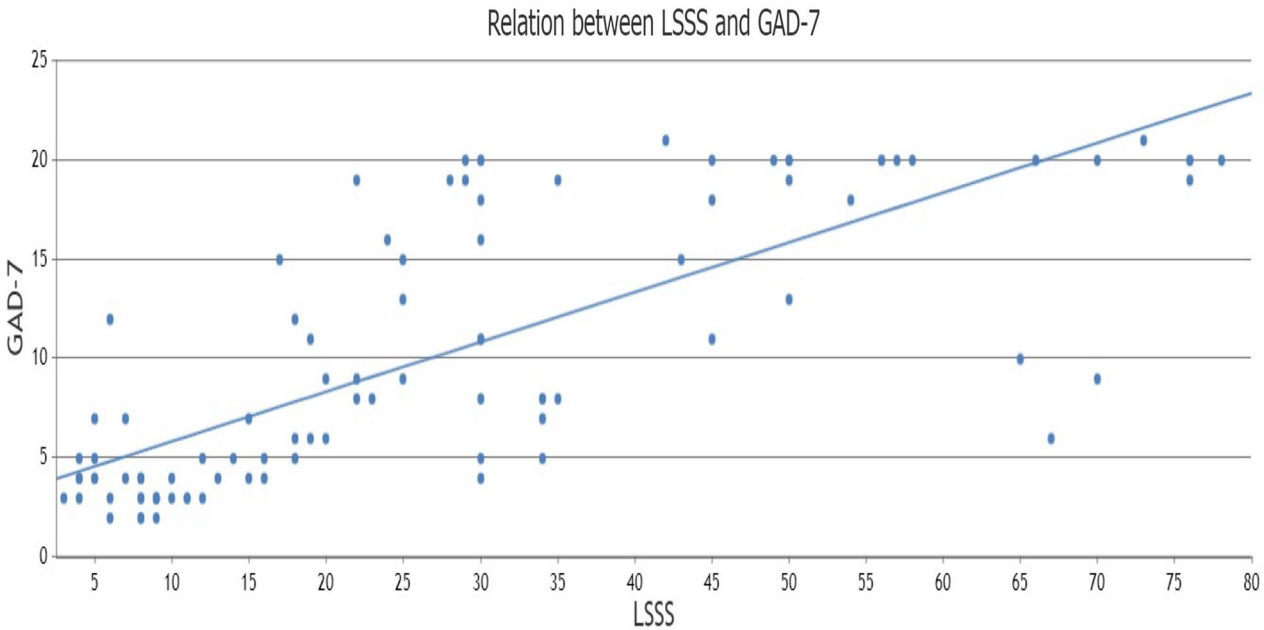

Fig. 1 Relation between the scores of Liverpool Seizure Severity Scale (LSSS) and of Generalized Anxiety Disorder 7-item (GAD-7)

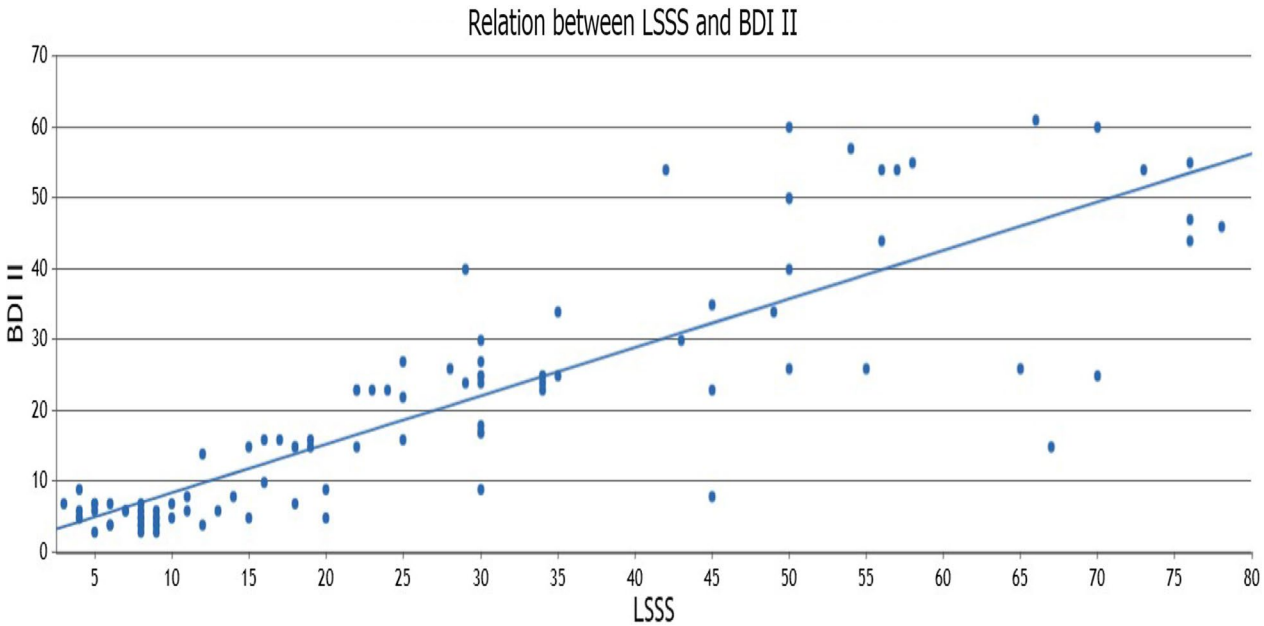

Fig. 2 Relation between the scores of Liverpool Seizure Severity Scale (LSSS) and of Beck's Depression Inventory II (BDI-II)

rates than those with normal anxiety score. Sex was not significantly associated with anxiety. Seizure severity was associated with generalized anxiety as patients with more severe seizures had higher scores on GAD-7. Family history of epilepsy was significantly associated with GAD-7 score as patients with severe anxiety had higher rate of family history of epilepsy as compared to those with mild and moderate anxiety.

Similar to these findings, Zhong and colleagues [21] mentioned that epileptic patients with anxiety had their seizures occurring more frequently, and they were more likely to be treated with polytherapy.

Contrary to the results of our study, Zhong and colleagues [21] found that GAD-7 questionnaire scores were higher in females with epilepsy than in males with epilepsy, and females were more probable to suffer from anxiety than males.

In a study on South Korean patients, conducted by Lee and colleagues [22], they have stated that seizure frequency may play a role in the development of anxiety.

Similar to our results, Zhong and colleagues [21] found that patients who had recurrent severe seizures reported higher depressive and anxiety symptoms levels. There was no relation between age, gender, epilepsy type, or family history of seizures and the presence of recurrent severe seizures.

There was a positive correlation between seizure severity measured by Liverpool Seizure Severity Scale (LSSS) with both of anxiety level measured by GAD-7, and depression measured by Beck's Depression Inventory II. Furthermore, score of quality of life in epilepsy-10 questionnaire showed that patients on polytherapy had a statistically significantly worse quality of life than those on monotherapy.

In agreement with the results of our study, Espinosa and colleagues [23] conducted a study on 220 epileptic patients in low-income countries and found that the score of the QOLIE-10 was significantly affected by epilepsy and multiple ASM intake which adversely affected quality of life. Alexander and colleagues [24] mentioned that patients on polypharmacy had worse QOLIE-10 scores even after controlling their seizure status. Harden and colleagues [25] examined a group of females aged from 18 to 45 years with refractory epilepsy, and found that even when controlling their depression, seizure severity was inversely correlated with quality of life.

However, the absence of an age, sex, and socioeconomic healthy control group that is compared with the epilepsy group is considered a major limitation in the study as the degree of impairment in epileptic patients' needs to be quantified relative to their non-epileptic peers.

Conclusion

We conclude that most patients with epilepsy had psychiatric comorbidities such as depression and anxiety which strongly reduce their quality of life and interfere with their compliance to anti-seizure medication. Moreover, patients' Intelligence Quotient (IQ) measured by Wechsler Adult Intelligence Scale Fourth Edition was found to be

negatively affected by taking multiple anti-seizure medication. Patients regularly taking more than one anti-seizure medication had a statistically significantly lower IQ score, more seizure severity, higher Beck's depression inventory II score, higher generalized anxiety disorder 7-item scale score, and worse quality of life than those on monotherapy.

Abbreviations

EEG	Electroencephalogram
LSSS	Liverpool seizure severity scale
QOLIE-10	Quality of Life In Epilepsy-10 Questionnaire
SD	Standard deviation
ASM	Anti-seizure medication
IQ	Intelligence quotient
CT	Computed tomography
MRI	Magnetic resonance imaging
IQR	Interquartile range
n	Number
%	Percent
P	*P* Value
PSI	Processing Speed Index
PRI	Perceptual Reasoning Index
WMI	Working Memory Index
VCI	Verbal Comprehension Index
PIQ	Performance IQ
VIQ	Verbal IQ
FSIQ	Full-Scale Intelligence Quotient
WAIS-IV	Wechsler Adult Intelligence Scale Fourth Edition
BDI II	Beck depression inventory II
GAD-7	Generalized Anxiety Disorder 7-item
FLAIR	Fluid attenuated inversion recovery

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Author contributions
RSN, AMM, SAY and EAM carried out the work. RSN designed the study, collected the patients, gathered the clinical data, coordinated the research team, had done the statistical analysis, wrote the manuscript and reviewed the manuscript. AMM, and SAY coordinated the research team, and participated in the formal analysis. EAM collected the patients, gathered the clinical data, and wrote the manuscript. All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved from the institute research board of Faculty of Medicine, Zagazig University, Egypt (ZU-IRB# 6115 at 2019). A written informed consent was obtained from all the participants after informing them about the study rationale and their right to withdraw from the study at any time without any consequences.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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