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Profile of adult -onset epilepsy in Zagazig university hospitals

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Abstract

Background Epilepsy has many neurobiological consequences. This study aimed to identify the profile of adult patients with new onset epilepsy in our university hospitals as regarding clinical picture, etiology, cerebral imaging and electroencephalogram (EEG) correlation, comorbidities, management, drug therapy and seizure severity and quality of life. We recruited one hundred patients with adult onset epilepsy, and we assessed them clinically, radiologically, and electrophysiologically. We performed Liverpool Seizure Severity Scale (LSSS) to assess seizure severity and the Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10) to assess quality of life of adult patients with new onset epilepsy.

Results Fifty-seven percent of the studied patients were males, and 43.0% were females with mean (± SD) of age was 52.83 (± 17.33), 13.0% of the studied patients had positive family history of epilepsy. 32.0% had focal epilepsy, and 68.0% had generalized epilepsy, 53% of patients had uncontrolled seizures, 49% of patients were on monotherapy, and 51.0% were on polytherapy. The mean (± SD) seizure frequency per month in the studied patients was 4.0 (± 3.15). Imaging abnormalities were found in 88% of studied patients. 43% of the studied patients had abnormal EEG. Post-traumatic epilepsy, focal cortical dysplasia and mesial temporal sclerosis were statistically significant higher in male patients than female patients. Arteriovenous malformations were significantly higher in females. Middle-aged adults' group had hypertension more than other age groups, older adult age group had atrial fibrillation, coronary heart disease, diabetes mellitus and dyslipidemia more than other age groups. Young adults had migraine more than other age groups. Post-stroke epilepsy was higher in older adult and middle-aged adult groups more than young adult age group. Intracranial neoplasms were higher in older adult age group than other age groups. Patients with moderate, severe, and very severe LSSS score had significantly more frequent uncontrolled seizures, abnormal EEG and higher rate of polytherapy as compared to those with mild LSSS score. Patients with impaired quality of life had more seizure frequency, less seizure control, higher seizure severity, more EEG abnormalities and were mostly treated by AEDs polytherapy than those with average life quality.

Conclusions Levetiracetam was the most preferred drug for treating patients with adult-onset epilepsy (40%), whether used as monotherapy or in combination with other drugs. Seizure severity, and seizure frequency per month strongly impaired patients' quality of life.

Keywords Epilepsy, Quality of life, Seizure severity

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Background

Epilepsy is one of the most common neurologic diseases in the world that affects approximately two million people in the United States and more than 50 million people worldwide, with 16–51 cases of new-onset epilepsy per 100,000 people every year [1]. With

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populations aging across the world and those with complex early onset epilepsies thankfully living into later life, the prevalence of epilepsy in aged people is raising rapidly. Assessment and management in this age group can be challenging. Seizures may present in unusual ways and the complex comorbidities and polypharmacy that often characterize older age, might make establishing a diagnosis of epilepsy and its management in older persons difficult [2].

In Arab countries, the estimated prevalence of epilepsy in children was found to be 3.6–10 .5/1000 [3].

In Egypt, the lifetime point prevalence of epilepsy among inhabitants of Al-Manial island was 6.9/1000 inhabitants, while the prevalence of active epilepsy was 5.1/1000 inhabitants. The age distribution showed bimodal peaks in adolescents and in elderly with equal sex ratio (6/855 versus 6/896). Focal seizures were the commonest type (58.3%) [4].

The prevalence of epilepsy among Fayoum inhabitants was 12/1000, with 95% CI (8.5–16.5)/1000 of the population [5]. A community based study conducted in Assiut Governorate showed that the prevalence of epilepsy was higher in rural areas (17.7/1000) than in urban areas (9.56/1000) with the highest prevalence rate recorded in the early and late childhood period (69.78/ 100,000 and 43.78/ 100,000, respectively) [6], while in the New Valley Governorate the prevalence of epilepsy was (6.76/1000) with the highest peak during early childhood [7].

Another study in Al-Quseir revealed that the lifetime prevalence rate of epilepsy was (5.5/1000), with the highest peak during early childhood, while that of active epilepsy was (3.3/1000) population. The annual incidence rate was (48/ 100,000) and the age-specific incidence rate had a U-shaped pattern with two peaks of incidence in early infancy and elderly life. Localization-related epilepsy was the most frequently encountered type 58.8%. The treatment gap of epilepsy in Al-Quseir was found to be 83.8% [8].

Sharkia Governorate is considered the third governorate in Egypt in population at the level of the Republic after Cairo and Giza governorates with 7.4% of the population of Egypt, where its estimated population for 2021 is 7.6 million people. The estimated total population in Zagazic city, according to the statement of the Central Agency for Public Mobilization and Statistics for the year 2020/2021 was 1406996. So, the aim of this work was to identify the profile of adult patients with new onset epilepsy in our university hospitals as regarding clinical picture, etiology, cerebral imaging and electroencephalogram (EEG) correlation, comorbidities, management, drug therapy and seizure severity and quality of life.

Methods

This is a prospective, cross-sectional, tertiary hospital-based study (the Zagazig university hospitals include about 1751 beds, and it is the main medical service provider of Sharika Government that includes about 7.64 million population). This study was carried out in our university 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.

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

The calculated sample size was 100 adult patients with new-onset epilepsy. Sample was calculated using open EPI program with confidence level 95% and power 80%.

We included one hundred patients with new onset epilepsy who fulfilled criteria for epilepsy diagnosis after the age of 18 years. We arranged them into three groups according to age: young adults (>18 years–40 years), middle-aged adults (>40 years–65 years) group, and older adult (>65 years) age group.

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 epilepsy or epileptic seizures and patients with acute symptomatic seizures {which are seizures occurring (1) during the period of 1 week in stroke, head trauma, or anoxic encephalopathy; (2) during the active phase in CNS infection or inflammatory disease, based on persistent clinical, laboratorial, or imaging findings; and (3) within 24 h in documented severe selected metabolic derangements} were excluded from the study.

All participants were subjected to the following: clinical assessment with detailed medical history with seizures history (age of onset, frequency per month, type and duration). Then, we arranged them into 3 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. Full general and neurological examination was done with focus on seizures time, onset (focal or generalized), level of consciousness, limbs tone and movement during the seizures, uprolling of eyes, frothy secretions from the mouth, duration and frequency of seizures, presence of eyewitness, hospital admission, occurrence of complications, status epilepticus, comorbid diseases, investigations done, treatment and compliance to treatment.

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Epilepsy was diagnosed according to International league against Epilepsy Commission on Classification and Terminology [9].

All patients were subjected to electroencephalography (EEG), and /or video_EEG monitoring when needed. Interictal scalp digital EEG was performed to all patients using EBNeuro machine (Italy) in quiet room while patient was relaxed under normal standard conditions. The electrodes were placed according to 10–20 transnational system of electrode placement. Bipolar as well as referential montages were applied. For every patient a 30-min awake record was obtained, using hyperventilation and photic stimulation as provocative methods. EEG traces were read by expert neurologists who are blinded to the clinical data of the patients. The EEG tracings were analyzed carefully 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), 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). Full routine laboratory investigations, available serum drug level of antiepileptic drugs and toxic/ drug screen was done if toxic causes were suspected.

Assessment of seizure severity was done using Liverpool Seizure Severity Scale [10]. We used the 20 questions scale translated into Arabic, each had 1 to 4 scores, and we measured seizure severity. The scores were calculated and arranged as follows [11]: mild seizures from 1 to 20, moderate seizures from 21 to 40, severe seizures from 41 to 60, very severe seizures from 61 to 80.

Assessment of quality of life was done using the Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10) [12]. QOLIE-10 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 QOLIE-10 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 scale score of 10 to 51 by answering all the questions. QOLIE-10 scores of 25 or more were considered as indicator for impaired quality of life [13]. It was used in Arabic language and was shown to be reliable in the current study.

Statistical analysis

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

Results

One hundred adult patients were studied, and the following results were obtained, 57.0% of the studied patients were males and 43.0% were females. The mean age (± SD) was 52.83 (± 17.33) with range from 19.0 to 82.0. Regarding educational level, 9.0% were illiterate, 31.0% had primary school level, 42.0% had high school level and 18.0% had college level. Regarding residence identity, 47.0% were living in urban areas, and 53.0% were living in rural areas. Regarding marital status, 77.0% were married, and 33.0% were unmarried.

There were 87.0% of the studied cases with no family history of epilepsy, and 13.0% had positive family history of epilepsy. 32.0% of the studied cases had focal epilepsy, and 68.0% presented with generalized epilepsy.

In this study, there were 47.0% of the studied cases had controlled seizure, and 53.0% had uncontrolled seizure (61.0% of cases had 1 to 4 seizures per month, 30.0% of cases had 5 to 8 seizures per month, and 9.0% had 9 to 15 seizures per month).

In this study 45% of cases had post-ictal confusion, 66% had post-ictal focal neurological deficit, 43% had ictal sphincteric incontinence, 11% had ictal tongue biting, 5% had fever and 5% had status epilepticus.

There were 12.0% of the studied cases had normal CT / MRI brain, and 88.0% had abnormal CT / MRI brain. Global brain atrophy was found in 34.0%, focal encephalomalacia was found in 30.0%, space occupying lesion was found in 22.0%, focal cortical dysplasia was found in 1.0%, and mesial temporal sclerosis was found in 1.0%.

There were 57% of the studied cases had normal EEG, and 43% had abnormal EEG. Generalized epileptiform activity was found in 19.0%, while focal epileptiform activity was found in 11.0%, and focal epileptiform activity with secondary generalization was found in 1.0%. Generalized non-epileptiform activity (diffuse slowing) was found in 10% of cases, and focal non-epileptiform activity (localized slow activity) was found in 2%.

As regarding antiepileptic drugs (AEDs), 49% of the studied patients had monotherapy and 51.0% had

Table 1 Distribution of the studied cases according to the comorbidities in different age groups

	Young adults (18 y–40 y) total No.26		Middle-age adults (>40 y-65 y) Total n = 41			Older adults (>65 y) Total n = 33			P value
	n	% Total patients	% Age group	n	% Total patients	% Age group	n	% Total patients	% Age group	
Hypertension	0	0.0	0.0	20	20.0	48.78	12	12.0	36.36	<0.001*
Migraine	15	15.0	57.7	3	3.0	7.3	0	0.0	0.0	<0.001*
Atrial fibrillation	0	0.0	0.0	6	6.0	14.6	10	10.0	30.30	0.0095*
Coronary heart disease	2	2.0	7.7	4	4.0	9.75	10	10.0	30.30	0.0430*
Diabetes mellitus	0	0.0	0.0	7	7.0	17.07	8	8.0	24.24	0.0224*
Dyslipidemia	0	0.0	0.0	3	3.0	7.3	6	6.0	18.18	0.0498*
Chronic kidney disease	0	0.0	0.0	1	1.0	2.4	2	2.0	6.06	0.3679
Chronic liver disease	0	0.0	0.0	0	0.0	0.0	1	1.0	3.03	0.4724

(n): number, (%): percent, (y): years, (P): p value for comparing between different age groups

* statistically significant at $p \leq 0.05$

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polytherapy of AEDs. 40.0% of cases had 2 AEDs, 9.0% had 3 AEDs and 2.0% had 4 AEDs. 42.0% of cases were on old AEDs (phenytoin, valproate and carbamazepine), 41.0% were on new AEDs (Levetiracetam, oxcarbazepine, topiramate, zonisamide and lacosamide), and 17.0% had combined therapy (old and new AEDs). Levetiracetam was the first line monotherapy in 40.0% of our patients, 34.0% were on valproate, 32.0% were on carbamazepine, and 20% were on phenytoin.

Thirty-two percent of the studied cases had hypertension, 18.0% had migraine, 16.0% had atrial fibrillation, 14.0% had diabetes mellitus, 9.0% had dyslipidemia, 5% had coronary heart disease, 3.0% had chronic kidney disease, and 1.0% had chronic liver disease. Middle-age adults' group (>40 years–65 years) had hypertension more than other age groups, older adults age group (>65 years) had atrial fibrillation, coronary heart disease, diabetes mellitus and dyslipidemia more than other age groups. Also, young adults age group (18 years–40 years) had migraine more than other age groups (Table 1).

Thirty-one percent of the studied patients had epilepsy due to cerebrovascular stroke, 22.0% had epilepsy due to intracranial neoplasms, 15.0% had epilepsy due to previous cranial trauma, 15.0% had epilepsy due to previous central nervous system infection, 2.0% had epilepsy due to arteriovenous malformations, 1.0% had epilepsy due to focal cortical dysplasia, 1.0% had epilepsy due to mesial temporal sclerosis, and 13.0% had epilepsy with undetermined etiology. The most common cause of epilepsy in young adults age group was post-traumatic brain injury, while old cerebrovascular stroke was the most common cause of epilepsy in both middle-age adults and older adults age groups (Table 2).

In the current study we found that post-traumatic brain injury, focal cortical dysplasia, and mesial temporal sclerosis as causes of epilepsy were statistically significantly higher in males. Arteriovenous malformations were statistically significantly higher in females.

Among our patients, 47% had mild seizure severity, 26% had moderate, 17% had severe, 10% had very severe seizures, and older adults group had higher scores in Liverpool Seizure Severity Scale than other age groups. Patients on polytherapy had a statistically significantly more seizure severity than those on monotherapy. Regarding laboratory investigations of the studied cases, serum valproic acid level, serum carbamazepine level, and serum phenytoin level (mg/dL) in patients with severe and very severe seizures are statistically significantly lower than in those with mild and moderate seizures' severity (Table 3).

There was a statistically significant relation between Liverpool Seizure Severity Scale Score and seizure control ($P < 0.001$), as patients with moderate, severe, and very severe LSSS had a significantly higher rate of uncontrolled seizures as compared to those with mild LSSS. Similarly, there was a statistically significant relation between LSSS score and seizure frequency ($P < 0.001$), as patients with moderate, severe, and very severe LSSS had higher frequency of seizures when compared to those with mild LSSS (Table 4).

There was a statistically significant relation between LSSS Score and presence of EEG abnormalities, number of AEDs taken regularly by patients (P $P < 0.001$), as patients with moderate, severe, and very severe LSSS had more abnormal EEG, and higher rate of polytherapy as compared to those with mild LSSS (Table 5).

In our study, concerning Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10) score, 70% of the studied patients had average quality of life, while 30% had impaired quality of life. There was a statistically significant relation between QOLIE-10 score and seizure control, and seizure frequency as patients with impaired quality of life had significantly higher rate of uncontrolled seizures and higher frequency of seizures as compared to those with average life quality (P < 0.001) (Table 6).

There was a statistically significant relation between QOLIE-10 and presence of EEG abnormalities, as patients having impaired quality of life had significantly higher rate of abnormal EEG as compared to those with average life quality ($P < 0.001$) Also, were mostly treated by AEDs polytherapy than those with average life quality (Table 7).

There was a positive correlation between seizure severity and QOLIE-10 score. The higher is the seizure severity, the higher is the score in QOLIE-10 with worse life quality Fig. 1.

Discussion

This study is a prospective, cross-sectional, tertiary hospital-based study aiming to identify the profile of adult patients with new onset epilepsy in Zagazig University hospitals that support investigations, treatment of patients at reduced prices, provides medical consultation and inpatient services almost free of charge.

In our study 57% of the studied patients were males, and 43% were females, with male to female ratio of 1.3 to 1. The mean age in years (± SD) was 52.83 (± 17.33) with range from 19.0 years to 82.0 years. Educational level varied among studied patients as 9.0% were illiterate, 31.0% had primary school level, 42.0% had high school level, and 18.0% had college level. Regarding residence identity, 47.0% were from urban areas, and 53.0% were from rural areas. Regarding marital status 77.0% were married, and 33.0% were unmarried.

Middle-age group (aged from 40 to 65 years) showed higher prevalence (41%) of epilepsy than young adults

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Table 2 Distribution of the studied cases according to the etiology of epilepsy in different age groups

	Young adults (18 y–40 y) total n=26			Middle-age adults (>40 y–65 y) total n=41			Older adults (>65 y) total n=33			P value
	n	% Total patients	% Age group	n	% Total patients	% Age group	n	% Total Patients	% Age group	
Post-stroke epilepsy	2	2.0	7.69	14	14.0	34.14	15	15.0	45.45	0.0066*
Intracranial neoplasm	4	4.0	15.38	5	5.0	12.19	13	13.0	39.39	0.0397*
Post-traumatic epilepsy	7	7.0	26.92	7	7.0	17.07	1	1.0	3.03	0.0907
Post-central nervous system infection	3	3.0	11.53	9	9.0	21.95	3	3.0	9.09	0.0907
Arteriovenous malformations	2	2.0	2.69	0	0.0	0.0	0	0.0	0.0	0.2231
Focal cortical dysplasia	1	1.0	3.84	0	0.0	0.0	0	0.0	0.0	0.4724
Mesial temporal sclerosis	1	1.0	3.84	0	0.0	0.0	0	0.0	0.0	0.4724
Undetermined	6	6.0	23.07	6	6.0	14.63	1	1.0	3.03	0.1506

(n): number, (y): years, (%): percent, (P): p value for comparing between different age groups

* statistically significant at p≤0.05

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Table 3 Distribution of the studied cases according to laboratory investigations findings and Liverpool seizure severity scale score

Laboratory investigation findings mean (± SD)	Liverpool seizure severity scale score				*P* value
	Mild	**Moderate**	**Severe**	**Very severe**	
Sodium (mEq\L)	139.64(± 2.1)	136.87(± 2.03)	141.34(± 1.9)	136.58(± 2.5)	0.068
Potassium (mEq \L)	4.26 (± 0.46)	4.56 (± 0.45)	5.12(± 0.48)	4.43(± 0.49)	
Calcium (mEq \L)	9.24 (± 0.41)	9.32 (± 0.32)	8.87(± 0.51)	9.66(± 0.45)	
Magnesium (mEq\L)	2.03 (± 0.36)	2.5 (± 0.65)	1.89(± 0.31)	1.59(± 0.23)	
Serum valproic acid level (mcg/mL)	91.66(± 10.45)	78.39(± 14.45)	25.35(± 10.3)	20.24(± 9.24)	< 0.001*
Serum carbamazepine level (mcg/mL)	9.11 (± 1.37)	10.01(± 1.45)	7.36(± 2.65)	7.23 ± (2.65)	0.0432*
Serum phenytoin level (mg/dL)	12.1 (± 3.31)	13.3 (± 2.12)	8.7 (± 4.76)	7.5 (± 4.25)	0.0456*
INR	1.2 (± 0.37)	1.17 (± 0.42)	1.11(± 0.37)	0.9(± 0.38)	0.076
Cholesterol level(mg \dL)	152.15 (± 29.45)	169.21 (± 38.29)	171.17 (± 42.26)	158.43 (± 37.31)	
ESR (mm\ hr)	31.2(± 13.12)	34.4(± 11.09)	35.5(± 15.26)	32.7(± 15.01)	
Blood glucose level (mg\dL)	118.49 (± 78.16)	112.38 (± 56.38)	121.56 (± 76.65)	123.78 (± 87.76)	0.088
Serum creatinine level (mg\dL)	1.25 (± 0.54)	1.87 (± 0.76)	1.49 (± 0.45)	1.28 (± 0.28)	
Serum bilirubin (mg\dL)	0.67 (± 0.45)	0.76 (± 0.38)	0.65(± 0.35)	0.39(± 0.78)	
Serum albumin (mg\ dL)	4.56 (± 0.42)	4.89 (± 0.59)	3.79(± 0.46)	3.98(± 0.52)	0.078
Hemoglobin level (g/dL)	13.52 (± 1.34)	14.48(± 1.45)	12.98(± 1.81)	13.52 (± 1.47)	
WBCs (per μL)	8340 (± 1400.73)	6980 (± 1354.61)	5400(± 1640.81)	4200 (± 1456.52)	

(IQR): interquartile range, (SD): standard deviation, (mcg/mL): microgram per milliliter, (mg \dl): milligram per deciliter, (ESR): erythrocyte sedimentation rate, (mm\ hr): millimeter per hour, (g/dL): gram per deciliter, (WBCs): white blood cells, (μL): microliter, (mEq\L): milliequivalent per liter, (INR): international normalized ratio

* statistically significant at *p* ≤0.05

(aged from 18 to 40 years) who showed prevalence of 26%, and older adults (aged more than 65 years) with prevalence of 33%.

In agreement with these results, Bhatia and colleagues [14] showed that male patients outnumbered female patients, 54.4% of the patients were males, and 45.6% were females, with an average age of 44.6 years, and the male to female proportion was 1.2 to 1. Similar results were reported by Kaur and colleagues [15] who stated that 65% were males, most of the patients (38%) were in the age group of 21 years–40 years and 41 years–60 years, only 9% were of< 20 years, and 15% were of more than 60 years.

Contrary to these results, Ali and colleagues [16] reported that the majority of patients were females (55.1%). On the other hand, Sheikh and colleagues [17] stated that both younger age group (25 years -34 years), and male patients showed higher prevalence. This difference in our study could be because most of the patients belonged to the middle-aged adult group (>40 years to 65 years), and also may be because older adult patients (>65 years) used not to seek medical advice as compared to other age groups.

In our study, 87% of the studied patients had no family history of epilepsy, and 13% had positive family history of epilepsy. That relatively higher percentage of absence of epilepsy family history in our study, is going with the relatively high percentage of presence of organic cerebral

pathology (88%), and of having acquired etiology (87%) in our study. Which may be expected when the included patients are all having adult-onset epilepsy, as in our study.

There were 32.0% of the studied patients having focal epilepsy (of them, 11% had epilepsy with focal onset aware seizures, and 21% had epilepsy with focal onset seizures with impaired awareness), while 68.0% of the studied patients had generalized epilepsy (of them, 42% had epilepsy with generalized onset motor seizures and 26% had epilepsy with generalized onset non-motor seizures (absence)). In agreement with these results, Sheikh and colleagues (17) stated that among the participating subjects, generalized tonic–clonic seizures were the most common type of seizures (48.8%), followed by focal seizures with impaired awareness (14.6%).

This is in accordance with Kaur and colleagues [15] who carried out a study on 100 patients with adult-onset epilepsy and reported that the majority (59%) had generalized seizures. Out of rest 41 with focal seizures, 16 (39%) had focal aware seizures, 15 (36.6%) had focal seizures with impaired awareness, whereas remaining 10 (24.4%) had focal seizures with secondary generalization.

These results are different from Bhatia and colleagues [14] who had reported that the most common seizure type of seizure was generalized tonic–clonic seizures, present in 98.9% of patients, whereas focal seizures were seen in 1.1%, and the percentage of patients having

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Table 4 Relation between Liverpool Seizure Severity Scale (LSSS) Score and different patients' characteristics

	Liverpool seizure severity scale score				P value
	Mild (*n* = 47)	Moderate (*n* = 26)	Severe (*n* = 17)	Very severe (*n* = 10)	
Age (years)					0.089
Min–Max	19 – 82	22–76	19–73	34–81	
Mean (± SD)	50.43 (± 15.43)	51.31(± 17.11)	52.76(± 16.2)	65.9(± 15.33)	
Sex					0.63
Male	29 (61.7%)	14 (53.8%)	10 (58.8%)	4 (40%)	
Female	18 (38.3%)	12 (46.2%)	7 (41.2%)	6 (60%)	
Family history					0.861
Absent	42 (89.4%)	22 (84.6%)	14 (82.4%)	9 (90%)	
Present	5 (10.6%)	4 (15.4%)	3 (17.6%)	1 (10%)	
Epilepsy type					0.254
Focal	14 (29.8%)	7 (26.9%)	5 (29.4%)	6 (60%)	
Generalized	33 (70.2%)	19 (73.1%)	12 (70.6%)	4 (40%)	
Seizure control					< 0.001*
Controlled	41 (87.2%)	5 (19.2%)	0 (0%)	1 (10%)	
Uncontrolled	6 (12.8%)	21 (80.8%)	17 (100%)	9 (90%)	
Seizure frequency /month					< 0.001*
Min.–Max.	1–6	1–8	4–15	2–15	
Mean (± SD)	1.81 (± 1.32)	4.35 (± 1.92)	7.35(± 2.87)	7.7 (± 3.71)	
Comorbidities					
Hypertension	13 (27.7%)	7 (26.9%)	8 (47.1%)	4 (40%)	0.427
Diabetes mellitus	7 (14.9%)	4 (15.4%)	2 (11.8%)	1 (10%)	0.962
Dyslipidemia	3 (6.4%)	3 (11.5%)	3 (17.6%)	0 (0%)	0.289
Coronary heart disease	5 (10.6%)	0 (0%)	0 (0%)	0 (0%)	0.115
Atrial fibrillation	7 (14.9%)	3 (11.5%)	2 (11.8%)	4 (40%)	0.261
Chronic kidney disease	1 (2.1%)	1 (3.8%)	0 (0%)	1 (10%)	0.514
Chronic liver disease	0 (0%)	1 (3.8%)	0 (0%)	0 (0%)	0.4361
Migraine	11 (23.4%)	3 (11.5%)	3 (17.6%)	1 (10%)	0.534

(SD): standard deviation, (n): number of patients, (p): p value for comparing between LSSS and different patients' characteristics

* statistically significant at p ≤ 0.05

generalized tonic–clonic seizures was more than those in our study, probably because all patients in their study were enrolled from emergency departments where most of the active epilepsy patients brought to emergency room are those having the grand mal presentation (generalized tonic–clonic seizures), particularly when they take the serial or status form.

In our study 47.0% of the studied patients had controlled seizure, and 53.0% had uncontrolled seizure. The mean (± SD) seizure frequency per month was 4.0 (± 3.15), with range from 1.0 to 15.0. The majority of the studied patients (61%) had 1 to 4 seizures per month, 30% had 5 to 8 seizures per month, and 9% had 9 to 15 seizures per month. Bhatia and colleagues [14] reported that the majority of their patients (92.2%) had one to five episodes of seizure per month, whereas 5.6% of patients were found to have six to ten episodes, and 2.2% were found to have 10 –15 episodes of seizure.

In our study 12.0% of the studied patients had normal computed tomography (CT) / magnetic resonance imaging (MRI) brain, and 88.0% had abnormal CT / MRI brain. Parallel to the results of our study, Bhatia and colleagues [14] showed that almost 72% had abnormal brain imaging and Sheikh and colleagues [17] stated that MRI showed abnormal findings in 59.7% of the patients.

Similar to our results, Mahmoud and colleagues [18] showed that abnormal findings in neuroimaging were detected among (75%) of adult-onset epilepsy patients. This can be going with the expected relatively higher percentage of organic cerebral pathology in adult-onset epilepsy as in our study inclusion criteria.

The findings of our study revealed that 57% of the studied patients had a within normal EEG, and 43% had abnormal EEG. In agreement with our study, Mahmoud and colleagues [18] found that electroencephalographic data were useful; where it detected abnormality in 37.5%,

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Table 5 Relation of Liverpool Seizure Severity Scale (LSSS) Score with Cerebral Imaging and EEG findings, and antiepileptic drugs profile

	Liverpool seizure severity scale score				*P* value
	Mild (*n* = 47)	Moderate (*n* = 26)	Severe (*n* = 17)	Very severe (*n* = 10)	
CT/MRI findings					0.077
Normal	5 (10.6%)	2 (7.7%)	5 (29.4%)	0 (0%)	
Abnormal	42 (89.4%)	24 (92.3%)	12 (70.6%)	10 (100%)	
EEG findings					< 0.001*
Normal	40 (85.1%)	10 (38.5%)	4 (23.5%)	3 (30%)	
Abnormal	7 (14.9%)	16 (61.5%)	13 (76.5%)	7 (70%)	
Number of AEDs					< 0.001*
Monotherapy	34 (72.3%)	8 (30.8%)	5 (29.4%)	2 (20%)	
Polytherapy	13 (27.7%)	18 (69.2%)	12 (70.6%)	8 (80%)	
2	10	17	8	5	
3	3	1	3	2	
4	0	0	1	1	
Type of AEDs					
Valproate	10 (21.3%)	11 (42.3%)	8 (47.1%)	5 (50%)	0.085
Phenytoin	7 (14.9%)	6 (23.1%)	5 (29.4%)	2 (20%)	0.61
Carbamazepine	12 (25.5%)	11 (42.3%)	6 (35.3%)	3 (30%)	0.517
Oxcarbazepine	3 (6.4%)	0 (0%)	2 (11.8%)	2 (20%)	0.107
Levetiracetam	19 (40.4%)	9 (34.6%)	7 (41.2%)	5 (50%)	0.863
Lacosamide	0 (0%)	1 (3.8%)	1 (5.9%)	1 (10%)	0.225
Topiramate	9 (19.1%)	5 (19.2%)	0 (0%)	2 (20%)	0.087
Zonisamide	2 (4.3%)	2 (7.7%)	1 (5.9%)	0 (0%)	0.693

(AEDs): antiepileptic drugs, (EEG): electroencephalogram, (CT): computed tomography, (MRI): magnetic resonance imaging, (n): number of patients, (p): p value for comparing between LSSS and different examinations and AEDs

* statistically significant at $p \leq 0.05$

and Sheikh and colleagues [17] reported that EEG findings were abnormal in 52.8% of their patients. Furthermore, Kaur and colleagues [15] reported that 44% of their patients had an abnormal EEG record suggestive of seizure activity, whereas 56% of their patients had a normal EEG record. The results of our study are different from those of Hosalli and colleagues [19], who reported that out of 100 cases, EEG was done in 45 cases only as demanded by clinical situation. About 14% had an abnormal EEG record while the rest 31% (n = 31) had a normal EEG record. The difference is probably because of not performing EEG for all patients in their study.

In our study, 45% of studied patients had post-ictal confusion, 66% had post-ictal focal neurological deficit (hemiparesis in 33.0%, cranial nerve affection in 18.0%, language and speech dysfunction in 9.0%, and monoparesis in 6.0%). Of the studied patients, 43% had ictal sphincteric incontinence, 11% had ictal tongue biting, 5% had pot-ictal fever, and 5% presented in status epilepticus.

In our study 32.0% of the studied patients were hypertensive on treatment, 18.0% had chronic migraine, atrial fibrillation was found in 16.0% of patients, 14.0% were diabetics, 9.0% had dyslipidemia, 5% had coronary heart disease, 3.0% had chronic kidney disease, and 1.0% had chronic liver disease. In our study post-traumatic epilepsy was of higher percentage in male than female patients, and focal cortical dysplasia and mesial temporal sclerosis were higher in males. Arteriovenous malformations were significantly higher in females. Post-traumatic brain injury, focal cortical dysplasia, and mesial temporal sclerosis as causes of epilepsy were statistically significantly higher in males. Arteriovenous malformations were statistically significantly higher in females.

Regarding distribution of comorbidities in different age groups, our study revealed that hypertension was significantly higher in middle-aged adults' group (40–65 years) than in other age groups. Atrial fibrillation, coronary heart disease, diabetes mellitus and dyslipidemia were significantly higher in older adults (> 65 years) age group than in other age groups. Also, chronic migraine was higher in young adults (18 years–40 years) age group than in other age groups.

Bhatia and colleagues [14] showed in their study that the majority of cases (81.1%) had no past history of medical diseases, whereas 7.7% had hypertension, 5.6% had diabetes. These figures are much lower than what is in

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Table 6 Relation between Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10) Score and different patients' characteristics

	Quality of life in epilepsy-10 questionnaire score		P value
	Average (n = 70)	Impaired (n = 30)	
Age (years)			0.175
Min–Max	19–82	19–81	
Mean (± SD)	52.24 (± 15.69)	54.2 (± 20.9)	
Sex			0.172
Male	43 (61.4%)	14 (46.7%)	
Female	27 (38.6%)	16 (53.3%)	
Family history			0.201
Absent	63 (90%)	24 (80%)	
Present	7 (10%)	6 (20%)	
Epilepsy type			0.092
Focal	26 (37.1%)	6 (20%)	
Generalized	44 (62.9%)	24 (80%)	
Seizure control			< 0.001*
Controlled	45 (64.3%)	2 (6.7%)	
Uncontrolled	25 (35.7%)	28 (93.3%)	
Seizure frequency / month			< 0.001*
Min.–Max	1–15	2–15	
Mean (± SD)	2.96 (± 2.61)	6.43 (± 2.99)	
Comorbidities			
Hypertension	21 (30%)	11 (36.7%)	0.513
Diabetes mellitus	10 (14.3%)	4 (13.3%)	> 0.999
Dyslipidemia	8 (11.4%)	1 (3.3%)	0.272
Coronary heart disease	5 (7.1%)	0 (0%)	0.318
Atrial fibrillation	9 (12.9%)	7 (23.3%)	0.236
Chronic kidney disease	2 (2.9%)	1 (3.3%)	> 0.999
Chronic liver disease	1 (1.4%)	0 (0%)	> 0.999
Migraine	13 (18.6%)	5 (16.7%)	0.82

(SD): standard deviation, (n): number of patients, (P): p value for comparing between (QOLIE 10) and different patients' characteristics

* statistically significant at p ≤ 0.05

Table 7 Relation of Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10) Score with Cerebral Imaging and EEG findings, and Antiepileptic Drugs Profile

	Quality of life in epilepsy-10 questionnaire score		P value
	Average (n = 70)	Impaired (n = 30)	
CT/MRI findings			0.338
Normal	7 (10%)	5 (16.7%)	
Abnormal	63 (90%)	25 (83.3%)	
EEG			< 0.001*
Normal	48 (68.6%)	9 (30%)	
Abnormal	22 (31.4%)	21 (70%)	
Number of AEDs			0.106
Monotherapy	38 (54.3%)	11 (36.7%)	
Polytherapy	32 (45.7%)	19 (63.3%)	
2	27	13	
3	4	5	
4	1	1	
Type of AEDs			
Valproate	20 (28.6%)	14 (46.7%)	0.08
Phenytoin	14 (20%)	6 (20%)	> 0.999
Carbamazepine	21 (30%)	11 (36.7%)	0.513
Oxcarbazepine	5 (7.1%)	2 (6.7%)	> 0.999
Levetiracetam	29 (41.4%)	11 (36.7%)	0.656
Lacosamide	2 (2.9%)	1 (3.3%)	> 0.999
Topiramate	11 (15.7%)	5 (16.7%)	> 0.999
Zonisamide	3 (4.3%)	2 (6.7%)	0.635

(AEDs): antiepileptic drugs, (EEG): electroencephalogram, (CT): computed tomography, (MRI): magnetic resonance imaging, (n): number of patients, (P): p value for comparing between QOLIE-10 with different examinations and AEDs

* statistically significant at p ≤ 0.05

our study, which may be attributed to differences in cultural and environmental factors, and in lifestyle and feeding habits, also it may be attributed to the much lower age range of their patients than ours, where two thirds of their patients aged from 13 to 55 years, while 74% of our patients aged from > 40 to > 65 years.

Our study revealed that post-stroke epilepsy was higher in older adults, and middle-age adults' groups more than in young adults age group and intracranial neoplasms were of higher percentage in older adults age group than other age groups. In agreement with our findings, Mahmoud and colleagues [18] revealed that post-stroke epilepsy is the most common etiology for adult new-onset epilepsy (44.17%), and the highest prevalence was in the older adults (> 65 years) age group (65.28%).

This is in accordance with study of Bhatia and colleagues [14] who illustrated that new-onset seizures have different etiologies in different age groups. In the middle-age group (between 36 and 55 years), cerebrovascular accidents were the dominant etiology present in 36.7% of the patients. The second most common etiology in this age group was CNS infection. The third most common cause was metabolic abnormalities in this age group. In the older age group (above 55 years), the most dominating etiology was cerebrovascular accident, followed by infective etiology.

Stroke was shown to be the most prevalent cause of seizures in older adults, according to a study by Kaur and colleagues [15].

According to study by Hirani and colleagues [20], CNS infections (38%), stroke (30%), and idiopathic seizures (25%) were the most common causes of adult-onset seizures. Infective causes of epilepsy were
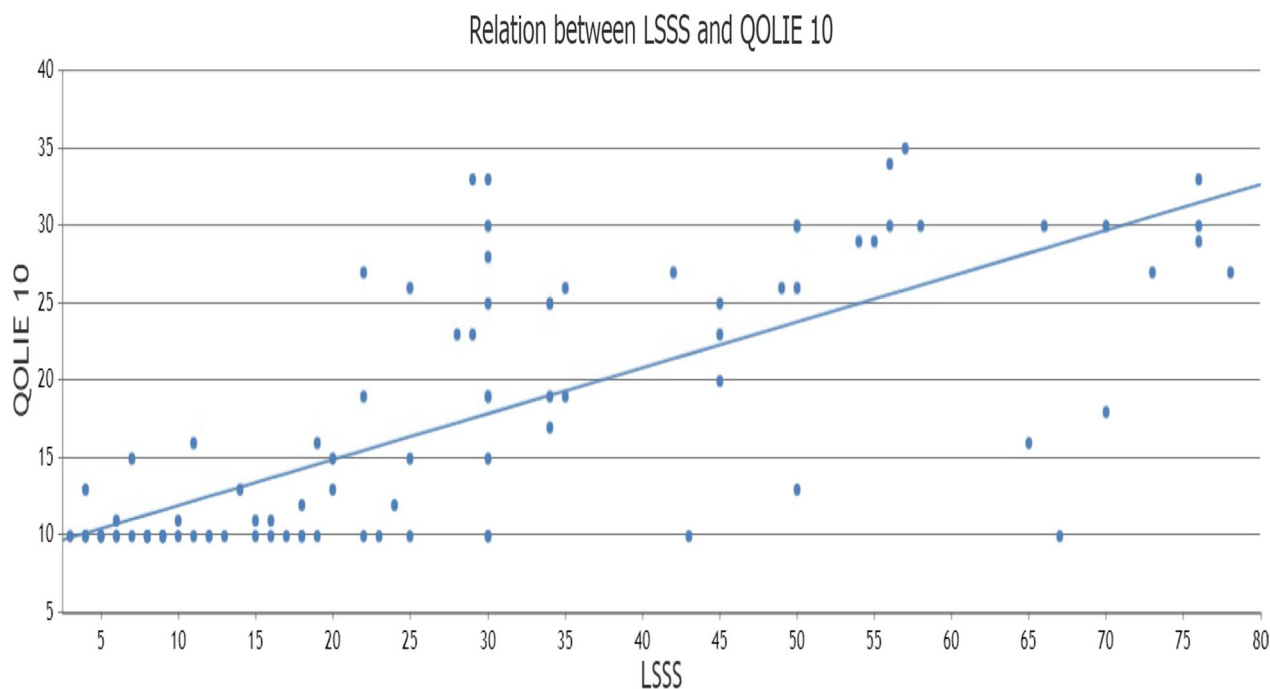
Fig. 1 Relation between the scores of Liverpool Seizure Severity Scale (LSSS) and of Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10)

predominant in young patients, and stroke became the dominant cause as age increased. Kaur and colleagues [15] documented that in their studied 23 patients with post-stroke seizures, the highest prevalence was among individuals aged more than 40 years (95.6%). Idiopathic seizures were more common in younger adults (68.1%) aged less than 40 years, followed by CNS infections (66.6%). Metabolic causes and brain tumors were the cause of seizures in minority of cases.

Our findings regarding laboratory investigations revealed that all the studied patients had normal serum electrolytes (sodium, potassium, calcium, magnesium), and serum antiepileptic drugs (AEDs) level (valproate, phenytoin, carbamazepine) was significantly lower in patients with severe seizures (measured by LSSS) than in those with mild, and moderate seizures. Contrary to our findings, Bhatia and colleagues [14] reported that the most common metabolic abnormality found was hyponatremia in 6.3% of patients, followed by hypoglycemia in 2.3% of patients, and the least common was hypocalcemia in 0.9% of patients. Also, Mahmoud and colleagues [18] revealed that epilepsy patients with new-onset seizure had significant findings in their metabolic profile included 10% of patients with hypocalcemia, 6.67% of patients with hyponatremia, 4.17% of patients with hypokalemia, 5.83% patients with hyperglycemia and 2.5% of patients with hypoglycemia.

Rayamahji and colleagues [21] showed that the most common cause of seizures was hyponatremia. According to a report in the United States of America, the prevalence of hyponatremia in the emergency department was 2.7%. Also, a survey in Taiwan performed by Hao and colleagues [22] showed that prevalence of hyponatremia was 2.9%. The reason for this difference is that acute symptomatic seizures within 24 h in documented severe selected metabolic derangements were excluded from our study (Methods, Exclusion Criteria).

Our findings regarding AEDs revealed that there were 49% of the studied patients regularly on a single antiepileptic drug, and 51.0% on multiple AEDs (40.0% on two AEDs, 9.0% on 3 AEDs and 2.0% on 4 AEDs). Also, 42.0% were on old AEDs, 41.0% were on newer AEDs, and 17.0% were on both old and new AEDs. Levetiracetam was the first line monotherapy in 40.0% of our patients, 34.0% were on valproate, 32.0% were on carbamazepine, and 20% were on phenytoin.

In agreement with our results, Lezaic and colleagues [23] mentioned that levetiracetam had better tolerability when compared with other AEDs in post-stroke epilepsy in the older adults, and was the most commonly used as first line therapy. Similarly, Martin and colleagues [24] demonstrated that the most commonly prescribed initial antiepileptic drug was levetiracetam in 45.5% of patients, followed by phenytoin in 30.6%. These results

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were compatible with Thurman and colleagues [25] who reported that levetiracetam was the most common antiepileptic drug prescribed for initial monotherapy.

In contrary to these results, an old study by Pugh and colleagues [26] which showed that phenytoin was the most commonly prescribed antiepileptic drug in older adult individuals with new-onset epilepsy.

Among our patients, 47% had mild seizure severity, 26% had moderate, 17% had severe, 10% had very severe seizures, and older adults group had higher scores in Liverpool Seizure Severity Scale than other age groups. Another important finding in our study was that patients regularly on AEDs polytherapy had significantly more score on LSSS than those on monotherapy.

Viteva and colleagues [11] done a study on 70 adult patients with refractory epilepsy, and 70 patients with pharmaco-sensitive epilepsy, and evaluated the seizure severity using LSSS. 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 Quality of Life In Epilepsy-10 Questionnaire (QOLIE-10) score, 70% of the studied patients had average quality of life, while 30% had impaired quality of life. Patients with impaired quality of life had more seizure frequency, less seizure control, and higher seizure severity. Also, they had more abnormal EEG findings and were mostly treated by AEDs polytherapy than those with average life quality.

Similar to the results of our study, a study in Ethiopia done by Muche and colleagues [27] on 354 patients showed that the mean QOLIE-10 score was 19.85 (±8.35), and 54.8% of participants had a good quality of life.

In agreement with the results of our study, Espinosa and colleagues [28] 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 AEDs intake which adversely affected quality of life.

Alexander and colleagues [29] mentioned that patients on polypharmacy had worse QOLIE-10 scores even after controlling their seizure status. Harden and colleagues [30] 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.

Bautista and colleagues [31] indicated that quality of life of patients with epilepsy was adversely affected by seizure severity.

Furthermore, Sancho and colleagues [32] indicated that the quality of life in patients with severe seizures has been consistently shown to be worse than for those with mild or moderate seizures.

However, the current study may be limited by the relatively small sample size So, further larger studies need to be done on choosing the best antiepileptic drugs in cases of adult-onset epilepsy taking patients' age, sex, occupation, and comorbidities in consideration, with follow up of their effectiveness in prevention of recurrence, and adverse effects.

Conclusions

Adult-onset epilepsy has increasing importance with the aging population. Cerebrovascular stroke was found to be the most common cause of adult-onset epilepsy representing 31%, followed by intracranial tumors representing 22%. EEG was found to be abnormal in 43% of all studied patients with adult-onset epilepsy. Levetiracetam was the most preferred drug for treating patients with adult-onset epilepsy (40%), whether used as monotherapy or in combination with other drugs. Seizure severity measured by Liverpool Seizure Severity Scale, and seizure frequency per month strongly impaired patients' quality of life as measured by Quality of Life In Epilepsy-10 Questionnaire.

It is advisable to do appropriate investigations looking thoroughly for an acquired pathology as a possible direct cause of recent-onset epilepsy in all patients whose history and physical examination are not suggestive of idiopathic primary epilepsy, particularly when it is an adult-onset epilepsy. Care should be taken when giving multiple antiepileptic drugs especially in elderly.

Abbreviations

EEG	Electroencephalogram
LSSS	Liverpool Seizure Severity Scale
QOLIE-10	Quality of Life In Epilepsy-10 Questionnaire
SD	Standard Deviation
AEDs	Antiepileptic drugs
IRB	Institutional Research Board
CT	Computed Tomography
MRI	Magnetic resonance imaging
IQR	Interquartile range
No	Number
%	Percent
y	Years
P	P value
mcg/mL	Microgram per milliliter
mg \dl	Milligram per deciliter
ESR	Erythrocyte sedimentation rate
mm\ hr	Millimeter per hour
g/dL	Gram per deciliter
WBCs	White blood cells
µL	Microliter
mEq\L	Milliequivalent per liter
INR	International normalized ratio

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.

Availability of data and materials
The corresponding author takes full responsibility for the data, has full access to all the data; and has the right to publish any and all data separate and apart from any sponsor.

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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