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# Etiological profile of new-onset seizures among adult Egyptians



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## Abstract

**Background:** New-onset seizure (NOS) is defined as the first seizure within a 24-h period ever experienced by the patient. A first-ever seizure can be the first manifestation of epilepsy. Or it may be a symptom of a brain tumor, a systemic disorder, an infection, or a syndrome that deserves special attention and treatment. This study aims to identify the etiology of NOS among different age and sex groups of adult Egyptian patients. A hundred and twenty adult Egyptian patients (> 18 years) presented with acute NOS were enrolled in a hospital-based cross-sectional observational study from the emergency room and neurology outpatient clinics of our hospitals within a time period of 6 months from March till September 2018. All patients were subjected to neurological examination, laboratory, neuroimaging, and electroencephalogram investigations.

**Results:** Among 120 adult patients presented with NOS, males were prevalent (63%). Older adults (age group > 55 years) were the most prevalent cohort (60%). Cerebrovascular diseases (CVDs) were the most common identified etiology of NOS (44.17%), followed by idiopathic epilepsy syndrome (18.33%), symptomatic mainly “metabolic” (11%), brain tumors (9.17%), post-traumatic epilepsy (6.67%), encephalitis (5.83%), and cryptogenic (5%). Idiopathic epilepsy syndrome was the most common etiology (55.56%) of new-onset seizures among the young adult age group (< 36 years), while CVDs were the most common etiology (65.28%) among older adults (> 55 years). Also, CVDs were the most common etiology among males (43.4%) as well as females (45.4%). However, male predominance was the highest among post-traumatic seizures (87.5%). And female predominance was the highest among brain tumors identified etiology of NOS (54.5%).

**Conclusion:** NOS among adults are prevalent in elder males. CVDs are the most commonly identified etiology of adult NOS across males and females. Idiopathic epilepsy syndromes are the predominant etiology among younger adults.

**Keywords:** New-onset seizure, Adult onset, Egyptian, EEG, Neuroimaging

## Background

Seizures are one of the important causes of morbidity and mortality in adults. Despite many studies are based on the seizure and epilepsy classification system, however, there are only a few studies on the clinical profile and causes of new-onset seizures [1].

New-onset seizure was defined as the first seizure (or the first cluster of seizures within a 24-h period) ever experienced by the patient [2].

A first-ever seizure can be the first manifestation of epilepsy, which is characterized by recurrent unprovoked seizures (two or more). Or it may be a symptom of a brain tumor, a systemic disorder, an infection, or a syndrome that deserves special attention and treatment [3].

Seizures are common in the general population, and about 1 in 10 people will experience a seizure in their

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lifetime. Most of these seizures are provoked by acute events and are not related to epilepsy [4].

Epilepsy was regarded as a disease of children for many years, but as researchers gathered more data on an aging population, they found that the incidence of new-onset epilepsy increased among people older than 50. They reported an incidence of 169/100,000 per year in this population, almost twice the incidence among children [5].

The incidence rate of new-onset epilepsy in older adults ranges from 1 to 3 per 1000 person per year and is estimated to be two to six times higher than in younger adults [6].

The etiology of seizures can be easily made out in most of the older patients. The causes include subdural hematoma, stroke, central nervous system (CNS) infections, degenerative disorders like Alzheimer's disease, and malignancy. They also can occur with systemic metabolic conditions like uremia, hyperglycemia, hypoglycemia, and hyponatremia [7].

An epidemiological study of the incidence, prevalence, underlying etiology of new-onset seizures, and distribution among different age and sex groups can help predict the course of treatment and prognosis of such patients.

## Methods

This is a hospital-based cross-sectional observational study. Patients were recruited over 6 months (from March 2018 till September 2018). A hundred and twenty patients presented by acute (within 24 h) new-onset seizure (NOS) were included in this study.

### Inclusion criteria

All adults aged (> 18 years old) presented by acute new-onset seizures were divided into 3 age subgroups: young adult (18–35 years); middle-aged adult (36–55 years), and older adult (> 55 years).

### Exclusion criteria

Exclusion criteria include patients known as epileptic or with a past history of seizure disorder, patients aged < 18 years old, and seizure mimics: syncope (cardiac arrhythmia, vasovagal syncope), migraine (especially presenting with isolated symptoms as vertigo, visual changes, and aphasia), vascular conditions (transient ischemic attacks), pseudoseizures/hysterical seizures, physiological nocturnal myoclonus, movement disorders, sleep disorders (cataplexy, narcolepsy, night terror), benign positional vertigo (BPV), hyperventilation syndromes, and psychiatric conditions (conversion, panic attacks).

**All patients were subjected to:** full medical history including past history of possible risk factors for

symptomatic seizures such as diabetes mellitus (DM), chronic liver disease (hepatic encephalopathy), chronic kidney disease (CKD) or first presentation of acute renal failure (uremic encephalopathy), hypertension (hypertensive encephalopathy), posterior reversible encephalopathy syndrome (PRES) in eclampsia, autoimmune diseases as (systemic lupus erythematosus), febrile seizures, cerebrovascular accidents (CVAs) including infarction and hemorrhage, head injuries such as road traffic accidents (RTA) with traumatic brain injuries (TBI), central nervous system infections (meningitis, encephalitis), drug intake and alcohol (especially drug abuse or withdrawal), brain tumors, and operative (neurosurgical) intervention.

A family history of epilepsy.

A detailed history of the new-onset seizure (type of seizure was established according to the ILAE 2017 classification of seizures).

Detailed neurological examination including Mini-Mental State Examination (MMSE), speech, cranial nerves examination, motor and sensory examination, and signs denoting a cause of seizure (fever, papilledema).

Laboratory investigations including complete blood count (CBC); liver function tests (LFTs): alanine transaminase (ALT), aspartate transaminase (AST) and albumin; kidney function tests (KFTs): urea and creatinine; random blood sugar (RBS); serum electrolytes: sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), and calcium (ionized Ca<sup>+</sup>); and others only if indicated as collagen profile, cerebrospinal fluid examination (CSF), and urine toxicology profile.

Neuroimaging including cranial computed tomography (CT) "GE Healthcare Computed Tomography Optima CT660 System, USA, 2010" scanning with/or without contrast to identify stroke (ischemic or hemorrhagic) and space-occupying lesions (SOLs) and magnetic resonance imaging (MRI) of the brain "Closed Refurbished GE 1.5 T HD xt MRI Machines, USA, 2015" (if epilepsy syndrome is suspected) for better resolution of abnormal brain structure as mesial temporal sclerosis, cortical dysplasia and with contrast (when indicated) for brain tumors.

Electroencephalogram (EEG) "Nihon Khoden EEG-1200, USA, 2017" short-term digital electroencephalogram (DEEG) within average 48–72 h of patient first presentation to help classify seizure type and risk of recurrent seizures.

### Sampling method

The sampling technique used in this study was a purposive sampling of adults with new-onset seizures with an estimated number to be at least eighty patients.

### Statistical methods

IBM SPSS statistics (V. 21.0, IBM Corp., USA, 2012) was used for data analysis.

Chi-square test to study the association between every 2 variables or comparison between 2 independent groups as regards the categorized data.

The probability of error at (*P* value 0.05) was considered significant, while *P* values 0.01 and 0.001 were highly significant.

**Ethical considerations**

All subjects were informed of the general aim of the study and their participation was fully voluntary. Informed written consent had been obtained and approved by the ethics committee for clinical research of the faculty of medicine.

**Results**

One hundred and twenty (120) patients presented to ER and Neurology Clinic, at the time of the first seizure. 63.33% were males (76 patients) and 36.67% were females (44 patients). NOS were more predominant in the older adult age group (72 patients) (60%) than in young adults (27 patients) (22.5%), with fewer incidence among the middle-aged group (21 patients) (17.5%).

Males with NOS were predominant among young and older adult age groups by (66.67%), while females with NOS were predominant among middle-aged adults by (52.38%) with a statistically non-significant difference (Table 1).

**Past medical history of study patient**

Twenty four (20%) patients had no PH for medical illness, 61 (50.83%) had PH of systemic HTN, 59 (49.17%) suffered from DM, 42 patients had PH of CVAs (35%), 28 (23.33%) had PH of IHD, 15 (12.50%) with CKD, and 8 patients had PH of head trauma (6.67%).

**Metabolic profile**

Patients with NOS with significant findings in their metabolic profile included twelve (10%) patients with hypocalcemia. Eight patients (6.67%) had hyponatremia, five patients had hypokalemia (4.17%), and 7 patients (5.83%) had hyperglycemia. Only 3 patients (2.5%) had hypoglycemia.

**Neuroimaging findings**

CT brain and MRI brain were done for all patients. Nearly 75% had abnormal neuroimaging findings. Fifty

patients (41.76%) had ischemic infarcts; three patients (2.5%) had IChge or hemorrhagic transformation. Three patients had subarachnoid hemorrhage (SAH) (2.5%), 3 patients (2.5%) had subdural hemorrhage (SDH), and one patient had EDH (0.83%). Twelve patients (10%) had a space-occupying lesion (brain tumor). MRI flair and T2WI hyperintensities and white matter lesions (WMLs) like vasculitis, encephalitis, PRES, and small vessel disease (SVD) were identified in 10 patients (8.34%). Congenital malformations, focal cortical dysplasia and mesial temporal sclerosis, were found in 4 patients (3.33%). Brain edema was found in 2 patients (1.65%) (Fig. 1).

**Electroencephalographic (EEG) findings**

Out of 120 patients, 79 were subjected to DEEG recording (65.83%), 34 patients (28.33%) had normal DEEG study, while EEG abnormalities were detected among 45 patients (37.5%). Epileptiform activities in the form of “spikes and sharp and slow waves” were detected among 23 patients (19.17%) and non-epileptiform activities in the form of “EEG slowing” were detected among 22 patients (18.33%) (Table 2)

**Etiology of new-onset seizures**

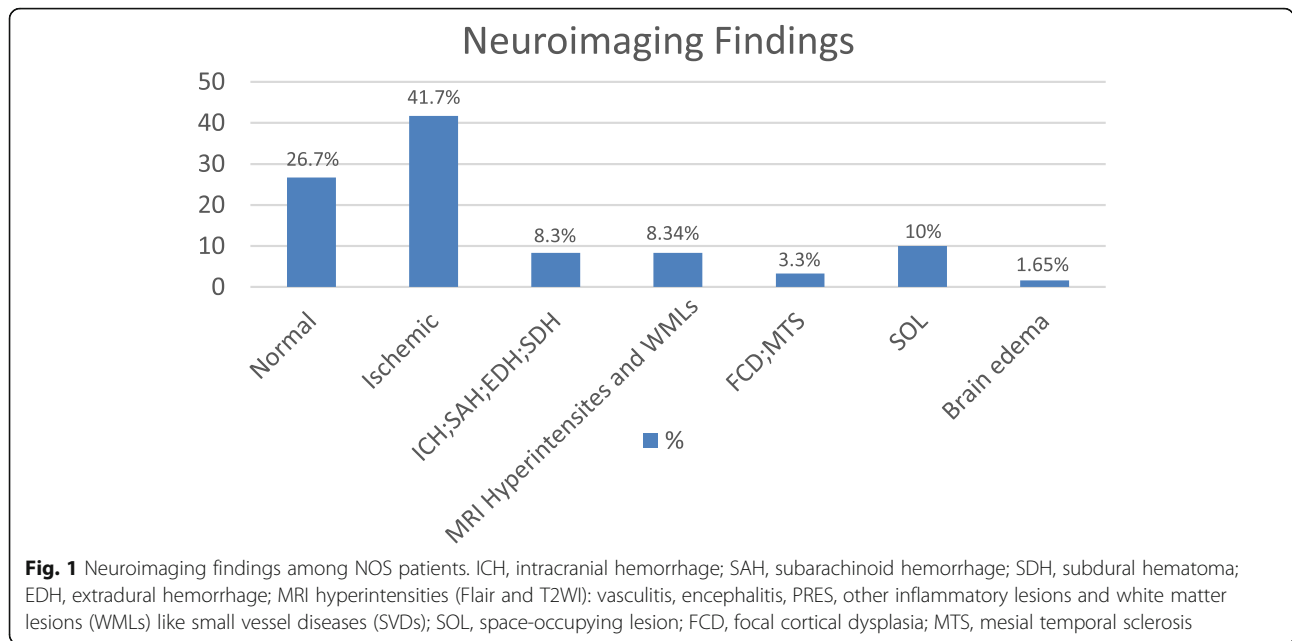
Cerebrovascular diseases (CVDs) were the most common identified etiology of new-onset adult seizures (post-stroke seizure/epilepsy) by 53 patients (44.17%) [50 patients with ischemic infarctions (41.67%) and 3 patients with intracranial hemorrhage (ICHge) (2.5%)], followed by idiopathic epilepsy syndrome by 22 patients (18.33%), other symptomatic etiologies by 13 patients (10.83%) [10 patients with metabolic (8.33%), 1 patient with vasculitis (0.83%), 1 patient with PRES (0.83%), and 1 patient with drug-induced seizures (0.83%)], 11 patients with brain tumors (9.17%), 8 patients with post-traumatic seizure/epilepsy (post-traumatic concussion and traumatic hemorrhage) (6.67%), 7 patients with encephalitis (5.83%), and 6 patients with cryptogenic (5%) (Fig. 2).

**Age in correlation with different etiologies of NOS**

Among the young adult age group (<36 years of age), the most common etiology was idiopathic epilepsy

**Table 1** Age and gender distribution of adult patients with NOS

Gender	Age group								Chi-square	
	Young adult		Middle-aged adult		Older adult		Total		$\chi^2$	P value
	N	%	N	%	N	%	N	%		
Male	18	66.67	10	47.62	48	66.67	76	63.33	2.707	0.258
Female	9	33.33	11	52.38	24	33.33	44	36.67		
Total	27	100.00	21	100.00	72	100.00	120	100.00		



syndrome (55.56%), while CVDs were the most common etiology among older adults (> 55 years) (65.28%).

Metabolic and other acute symptomatic etiologies (13.89%), brain tumors (9.72%), and encephalitis (6.94%) were more prevalent in the older adults, while post-traumatic seizures were more prevalent among middle-aged (14.3%) and young adults (11%) with statistically significant value (*P* value < 0.001) (Table 3).

Sex is in correlation with different etiologies of NOS: among males, CVDs were the most prevalent etiology for new-onset seizures (43.4%), followed by idiopathic epilepsy syndrome (18.4%) and then an equal distribution of both symptomatic and post-traumatic seizures (9.2%).

Among females, CVDs were also the most prevalent etiology (45.4%), followed by idiopathic epilepsy syndrome (18.2%) as the same as among males. However, brain tumors were in equal distribution as metabolic and other symptomatic seizures (13.6%). (Table 4)

Male predominance was the highest among post-traumatic epilepsy (87.5%), while female predominance

was the highest among brain tumors identified etiology of new-onset seizures (54.5%) (Fig. 3).

### Discussion

As far as we know, there were no major hospital-based studies which evaluated new-onset seizures in adults especially from Egypt.

Most epidemiologic studies of seizure disorders are studies of the prevalence of epilepsy and only a few prospective incidence studies of cases with a first seizure in the adult population exist [8].

The importance of adult-onset seizures stems from their frequent association with secondary causes. If proper analysis of etiology is made with history taking, clinical examination, and appropriate investigations, the presenting seizures can be treated accordingly, thus reducing associated morbidity and mortality [2].

In 2010, the International League against Epilepsy (ILAE) Commission for Classification of Epilepsy divided epilepsies into three main categories (idiopathic mainly “genetic”, structural or/metabolic, unknown cause “cryptogenic”) according to the etiologies of epilepsy [9].

In the present study, we evaluated the data of 120 patients presented to ER and Neurology Clinics, who aged (≥ 18 years old) at the time of first seizure. Males represented (63.33%) of our cohort, while females represented (36.67%) with male to female ratio (1.7:1).

Our results are in concomitant with two studies reporting M:F ratio 1.85:1 and 1.9:1, respectively [2, 8].

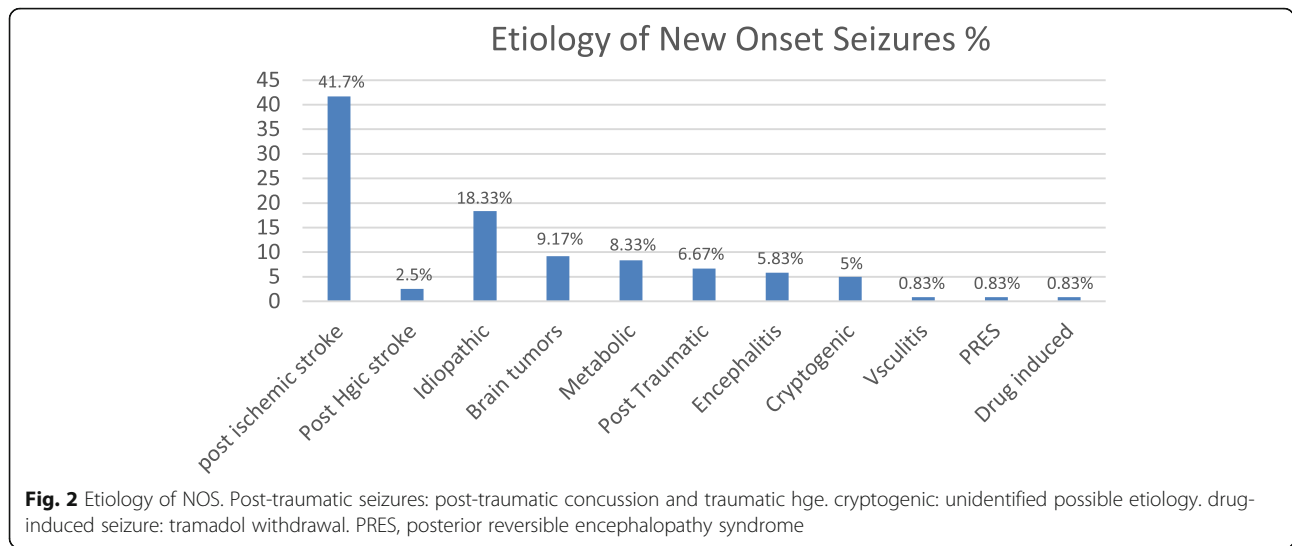
Another study group reported that the rate of new-onset seizures was considerably higher in men than in women. The same study group reported that acute symptomatic seizure is also common in older patients.

**Table 2** EEG Findings among study patients

DEEG finding	N	%
Not done	41	34.17
Normal DEEG	34	28.33
Non-epileptiform activity	22	18.33
Epileptiform activity	23	19.17
Total	120	100.00

Epileptiform activity: Spikes/sharp and slow waves

Non-epileptiform activity: EEG slowing



The incidence of acute seizures in patients over age 60 was estimated at 50 to 100 per 100,000 per year [10].

In the current study, we reported that new-onset seizures (NOS) were more common in the older age group (> 55 years), accounting for 60% of total cases.

Another community-based epidemiological study showed that the average annual incidence of epilepsy in the elderly aged 65 years and older is up to 240 per 100,000 [11].

In concomitant to our study, a study group reported that the number of patients with first seizure is more in the age group > 60 years [12].

It is in contrary to other studies done in India, where the majority of cases were the young and middle-aged groups < 40 years, with a higher prevalence of CNS infections in these age groups provoking symptomatic NOS [2, 8, 13].

Past medical illnesses usually give a clue to the possible etiology. History of hypertension was significantly associated with unprovoked seizures, whether associated or not with stroke [14].

In the current study, 61 patients (50.83%) had PH of systemic HTN and 42 patients had PH of CVA (35%).

Subjects with a history of both had a fourfold increase in seizure risk compared with subjects with neither, probably due to the synergism between PH of CVA and PH of HTN [14].

Another study group found that hypertension was present in 16% of their cohort with NOS and PH of CVA among 8% [12].

Alterations of metabolic homeostasis are associated with seizures in many situations and may be the only symptom of electrolyte imbalances. These are commonly seen in people with hyponatremia, hypocalcemia, hypoglycemia, and hyperglycemia. The more rapid the disturbance develops the more likely it is to induce seizures [15, 16].

In the present study, 10 patients had acute symptomatic metabolic seizures. Five patients were diagnosed with hypocalcemia-induced NOS, 3 patients had NOS out of hyperglycemia, 1 patient had NOS secondary to uremia, and 1 patient had hyponatremia-induced NOS.

**Table 3** Distribution of etiology in accordance with different age groups

Etiology	Age group								Chi-Square	
	Young adult		Middle-aged adult		Older adult		Total		$\chi^2$	P value
	N	%	N	%	N	%	N	%		
Cerebrovascular (CVDs)	1	3.70	5	23.81	47	65.28	53	44.17	74.807	< 0.001*
SOL (brain tumor)	0	0.00	4	19.05	7	9.72	11	9.17		
Metabolic and other acute symptomatic*	3	11.11	0	0.00	10	13.89	13	10.83		
Idiopathic epilepsy syndrome	15	55.56	7	33.33	0	0.00	22	18.33		
Cryptogenic	4	14.81	1	4.76	1	1.39	6	5.00		
Encephalitis	1	3.70	1	4.76	5	6.94	7	5.83		
Post-traumatic Seizure	3	11.11	3	14.29	2	2.78	8	6.67		

\*Other acute symptomatic seizures: PRES, vasculitis, drug-induced seizure

**Table 4** Distribution of different etiologies in accordance to sex

Etiology	Sex						Chi-square	
	Male		Female		Total		$\chi^2$	P value
	N	%	N	%	N	%		
Cerebrovascular	33	43.42	20	45.45	53	44.17	5.596	0.470
SOL (brain tumor)	5	6.58	6	13.64	11	9.17		
Metabolic and other acute symptomatic*	7	9.21	6	13.64	13	10.83		
Idiopathic epilepsy syndrome	14	18.42	8	18.18	22	18.33		
Cryptogenic	4	5.26	2	4.55	6	5.00		
Encephalitis	6	7.89	1	2.27	7	5.83		
Post-traumatic epilepsy	7	9.21	1	2.27	8	6.67		
<b>Total</b>	<b>76</b>	<b>100.00</b>	<b>44</b>	<b>100.00</b>	<b>120</b>	<b>100.00</b>		

\*Other acute symptomatic seizures: PRES, vasculitis, drug-induced seizure

Regarding neuroimaging investigations, in patients in whom lesions could not be picked up by CT brain in spite of clinical evidence of structural lesion, MRI brain (with or/without contrast) was done.

Two studies revealed that CT failed to detect the abnormality in MRI-positive cases 26% and 57% of the time [17].

In the current study, neuroimaging abnormal findings were detected among (75%) of the participants. A recent study recruited 416 adult patients with NOS, detected neuroimaging abnormalities among 53% of its cohort [17].

Ischemic infarctions were the most common brain scan finding among our cohort (41.76%), followed by SOLs (10%).

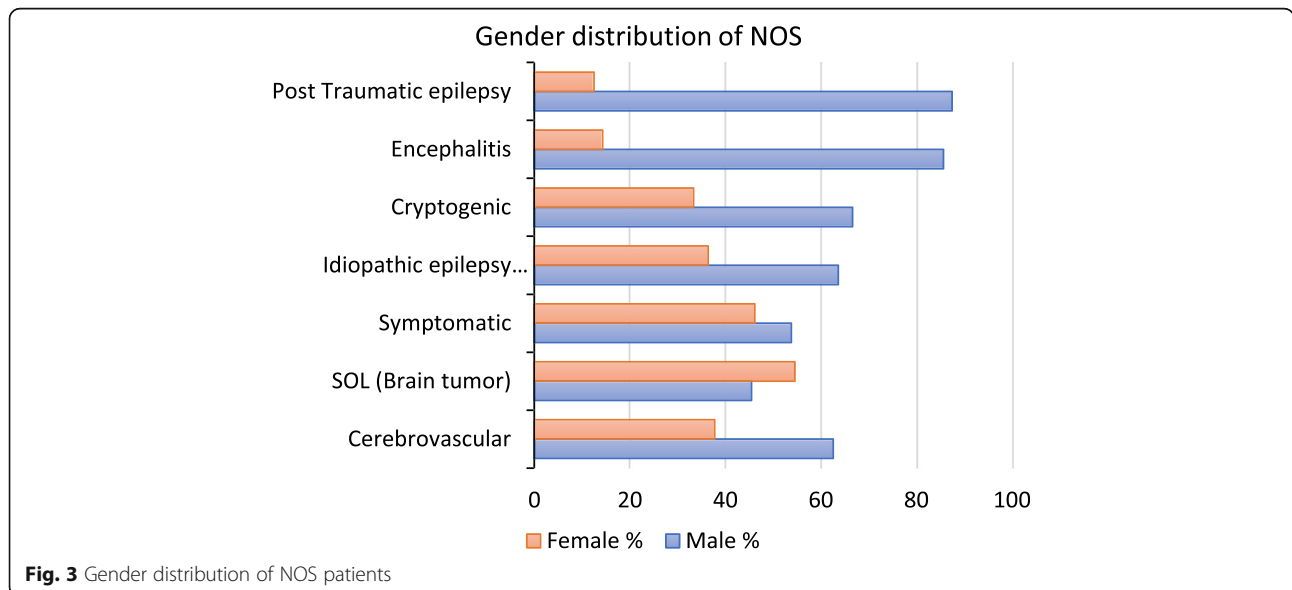
These findings are in concomitant to other studies which recruited 100 cases presented with adult new-onset seizures. The most common abnormal CT findings

were ischemic infarcts (18%), followed by brain tumors (either primary or secondary) (8%) [2].

However, different study results were influenced by endemic infectious diseases. One group study concluded that the most common abnormality in CT scan was a ring-enhancing lesion (mostly tuberculoma) (12%) as well as cerebral infarcts (12%), followed by generalized cerebral atrophy (4%) and meningioma, gliosis, and calcification (2%) for each [13].

The above findings highlighted the importance of neuroimaging among adult-onset seizures patients for appropriate etiological diagnosis of seizures.

Electrophysiological data were useful; it detected abnormality among 37.5% of our cohort. EEG epileptiform activity (spikes and sharp waves) was detected in 19.1% of the patients, while non-epileptiform activity (cerebral slowing) was detected in 18.3%.



**Fig. 3** Gender distribution of NOS patients

In the current study, out of 30 patients with normal neuroimaging studies, 24 patients underwent DEEG study; of those, 15 patients had abnormal DEEG findings, revealing the yield of post-ictal DEEG in NOS.

Our results were in concomitant with other studies. One study reported that out of 100 patients with new-onset seizures, 44% had abnormal DEEG records suggestive of seizure activity where as the remaining 56% had normal DEEG records [2].

The same results were reported in another study with DEEG abnormalities among 40% of their patient and normal DEEG among 20% [12].

In contrast to another group who studied NOS among the older age cohort only (> 65 years old), they reported abnormal EEG in 18.8% of their cohort and normal EEG in (49.3%) [18].

Younger patients with epilepsy often show a genetic cause. However, new-onset epilepsy in the elderly is mainly the consequence of accumulated injuries to the brain and other secondary factors [19].

New-onset epilepsy in elderly people often has underlying etiology including cerebrovascular diseases, brain tumors, and traumatic head injury. Post-stroke seizure is likely to increase because of the increasing aging population, and age itself is an independent risk factor for stroke [20].

The present study revealed that CVDs are the most common etiology for adult new-onset seizures by post-stroke seizure/epilepsy (44.17%). CVDs had the highest prevalence in the older adult (> 55 years) age group (65.28%).

Therefore, a close follow-up of stroke patients is needed for early detection of subtle fits which are hardly identified by the patients themselves or their caregivers, as well as understanding the characteristics of post-stroke seizures, etiological causes, and drug-drug interactions while treating those patients is necessary for effective patient management.

The second most common identified etiology for adult new-onset seizures was idiopathic epilepsy syndrome (18.33%), followed by SOLs (brain tumors) (9.17%), acute symptomatic metabolic seizures (8.33%), post-traumatic epilepsy (6.67%), encephalitis (5.83%), and cryptogenic (5%).

Among identified etiologies of new-onset seizures in relation to age, idiopathic seizures were more common in younger adults (55.56%) followed by cryptogenic (14.8%) and post-traumatic epilepsy (11%) with *P* value (< 0.001).

Encephalitis-related seizures were common in the older age group (6.94%) in comparison to young adults (3.7%) and middle-aged adults (4.7%); post-traumatic seizures were more common among middle-aged (14.29%) and young adult (11.11%) groups in comparison to older age group (2.78%).

The mentioned results were in concomitant with other study groups' results. One study found that stroke was the most common etiology of adult new-onset seizures (23%), followed by idiopathic (22%) [2].

Another group studied 50 cases of adult new-onset seizures and found that CVDs were the most common etiology (34%) followed by idiopathic (22%) being the second most common etiology [12].

The same results were revealed by a study group that recruited 100 cases presented with new-onset seizures in adults and found that stroke was the leading cause of seizures accounting for 21%; infection was the next leading cause of seizures accounting for 17% and metabolic causes account for 15% [1].

However, endemic CNS infections in some areas dramatically changed the results of a study done in India, which enrolled 98 cases presented with new-onset seizures after age 20 years. They reported that CNS infections mainly "neurocystercosis" were the leading cause of first seizure in adults accounting for 39.7%, followed by CVDs (26.5%) [8].

The present study revealed that CVDs were the most prevalent etiology of new-onset seizures among males (43.4%), as well as females (45.4%). However, male predominance was the highest among post-traumatic epilepsy (87.5%), while female predominance was the highest among brain tumors identified etiology of new-onset seizures (54.5%).

The different heterogeneity of etiologies, i.e. CVDs, idiopathic, post-traumatic, SOLs, metabolic, and CNS infections among adult patients with new-onset seizures and their relative contributions, depend on the age composition of the study population, sample size, and endemicity of CNS infections.

One of our study limitations is the narrow window for post ictal EEG 48–72 h that resulted into 34% dropping and missing of this pivotal investigation in our epileptic patients. Future research direction for recruitment of more patients through multicenter contribution can aid in making a national registry system and database for NOS patients across the country.

## Conclusion

New-onset seizures among adults are prevalent in elder males. CVDs are the most common identified etiology of adult new-onset seizures across males and females. However, idiopathic epilepsy syndromes are the predominant etiology of NOS among younger adults.

## Abbreviations

NOS: New-onset seizures; ER: Emergency room; OPCs: Neurology outpatient clinics; MMSE: Mini-Mental State Examination; EEG: Electroencephalogram; CVDs: Cerebrovascular diseases; CNS: Central nervous system; BPV: Benign positional vertigo; DM: Diabetes mellitus; CKD: Chronic kidney disease; RTA: Road traffic accidents; TBI: Traumatic brain injury; ILAE: International League Against Epilepsy; SOLs: Space-occupying lesions; CT: Cranial

computed tomography; MRI: Magnetic resonance imaging; ICHge: Intracranial hemorrhage; SDH: Subdural hematoma

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#### Authors' contributions

Professor MH proposed the idea of the study. Doctor AK collected the data. Professor EA revised the data. Doctor MS revised the results and wrote the manuscript. All authors have read and approved the manuscript.

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#### Availability of data and materials

From the corresponding author.

#### Declarations

##### Ethics approval and consent to participate

All subjects were informed of the general aim of the study and their participation was fully voluntary. Informed written consent had been obtained and approved by the ethics committee for clinical research of faculty of medicine ASU.

Date of Ethical Approval: 28/12/2017.

Reference Number: FMASU Msc 473/2017

##### Consent for publication

Not applicable.

##### Competing interests

The authors declare that they have no competing interests.

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