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Original Research Article

Structural Causes and Classification of First Ever Seizures in Adult Patients

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Abstract: *Seizures represent a common neurological emergency, and identifying the underlying cause of a first seizure episode is crucial for management and prognosis. Brain structural abnormalities are frequently implicated in adults, yet their distribution and association with seizure types remain variable across populations.* ***Objective:*** *To determine the frequency of brain structural causes and types of the first episode of seizures in adult patients.* ***Methodology:*** *This cross-sectional study was conducted in the ER and Neurology departments of Sheikh Zayed Hospital, Rahim Yar Khan, among adult patients presenting with first-onset seizures. A sample size of 280 was calculated, and demographic data, structural causes, and types of seizure were noted. After setting seizure and initial stabilization, all patients underwent an NCCT scan of the brain to determine the structural cause of the seizure. Structural causes were studied, including juxtacortical microvascular disease, neurodegenerative disease, post-stroke, and focal gliosis. When no cause was found after brain imaging and EEG, it was counted under idiopathic etiology, excluding metabolic and infectious causes. Seizures were also classified into focal, generalized, and undetermined seizures. The data were analyzed using SPSS version 26.0. Mean and standard deviations were reported for continuous variables. The chi-square test was used to compare the qualitative variables, with a p-value of less than 0.05 considered statistically significant. The result was as follows****:*** *This study comprised 280 subjects. Mean age ± SD of participants was 42.53±16.14 years, comprising 148 males (52.9%) and 132 females (47.1%). Idiopathic cause was found in 28.6%, post-stroke in 20.7%, juxtacortical microvascular disease in 20.4%, neurodegenerative disease in 12.5%, brain tumors in 9.3%, and focal gliosis in 8.6% patients. Generalized seizures were seen in 62.1%, and focal fits in 37.9% patients. Idiopathic causes of seizures were more prevalent in the younger age group (71.25%) from 20-39 years, whereas post-stroke (70.64%) and focal gliosis (41.7%) were more prominent in the elderly group (50-70 years) (p value = 0.00). Neurodegenerative causes of seizures were dominant in females (62.9%), whereas brain tumors, post stroke, and focal gliosis backed seizures dominated males by 61.5%, 67.2% and 66.7% respectively (p value 0.021). Generalized seizures were more common (58%) in patients aged 20 - 39 years, whereas focal seizures included 49.1% patients between 50 and 70 years (p value 0.003). Focal seizures are more prevalent in male patients, at a significant percentage of 60.4% (p value 0.049). Idiopathic and juxtacortical microvascular seizures dominantly showed the generalized type (90% and 73.7%). Focal gliosis (95.8%), post-stroke (75.9%), and brain tumors (61.5%) caused focal seizures. Neurodegenerative diseases showed only the generalized type of seizures (p-value 0.00).* ***Conclusion:*** *First-onset seizures in adults are more common in males than in females. Generalized seizures were seen more than focal seizures. Idiopathic causes were dominant overall; however, post-stroke causes were more prominent in the structural category. Generalized seizures were mainly due to idiopathic, neurodegenerative, and juxtacortical microvascular causes, whereas focal seizures were due to stroke, tumors, and focal gliosis.*

Keywords: Seizure, Idiopathic, post-stroke, juxtacortical microvascular, focal gliosis, brain tumors

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Introduction

While all people with epilepsy experience seizures, not all individuals with seizures have epilepsy. Epileptic seizures may also occur after an acute central nervous system (CNS) insult (structural, systemic, toxic, or metabolic). These events (acute symptomatic or provoked seizures) are intended as acute manifestations of the insult. They may not recur when the underlying cause has been removed or the acute phase has elapsed. According to the International League Against Epilepsy (ILAE), epilepsy is defined by any of the following conditions: (1) at least 2 unprovoked (or reflex) seizures occurring >24 h apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after 2 unprovoked seizures, occurring over the next 10 years; (3) And the Diagnosis of an epilepsy syndrome.

Smoking predisposes individuals to, among other things, stroke and cancer, which are both important seizure etiologies in adults and the elderly. (4) Some studies have shown a correlation between social deprivation and the prevalence of epilepsy. (5) A higher prevalence of epilepsy among residents living in socially deprived areas may be due to "social drift," whereby factors associated with a Diagnosis of epilepsy, for example, decreased employability, lead to a downward drift of the socioeconomic status of an individual. An alternative explanation is "social causation," whereby factors associated with living in an area of social deprivation put an individual at increased risk of developing epilepsy. (6)

Assessment of patients presenting with first seizures is critical to differentiating epileptic seizures from other conditions that resemble epileptic seizures ("seizure mimics"). (7) Appropriate management of patients with epilepsy requires precise classification of their disease. (8) In one study, it was found that the type of seizure was focal seizures in 71% cases, generalized seizures in 11% cases, and non-specific seizures in 18%. Cause of seizure was idiopathic in 25% cases, juxtacortical microvascular disease in 15%, brain tumor in 9%, neurodegenerative disease in 9%, post-stroke in 6% and focal gliosis in 3%. (9)

The rationale of this study is to determine the causes and types of first episodes of seizures in patients presenting in the outdoor, emergency, and labor rooms. Previous studies were conducted only in emergency departments of neurology units. In contrast, our study will enroll patients from different specialties, resulting in diverse data collection regarding

etiology and types of seizures. This will help further formulate the management plan based on the reported disease burden.

Methodology

This cross-sectional study was conducted in the ER and Neurology departments of Sheikh Zayed Hospital, Rahim Yar Khan, on patients who presented with seizures for the first time in their lives, with no prior history, from February 2024 to September 2024. Data collection commenced after obtaining ethical approval from the Institutional Review Board of the institute (Ref. No. 780/IRB/SZMC/SZH) and obtaining informed written consent from the study subjects. A sample size of 280 was calculated using the WHO calculator, with a 95% confidence level, 2% absolute precision, and an expected frequency of 3% for the least common cause of seizure. (9) In accordance with the inclusion criteria, patients aged between 20 and 70 years, of both genders, and having a first afebrile seizure were included. Patients who were known cases of epilepsy, who had head trauma, had febrile seizures, or were pregnant were not included. Demographic data, including age, gender, and type of seizure, were noted. Complete history regarding drug intake, history of hypertension, hepatic or renal failure was taken. A physical examination was also performed to determine signs of meningeal irritation and any neurological deficits. Benzodiazepines control seizures. Patients presenting with tonic colonic movement of one or both halves of the body were labelled as seizures. After setting seizure and initial stabilization, all patients underwent an NCCT scan of the brain to determine the structural cause of the seizure. Structural causes were studied, excluding hypertensive encephalopathy, uremic encephalopathy, hepatic encephalopathy, metabolic causes, and drug intake based on blood pressure (110-130mmHg systolic BP), LFT, RFT, serum electrolyte, serum calcium, and drug history. The following structural causes were studied using a CT scan.

i. Juxtacortical microvascular disease: CT scan showing one or more juxtacortical small lesions (JCSLs, < 5 mm in diameter, within 10 mm from the corticomedullary junction).
ii. Brain tumor: Seen as hyperdense opacities on CT scan of the brain with IV contrast.
iii. Neurodegenerative disease: Both grey and white matter diseases as appreciated on CT scan.
iv. Post-stroke: Old healed scar in cortical regions with a previous history of stroke.
v. Focal gliosis: It is a reactive process occurring after some time following most types of central nervous system injuries and is the result of focal proliferation of glial cells, particularly astrocytes. It is seen as an area of white matter hypoattenuation.

When no cause was found after brain imaging and EEG, it was counted under idiopathic etiology. Seizures were also classified into three categories depending upon types, such as:

i. Focal seizures: Seizures arising in one hemisphere of the brain were determined by the presence of tonic-clonic movement involving only one half of the body.
ii. Generalized seizures: seizures originating in both hemispheres simultaneously were determined by the presence of tonic-clonic movement involving both sides of the body.
iii. Undetermined seizures: Seizures which cannot be classified as focal or generalized were labelled as undetermined seizure type.

Data were recorded in a specially designed proforma, which was later entered and analyzed using SPSS version 26.0. The mean and standard deviation were calculated for quantitative variables, such as age. The Shapiro—Wilk test was used to check the normal distribution of the data, which showed a normal distribution (P value = 0.000). Frequency and percentage were calculated for categorical variables, such as gender, cause of seizure, and classification of seizure. Effect modifiers, such as age and gender, were addressed through the stratification of data by cause and seizure classification. Post-stratification chi-square was applied (Fisher's test in cases n = 5). A p-value ≤ 0.05 was considered statistically significant.

Results

This study includes 280 patients who experienced their first seizure in adulthood, comprising 148 males (52.9%) and 132 females (47.1%). Although the study discusses first-onset seizures in adults only, the age range fluctuates from a minimum to a maximum; the mean age of the participants was calculated as 42.53 with a standard deviation of 16.15. The patients presented with different etiologies of seizures. Idiopathic cause stands out as the most common cause of first-onset epilepsy, i.e., 80 patients (28.6%), post-stroke seizures remain the second most frequent cause of epilepsy (20.7%) according to our data. Juxtacortical microvascular disease accounts for 20.4%, neurodegenerative disease for 12.5%, brain tumors for 9.3%, and focal gliosis accounts for 8.6% (Table 1). Patients presenting in the emergency department during our study exhibited various types of seizures, which were primarily categorized as focal, generalized, or undetermined, regardless of their etiology or age. A major portion was classified under generalized seizures (62.1%). The rest were categorized as focal fits (37.9%). Most idiopathic causes of seizures were found in a younger age group (39, 48.8%, p value 0.00), specifically those aged 20-29. In contrast, focal gliosis and post-stroke etiologies made up the majority of the elderly group (Table 2). However, the rest of the causes had more or less equal shares in all age ranges—idiopathic and juxtacortical microvascular disease affects both genders almost equally. Patients with an idiopathic cause of seizures had 48.8% males and 51.3% females (p value 0.021). Similarly, patients in whom juxtacortical microvascular disease was the cause of seizures had 43.9% males and 56.1% females (p value 0.021). Neurodegenerative disease, causing seizures, dominated females in the study with 62.9% whereas brain tumors, post stroke, and focal gliosis backed seizures dominated males by 61.5%, 67.2% and 66.7% respectively (p value 0.021) (Table 3).

Focal and generalized seizures were reported in our patients included in the study, where there was a clear dominance of generalized seizures. Different age groups had a clear distinction in terms of types of fits. The younger age group has a greater incidence of generalized seizures, i.e., 101 (58%) out of the 174 patients in the 20-39 years age group, which accounts for 36% of all participants in the study (p value 0.003). Patients who had focal seizures included 52(49.1%) out of 106 between the age range of 50 to 70 years, making up 18.6% of the total participants (p value 0.003). Focal seizures are more prevalent in male patients, at a significant percentage of 60.4% (p value 0.049), whereas the incidence of generalized seizures is almost equal in both male and female patients.(Table 4) In our study, we identified a significant relationship between a specific cause of first-onset seizures and a specific type of seizure. Idiopathic seizures dominantly showed the generalized type of seizure (90%, P value 0.00). Seizures that were caused by juxtacortical microvascular disease mostly showed a generalized pattern of seizures (73.7%, P value 0.00). Brain tumors caused focal seizures in 61.5 % (P value 0.00) of the cases in our study. Neurodegenerative diseases showed only the Generalized type of seizures (100%, P value 0.00) (Table 5).

Seizures that had a post-stroke and focal gliosis etiology showed focal seizures in 75.9% and 95.8% of the cases, respectively (P value 0.00). (Table 6)

Table 1 Frequency of causes of seizures

	Frequency	Percent
Idiopathic	80	28.6
Juxtacortical microvascular disease	57	20.4

Brain tumor	26	9.3
Neurodegenerative disease	35	12.5
Post-stroke	58	20.7
Focal gliosis	24	8.6
Total	280	100.0

Table 2: Causes of seizures in different age groups

		Age range					Total	P-value
		20-29	30-39	40-49	50-59	60-70		
Causes of Seizures	Idiopathic	39 (48.8%)	18 (22.5%)	16 (20%)	2 (2.5%)	5 (6.3%)	80 (100%)	0.00
	Juxtacortical microvascular disease	13 (22.8%)	14 (24.6%)	9 (15.8%)	5 (8.8%)	16 (28.1%)	57 (100%)	0.00
	Brain tumor	5 (19.2%)	9 (24.6%)	2 (7.7%)	4 (15.4%)	6 (23.1%)	26 (100%)	0.00
	Neurodegenerative disease	10 (28.6%)	9 (25.7%)	1 (2.9%)	11 (31.4%)	4 (11.4%)	35 (100%)	0.00
	Post-stroke	6 (10.3%)	7 (12.1%)	4 (6.9%)	20 (34.5%)	21 (36.2%)	58 (100%)	0.00
	Focal gliosis	6 (25%)	5 (20.8%)	3 (12.5%)	0 (0%)	10 (41.7%)	24 (100%)	0.00
Total		79 (28.2%)	62 (22.1%)	35 (12.5%)	42 (15%)	62 (22.1%)	280 (100%)	0.00

Table 3: Causes of Seizures in Both Genders

		Gender		Total	P value
		Male	Female		
Causes of Seizures	Idiopathic	39 (48.8%)	41 (51.3%)	80 (100%)	0.021
	Juxtacortical microvascular disease	25 (43.9%)	32 (56.1%)	57 (100%)	0.021
	Brain tumor	16 (61.5%)	10 (38.5%)	26 (100%)	0.021
	Neurodegenerative disease	13 (37.1%)	22 (62.9%)	35 (100%)	0.021
	Post-stroke	39 (67.2%)	19 (32.8%)	58 (100%)	0.021
	Focal gliosis	16 (66.7%)	8 (33.3%)	24 (100%)	0.021
Total		148 (52.9%)	132 (47.1%)	280 (100%)	

Table 4: Types of Seizures in different age ranges

		Age range					Total	P value
		20-29	30-39	40-49	50-59	60-70		
Type of Seizures	Focal Seizures	17 (16.0%)	23 (23%)	14 (13.2%)	23 (21.7%)	29 (27.4%)	106 (100%a)	0.003
	Generalized Seizures	62 (35.6%)	39 (22.4%)	21 (12.1%)	19 (10.9%)	33 (19.0%)	174 (100%)	0.003
Total		79 (28.2%)	62 (22.1%)	35 (12.5%)	42 (15.0%)	62 (22.1%)	280 (100%)	

Table 5: Types of Seizures in Different Genders

		Gender		Total	P Value
		Male	Female		
Type of Seizures	Focal Seizures	64 (60.4%)	42 (39.6%)	106 (100%)	0.049
	Generalized Seizures	84 (48.3%)	90 (51.7%)	174 (100%)	0.049
Total		148 (52.9%)	132 (47.1%)	280 (100%)	

Table 6: Causes of Seizures with Type of Seizures

		Type of Seizures		Total	P value
		Focal Seizures	Generalized Seizures		
Causes of Seizures	Idiopathic	8 (10%)	72 (90%)	80 (100%)	0.00
	Juxtacortical microvascular disease	15 (26.3%)	42 (73.7%)	57 (100%)	0.00
	Brain tumor	16 (61.5%)	10 (38.5%)	26 (100%)	0.00
	Neurodegenerative disease	0 (0%)	35 (100%)	35 (100%)	0.00
	Post-stroke	44 (75.9%)	14 (24.1%)	58 (100%)	0.00
	Focal gliosis	23 (95.8%)	1 (4.2%)	24 (100%)	0.00
Total		106 (37.9%)	174 (62.1%)	280 (100%)	

Discussion

Most of the cases in our study on first-onset seizures in adults depicted an idiopathic cause for seizures, followed by post-stroke and juxtacortical microvascular disease. Generalized type of seizures dominated the focal seizures in our study, where idiopathic, juxtacortical microvascular, and neurodegenerative causes contributed to generalized seizures; on the other hand, focal gliosis, post-stroke, and brain tumors contributed to

focal seizures. Age has an impact on both causes and types of seizures in our study. Idiopathic reasons mostly caused seizures in younger age; however, the older age groups had post-stroke and focal gliosis as dominant causes. Juxtacortical microvascular disease caused disease in all age groups; however, neurodegenerative causes affected the participants at both extremes and somewhat spared the Middle Ages. As we examine the data on seizure types in different age groups, a slight difference is observed, with the balance slightly more tilted towards the younger age group for general seizures and the older age group for focal seizures. The overall impact of gender on the types of seizures marked more men presenting with focal seizures. However, there was no obvious difference between the two genders in presentation with generalized seizures. Causes of seizures, such as post-stroke, focal gliosis, and brain tumors, had a deflection towards the male gender, whereas the neurodegenerative causes were more prominent in females than males.

Kaur, S et al found in Faridkot, India, in a study in 2018, that the type of first onset seizure in adults was generalized seizures in 59% and focal seizures in 41% of the participants. Both these results are consistent with our findings. Additionally, in their study, they found that stroke was the cause of seizures in 23% of the participants, and 22% had idiopathic causes of seizures. Our study, however, is dominated by idiopathic causes of seizures (28.6%) and secondly by stroke (20.7%). They also found that the major etiology in the generalized type of seizures was idiopathic, i.e., 33.9% which was also relatable to 41.3% (idiopathic) in our study. Similarly, the major cause of focal type of seizures was stroke in both studies, i.e., 41.4% and 41.5% respectively. (10) Kaur S et al. found the idiopathic cause of seizures was common in younger age groups and post-stroke was seen more in the elderly, which is also similar to our findings. Bhatia et al. in Chandigarh, India, in 2022, along with their colleagues, obtained similar results to those of our study. The included participants were 54.4% male and 45.6% female, which is similar to our study, comprising 52.9% males and 47.1% females. The dominant type of seizure in their study was also generalized, but its incidence was much higher, at 98%, compared to 62.1%. (11)

In another study conducted in Egypt by Mahmuod et al. in 2021, a greater number of males (63%) presented with seizures in the emergency room, a finding also observed in our study. Among the etiologies, post-stroke causes were most prevalent in their study, preceding idiopathic causes, whereas in our study, idiopathic causes led the etiologies for new-onset seizures. Brain tumors account for 9.17 % which is very close to 9.3% in our study. Idiopathic causes were still dominant in the younger age group in comparison to post-stroke causes, which were more prevalent in older age groups, in line with the findings of our study.

A cohort study was conducted in 2024 by Arturo Caprio et al. in five Latin American countries, involving 180 adults, to investigate the causes of first-onset seizures. The findings of this study revealed post-stroke as the prominent cause of adult-onset epilepsy (23.5%), tumors contributed 9.8% but a major chunk was from infectious causes, i.e., 18.6%. Idiopathic causes of seizures remained a dominant entity in the causes of unprovoked seizures. (13) Showing slightly different results from our study, mainly due to differences in regions and ethnicity, most of the findings were in accordance with our study.

Considering the little amount of work done in this part of the world on epilepsy and its etiology, where there is less understanding in patients as well, (14) studying 280 participants for first onset seizures in adults extracts a lot of undiscovered facts and findings about epilepsy in Pakistan. The existing literature is scarce and too brief to be applied to the general population. (15) Patients who present with fits in the emergency department are focused on treatment rather than looking for the cause. (16) Therefore, more data is needed to address the needs of the patient in terms of management and a longer seizure-free period. Knowing the gender more affected, age groups more at risk for a certain type and etiology of first onset seizure ensures a better approach towards the treatment of epilepsy. In Pakistan, where there is a general belief in public that evil spirits cause epilepsy and cannot be cured by medicine (17), conducting such studies to provide a scientific basis to demolish false beliefs is necessary. More efforts are required to encourage medical practitioners and smaller medical units to raise awareness of various patterns and causes of seizures presenting in emergency departments, as well as in outdoor patient departments. Moreover, a good control of epilepsy with antiepileptic drugs, achieving a complete seizure-free state, is essential to mark an efficient regime and overall management. (18) These goals cannot be achieved unless comprehensive data is available about the local population in terms of causes and types of seizures.

This study has some limitations; the first is the small number of participants enrolled in the study. A sample of 280 obviously cannot accurately portray the ground realities. The seizures were sometimes not observed by the researcher, and the types of seizures were assumed mainly based on the history presented by the attendants. Accurate measurement of the seizure duration was also not possible, as the attendants did not use any measurement tools, and the data they provided was an approximation of their understanding. Finally, we could not control for every possible lifestyle factor; moreover, the observational nature of this design leaves the possibility of residual confounding.

Conclusion

First-onset seizures in adults are more common in males than in females. Generalized seizures were seen more than focal seizures. Idiopathic causes were dominant overall; however, post-stroke causes were more prominent in the structural category. Younger patients presented mainly with idiopathic etiology, whereas older age groups had stroke and focal gliosis as a cause of epilepsy. Neurodegenerative diseases affect extremes of age groups, but somehow spare middle-aged groups. Focal seizures were caused mainly by stroke, focal gliosis, and brain tumors. On the contrary, generalized seizures were mainly because of idiopathic, neurodegenerative, and juxtacortical microvascular causes.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (780/IRB/SZMC/SZH)

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The authors declared the absence of a conflict of interest.

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All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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