

Adult onset seizures: Clinical, etiological, and radiological profile

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ABSTRACT

Introduction: Adult onset seizure disorder is a major public health concern in terms of burden of disease, nature of illness, and its impact on individual, family, and community. This study was done to assess the clinical profile and etiology of adult onset seizures and correlates of clinical and radiological pattern. **Materials and Methods:** This was a prospective cross-sectional hospital-based study conducted on 100 cases presenting with adult onset seizures. **Results:** Adult onset seizures were most prevalent in the young and middle-aged adults than elderly; generalized seizures were more common than focal seizures. However, the incidence of generalized seizures showed a falling trend as the age advanced whereas focal seizures increased in incidence with advancing age. Overall, the most common etiology of seizures was stroke, followed by idiopathic and central nervous system infections; yet, most common etiology of adult onset generalized and focal seizures was idiopathic and stroke, respectively. Regarding etiology, among younger adults, idiopathic seizures were predominant, whereas among middle aged and elderly, stroke was the most common etiology. **Conclusions:** It is mandatory to deal carefully with each case of adult onset seizure with a tailor-made approach. Identification and awareness about the etiological factors and seizure type help in better management of these patients. Primary care physicians play a pivotal role in identifying patients with adult onset seizures and should encourage these patients to undergo neuroimaging so as to arrive at an appropriate etiological diagnosis. In the face of recent advances in neuroimaging techniques, the future prospective management of adult onset seizures appears bright and convincing.

Keywords: Adult onset, focal seizures, generalized seizures, seizure

Introduction

Globally, seizures are common disorders recognized since antiquity and are encountered frequently during medical practice; up to 10% of general population experience at least one seizure in their lifetime with the highest incidence occurring in early childhood and late adulthood. Seizures beginning in the adult life require special attention as regards to their etiology because these are likely to be due to an identifiable cause. These are mainly due to trauma, central nervous system (CNS) infections,

space-occupying lesions, cerebrovascular accidents (CVA), metabolic disorders, and drugs. On the other hand, seizures beginning in childhood are more likely to be idiopathic. In addition, the etiology and clinical profile of seizures in adults necessitate decisions about the initiation and discontinuation of pharmacotherapy that are different from those in younger patients.^[1,2] All patients with adult onset seizures should have a neuroimaging study to determine whether there is an underlying structural abnormality or not. For evaluation of adults with new onset seizures, magnetic resonance imaging (MRI) has been shown to be superior to computed tomography (CT) scan for the detection of cerebral lesions causing seizures; however, CT scan is an appropriate choice in emergency settings. Magnetic

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resonance spectroscopy (MRS) is a valuable tool that can be used to study the metabolic changes seen in epileptogenic zone.^[3]

In the above scenario, the aim of the study was to assess clinical profile and etiology of adult onset seizures and correlates of clinical and radiological pattern.

Methods

This study was conducted in the Department of Medicine of a tertiary care teaching hospital of Punjab, India. It was a prospective cross-sectional study of 100 patients with adult onset seizures admitted in the medical wards or attending the outpatient department. The study was conducted after obtaining the permission of the Institutional Ethics Committee. Written informed consent was obtained from each participant before enrolling him/her for the study. The data were collected by the first author as per the detailed questionnaire (copy attached). Following detailed history and thorough clinical examination, necessary investigations were undertaken in all the patients such as hematological profile, random blood sugar, renal function tests, liver function tests, serum electrolytes including calcium and magnesium, serum albumin, electroencephalogram (EEG), CT/MRI brain (contrast wherever required), and cerebrospinal fluid analysis (wherever required).

Inclusion criteria

Patients of seizures with age of onset 18 years and above were taken, and seizures were diagnosed according to International League against Epilepsy Commission on Classification and Terminology.

Exclusion criteria

Patients of seizures with age of onset <18 years, seizures due to recent traumatic brain injury (≤ 6 months), postoperative seizures (including neurosurgical procedures), and seizures due to obstetric causes (including eclampsia) were excluded from the study.

EEG was done in all 100 patients using Medicaid Sleepcare SC-32 machine and recordings were carefully evaluated for any abnormalities.

Noncontrast CT of head was done in all cases, and contrast-enhanced CT was done, wherever indicated on dual slice CT scanner (GE CT/E). MRI of brain was carried out in 73 patients on Siemens Magnetom Avanto 1.5 Tesla MRI scanner using standard protocols. Contrast = enhanced MR and MRS were done wherever required.

Statistical analysis

Statistical analysis was performed using GraphPad InStat software (version 3.05 for Windows, San Diego, CA, USA). At 95% confidence interval, $P < 0.05$ was considered statistically significant.

Results

Among the 100 patients, 65% were males; maximum patients (38%) were in the age group of 21–40 and 41–60 years, only 9% were aged <20, years and 15% more than 60 years; majority (59%) had generalized seizures. Out of rest 41 with focal seizures, 16 (39%) had focal seizures without discognitive features (simple partial seizures), 15 (36.6%) focal seizures with discognitive features (complex partial seizures), whereas remaining 10 (24.4%) focal seizures with secondary generalization. Out of total 100 patients, 17 presented with status epilepticus; 14 with generalized seizures and three with focal seizures with secondary generalization. In the productive age group of 21–50 years, majority (64.9%) had generalized seizures [Table 1].

Overall, the most common etiology of seizure was stroke (23%), next common was idiopathic seizures with no certain cause (22%), and CNS infections followed next (21%). Other common causes were metabolic (12%), brain tumors (8%), encephalomalacia with gliosis (7%), and cortical venous thrombosis (4%). Relatively rare causes of adult onset seizure were acute disseminated encephalomyelitis (ADEM), multiple sclerosis (MS), and posterior reversible encephalopathy syndrome (PRES) [Table 1].

The most common etiology among 59 patients presenting with generalized seizures was idiopathic (33.9%), followed by metabolic causes (20.3%) and CNS infections (16.9%) [Table 1].

The most common etiology among 41 patients presenting with focal seizures was stroke (41.4%), followed by CNS infection (26.8%) and brain tumors (14.6%) [Table 1].

Among the 17 patients who presented in status epilepticus, most common cause was metabolic (35.3%), followed by stroke (17.4%), CNS infections (11.8%), and brain tumors (11.8%).

Age-wise analysis of etiology revealed significant findings. Among the 23 patients with poststroke seizures, highest prevalence was among individuals aged more than 40 years (95.6%). Idiopathic seizures were more common in younger adults (68.1%) aged <40 years followed by CNS infections (66.6%). Metabolic causes and brain tumors were responsible for causing seizures in minority cases [Table 1].

Among the 23 patients with poststroke seizures, majority (78.3%) had infarct as the underlying etiology whereas 21.7% had intracranial hemorrhage. Among 18 patients with infarct, great majority (83.3%) presented with focal seizures. CNS infections contributed to adult onset seizures among 21 patients; most common etiology was CNS tuberculosis (42.8%), followed by neurocysticercosis (28.5%) and viral meningoencephalitis (14.3%) [Figure 1].

Metabolic causes constitute an important etiology (12%) of adult onset seizures. Of these, alcohol withdrawal and

Table 1: Age-gender distribution of adult onset seizures

Clinical parameters	Type of seizures	Age distribution (years)											
		Under 20		21-30		31-40		41-50		51-60		61 and above	
		Gender											
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Stroke	GS							2	1	1		2	
	FS					1		5	2	3		5	1
Idiopathic	GS	3	1	4	1	3	2	1	1	2	1	1	
	FS						1			1			
CNS infections	GS		1	2	2	1		1	1	1		1	
	FS	2		1	3	2			1		1		1
Metabolic	GS	1		1		3	1	2		2		1	1
	FS												
Brain tumors	GS				2								
	FS			1		1				1	2		1
Encephalomalacia with gliosis	GS					1		1			1		
	FS					1				2		1	
Cortical venous thrombosis	GS		1		1		2						
	FS												
ADEM	GS								1				
	FS												
MS	GS												
	FS				1								
PRES	GS									1			
	FS												

GS: Generalized seizures; FS: Focal seizures; CNS: Central nervous system; ADEM: Acute disseminated encephalomyelitis; MS: Multiple sclerosis; PRSE: Posterior reversible encephalopathy syndrome

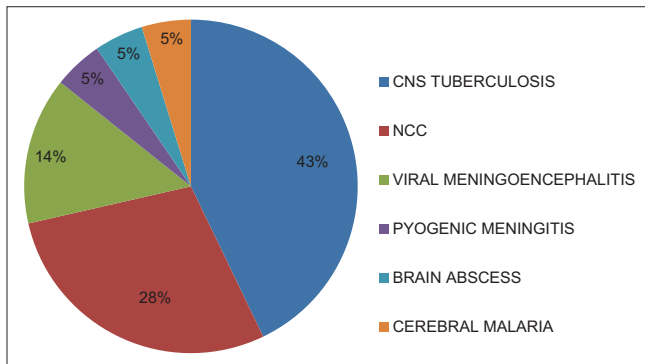


Figure 1: Distribution of central nervous system infections causing adult onset seizures

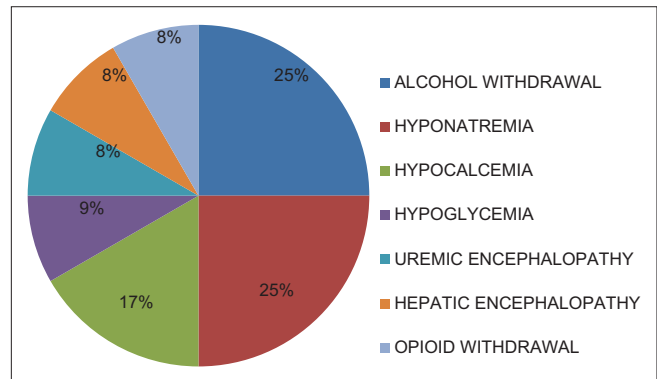


Figure 2: Distribution of metabolic causes of adult onset seizures

hyponatremia were the most common causes (25%), followed by hypocalcaemia (16.8%) [Figure 2].

EEG was done in all the 100 patients studied. Forty-four had an abnormal EEG record suggestive of seizure activity whereas the remaining 56 patients had a normal EEG record.

Comparing the yield of CT with that of MRI, it was noted that the nature of the focal lesion was better delineated on MRI, giving a better diagnostic yield. CT head, done in all cases, unearthed that 30% had normal CT scan; most common abnormal CT finding was infarct (18%), followed by brain tumors, either primary or secondary (8%) and gliosis (7%). MRI brain was done in 73% in our series observed that MRI was normal in 30.1% cases. In remaining 53 patients (69.9%), the most common MRI finding

was infarct (16.3%) followed by gliosis and brain tumors (8.3%); other notable findings were tuberculoma, neurocysticercosis, and meningitis/encephalitis (6.9%) [Table 2].

Discussion

The importance of adult onset seizures stems from its frequent association with secondary causes. With history, clinical examination, and appropriate investigations, including neuroimaging, if proper analysis of etiology is made, the presenting seizures can be treated accordingly, thus reducing associated morbidity and mortality.

Age

In this study, 47% patients were aged <40 years, 38% patients among 41–60 years, and 15% more than 60 years. Similar

Table 2: Neuroimaging findings of adult onset seizures

	Age distribution (years)											
	Under 20		21-30		31-40		41-50		51-60		>61	
	Gender											
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
CT scan (head) findings												
Normal	3	1	6	2	5	3	3	1	3	1	1	1
Infarct					1		6	2	2		7	
Tumor			1	2	1				1	2		1
Gliososis					2		1		2	1	1	
Cortical atrophy					1				3		1	
Hemorrhage							1	1	1		1	1
Ring enhancing lesion	2			1	1			1				
Diffuse cerebral edema			1				1	1	1			
Hydrocephalous				2					1			
Calcified granuloma				1	1							1
Focal edema (postictal)		1					1		1			
Tuberculoma				1	1					1		
Cortical venous thrombosis		1		1			1					
Brain abscess			1									
Basal ganglion calcification	1											
Multifocal white matter edema								1				
MRI (brain) findings												
Normal	2	1	4		2	4	3	1	3	1		1
Infarct							5	2	2		3	
Gliososis					2		1		2		1	
Tumor			1	2	1					1		1
Tuberculoma	1			1	2					1		
NCC				2	1			1				1
Encephalitis/meningitis		1	2	1				1				
Hemorrhage									2			1
Diffuse cortical atrophy					2				1			
CVT							2					
Brain abscess			1									
ADEM									1			
MS				1								
PRES									1			

CVT: Cerebral venous thrombosis; ADEM: Acute disseminated encephalomyelitis; MS: Multiple sclerosis; PRSE: Posterior reversible encephalopathy syndrome; NCC: Neurocysticercosis; CT: Computed tomography; MRI: Magnetic resonance imaging

findings were reported by Chalasani and Kumar where 46.9% were in the age group of 21–40 years.^[4] In studies by Muralidhar and Venugopal^[5] (64%), Hirani and Shrivastva^[6] (54%), and Saha *et al.*^[7] (40%), highest proportion of patients were also aged <40 years.

Gender

Male-to-female ratio was 1.85:1 in our study. Literature reported mild to moderate preponderance of males, as seen in studies by Muralidhar and Venugopal^[5] (2.12:1), Hirani and Shrivastva^[6] (1.17:1), and Sendil *et al.*^[8] (1.63:1).

Type of seizures

Generalized tonic–clonic seizures were the predominant seizure type overall, encountered in 59% patients. Narayanan and Murthy,^[9] Kanitkar *et al.*,^[10] Sendil *et al.*,^[8] and Hirani and Shrivastva^[6] also reported a higher prevalence of

generalized tonic–clonic seizures in adults (55%, 70%, 64%, and 60%, respectively).

Age-wise distribution of types of seizures

With advancing age, prevalence of generalized seizures reduces while focal seizures become the predominant seizure type. In this study, in patients aged more than 60 years, 60% had focal seizures whereas 40% had generalized seizures. Similar finding was reported by Sinha *et al.*^[11] in their study on new-onset seizures in elderly patients (aged more than 60 years), with majority (69.7%) having focal seizures. Similar trend was also noted by Sendil *et al.*^[8] and Hirani and Shrivastva^[6] The increased occurrence of focal seizures among elderly is linked to the common occurrence of stroke in this population. Other researchers reported acute stroke as up to half causes of acute symptomatic seizures in the elderly.^[12]

Etiology of seizures

In this study, stroke was the most common cause (23%) of adult onset seizures, followed by idiopathic (22%), CNS infections (21%), metabolic (12%), brain tumors (8%), encephalomalacia with gliosis (7%), and cortical venous thrombosis (4%). Kanitkar *et al.*^[10] reported that stroke was the most common cause of seizures (44%), followed by metabolic (26%), idiopathic (16%), tumors (8%), granulomas (6%), and neurocysticercosis (4%). Sendil *et al.*^[8] also reported similar findings. Pradeep *et al.*^[13] reported that seizures beginning at the age of 20 years or more were idiopathic in 44% and common etiologies were cerebrovascular diseases (20%), neurocysticercosis (12%), tuberculoma (6%), posttraumatic (6%), and tumor (4%). Jiménez *et al.*^[14] and Hirani and Shrivastva^[6] also reported a high prevalence of idiopathic seizures in adults (51% and 40%, respectively). Quraishi *et al.*^[15] observed that the most common causes of adult onset seizures were CNS infections (38%), stroke (30%), and idiopathic (20%). Mexican study^[6] reported neurocysticercosis as the cause in 50% of their participants. CVA, CNS infections, and idiopathic contributed to major fraction of adult onset seizures and their relative contributions depend on age composition of study population, sample size, and endemicity of CNS infections.

Etiology of generalized seizures

In our study, among generalized seizure cases, most common underlying etiology was idiopathic (33.9%) followed by metabolic (20.3%), CNS infections (16.9%), and stroke (10.2%). Similar results were obtained by Sendil *et al.*^[8] and Hirani and Shrivastva^[6] in their studies. On the contrary, Quraishi *et al.*^[15] reported that the most common etiologies of generalized seizures in adults were CNS infections and stroke (29.7% each), followed by idiopathic (27%), metabolic (10.8%), and tumors (2.7%).

Etiology of focal seizures

Among our patients with focal seizures, most common cause was stroke (41.5%), followed by CNS infections (26.8%), brain tumors (14.6%), encephalomalacia with gliosis (9.8%), idiopathic (4.9%), and MS (2.4%). Sendil *et al.*^[8] also observed stroke as the most common etiology (38.8% cases); other causes were idiopathic (33.3%), brain tumors (22.2%), and CNS infections (5.5%). Hirani and Shrivastva^[6] and Amaravathi *et al.*^[17] reported similar results in their studies. Chalasani and Kumar,^[4] however, observed that the most common etiology of adult onset focal seizures was CNS infections (52.7%), followed by stroke (27.3%), idiopathic (10.9%), brain tumors (5.4%), and trauma (3.6%).

Etiology of status epilepticus

In this study, 17 patients presented with status epilepticus with most common cause as metabolic (35.3%), followed by stroke (17.5%), CNS infections (11.8%), and brain tumors (11.8%). Narayanan and Murthy^[9] also observed similar findings.

Age-wise distribution of etiology of seizures

In our study, different etiologies of adult onset seizures were noted according to different age groups. In participants <20 years of age, the most common etiology was idiopathic (44.4%). CNS infections were most common in participants aged <40 years; 66.7% cases of seizures due to CNS infections were seen in patients aged <40 years. Stroke becomes a major cause of adult onset seizures after 40 years of age; 95.6% cases of seizures secondary to stroke were seen after the age of 40 years. Brain tumors causing seizures were equally prevalent in younger adults and elderly participants. All cases of cortical venous thrombosis leading to seizures were seen in participants of age <40 years. Chalasani and Kumar^[4] also reported similar findings. Similar analysis of etiology of seizures in different age groups by Quraishi *et al.*^[15] revealed that CNS infections were the most common causes of seizures in the age groups of 15–20 years (77.8%) and 21–30 years (57.1%). Stroke was the most common etiology in patients with age groups of 41–50 years, 51–60 years, and above.

Distribution of seizures in stroke

Among the patients having seizures due to stroke, 78.3% had infarct while 21.7% had intracranial hemorrhage. Among the patients having infarct, majority (83.3%) presented with focal seizures, whereas in patients having hemorrhage, predominant seizure type was generalized (60%). Sendil *et al.*^[8] also reported that among patients having seizures due to stroke, majority (75%) had an underlying infarct and most of these patients presented with focal seizures. Assis *et al.*,^[18] Quraishi *et al.*,^[15] and Amaravathi *et al.*^[17] observed similar findings.

Distribution of central nervous system infections causing seizures

Of the CNS infections causing seizures, most common was CNS TB (42.8%), followed by neurocysticercosis (28.5%) and viral meningoencephalitis (14.3%). Less common CNS infections were pyogenic meningitis, brain abscess, and cerebral malaria. Kanitkar *et al.*^[10] reported that among infectious causes of seizures, CNS TB contributed to 60% and neurocysticercosis to 40% cases. Quraishi *et al.*^[15] also reported that among neuro-infections causing seizures, tuberculoma was the most common (36.8%), followed by neurocysticercosis (31.5%), meningitis (15.8%), meningoencephalitis (10.5%), and cerebral malaria (5.3%).

Distribution of metabolic causes of seizures

Among metabolic causes, alcohol withdrawal and hyponatremia were found to be most common (25% each). Hypocalcemia was the next most common cause (16.8%), followed by hypoglycemia, uremic encephalopathy, hepatic encephalopathy, and opioid withdrawal. Similarly Kanitkar *et al.*^[10] noted that alcohol withdrawal was the most common metabolic cause of adult onset seizures (31%). Alcohol-related seizures occurred in 9% of total patients in Sander *et al.*^[19] study, 11% in Hauser *et al.*^[20] study, and 3% by us.

Abnormal electroencephalogram record

EEG record was abnormal only in 44% among our cases. Similar results were obtained by Kanitkar *et al.*^[10] (42%), Hirtz *et al.*^[21] (42%), and Sendil *et al.*^[8] (32%).

Computed tomography head findings

CT head was done in all cases, noted normal in 30%. Among abnormal CT findings, the most common features observed were infarct (18%), tumor (8%), gliosis (7%), ring enhancing lesion, hemorrhage, and cortical atrophy (5% each). Hirani and Shrivastva^[6] reported comparable findings as CT head was normal in 40% patients; most common CT finding was infarct (16%), followed by ring enhancing lesions (12%), tuberculoma (12%), brain tumor (8%), intracranial hemorrhage (8%), and brain abscess (2%). Sinha *et al.*^[11] observed that CT head was normal in 40.7% cases; in remaining patients, most frequent CT findings were infarct (22%), diffuse edema (10%), intracranial hemorrhage (9%), tumors (7%), calcified granuloma (5%), neurocysticercosis (3%), and brain atrophy (3%).

Magnetic resonance imaging brain findings

MRI brain was done in 73% among total patients; in 30% patients, it was normal. The most common MRI abnormal findings were infarct (16.3%), followed by gliosis and tumor (8.3% each); tuberculoma, neurocysticercosis, and encephalitis/meningitis (6.9% each). Sinha *et al.*^[11] also observed that MRI brain was normal in 44.2%, whereas in remaining patients, MRI revealed ischemic infarcts (16.3%), intracranial hemorrhage (14%), tumor (11.6%), calcified granuloma (7%), NCC (4.6%), and gliosis (2.3%). In a similar study, Pannag and Ravi^[22] reported that MRI brain was normal in 46% and the most common pathological findings on MRI were postischemia/hemorrhagic changes (20%), followed by tuberculoma (9.7%), tumor (9%), mesial temporal sclerosis (3%), neurocysticercosis (2.4%), encephalitis (2.4%), vascular malformation (1%), and progressive multifocal leukoencephalopathy (0.6%).

Strengths of the study

This study highlights the current scenario of the pattern of adult onset seizures in a tertiary care center. Seizures beginning in adult life require special attention with regard to their etiology as most of them are secondary to some underlying etiology. Primary care physicians play a pivotal role in identifying patients with adult onset seizures and should encourage these patients to undergo neuroimaging so as to arrive at an appropriate etiological diagnosis of adult onset seizures.

Limitations of the study

We had limitations as this was a single-center study with limited sample in resource-poor setting.

Conclusions

The incidence of generalized seizures showed a falling trend as the age advances whereas focal seizures show reverse trend with advancing age. Overall, the most common etiology of adult onset seizures is stroke. Other causes in descending order are idiopathic seizures, CNS infections, metabolic causes, and brain tumors. Gliosis, CVT, ADEM, MS, and PRES are the less common causes. MRI is superior to CT for the diagnosis of conditions such as acute infarcts, neurocysticercosis, tuberculomas, encephalitis/meningitis, CVT, MS, ADEM, and PRES. However, MRI brain can be normal in up to 30% patients with adult onset seizures. It is mandatory to deal carefully with each case of adult onset seizure, and in addition to proper history, physical and neurological examination, each patient must get EEG, CT/MRI brain, and other ancillary investigations to exclude structural or metabolic causes of adult onset seizures.

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Conflicts of interest

There are no conflicts of interest.

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