

# Aetiological and Clinical Profile of New Onset Seizures in Adults: An Institutional Experience

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## Abstract

**Objective:** This study was conducted with the objective to identify the aetiology of first seizure in adults and to evaluate their clinical profile, treatment practices and seizure recurrence.

**Methods:** A prospective observational study was conducted at the Neuro-sciences department of a tertiary care hospital cum medical research institute of Northern India from April-2017 to October-2018. A total of 114 adult patients aged 18 years or above, who presented to the hospital within 15 days of new onset seizures or developed first seizure in this hospital during the study period, were included in the study. Patients were followed up for 3 months to determine recurrence rate.

**Results:** First seizure occurred before 50 years age in most patients (65%). Generalized Tonic Clonic Seizure was most common noticed type. Most patients (63.2%) had single seizure, while status epilepticus occurred in 13.2% cases. Nearly 3/4 patients had provoked seizures. Neuro-infections and systemic/metabolic causes were relatively more common in 18-29 years group, while in older age group, cerebrovascular accidents and neuro-infections were more common. Amongst the cerebrovascular causes infraction (ischemia) was the most common. Neuro-cysticercosis was the most common infection followed by Tuberculosis. Recurrence was seen in 23 (20.2%) cases during 3 months follow up. Recurrence was significantly more common in noncompliant patients and in patients with seizure cluster at initial presentation.

**Conclusion:** Aetiology of adult new onset seizure varies with age and can vary geographically. Local etiological studies can help in early diagnosis and individualized treatment to prevent recurrence.

**Keywords:** New Onset Seizure, Adult Onset Seizure, Epilepsy

## Introduction

‘Seizure’ is a transient event which includes symptoms and/or signs of excessive abnormal hyper-synchronous activity in the brain,<sup>1</sup> and embraces all paroxysmal electrical discharges of the brain.<sup>2</sup> A solitary seizure can be caused by many medical illnesses affecting cerebral cortex primarily or secondarily. Nearly 5-10% of the population suffers at least one seizure, with highest incidence in early

childhood and late adulthood.<sup>3</sup> India harbors an estimated 6–10 million people with active epilepsy<sup>4-6</sup>, and less than half of these receive appropriate and sufficient epilepsy treatment.<sup>7</sup>

Epilepsy was defined as a disease of the brain defined by any of the following conditions: (1) at least two unprovoked (or reflex) seizures occurring >24 hours apart, or (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years, or (3) diagnosis of an epilepsy syndrome.<sup>8</sup>

Risk factors responsible for converting first seizure to epilepsy include head trauma; Vascular malformations like arteriovenous and cavernous malformations; Brain tumors; stroke; Inflammatory and autoimmune disorders like systemic lupus erythematosus (SLE), multiple sclerosis, acute disseminated encephalomyelitis, hashimoto encephalopathy, limbic encephalitis; chronic alcoholism, heroin, cocaine etc.<sup>9</sup>

First seizure has been classified as provoked seizure (due to toxin, medication, or metabolic factors); acute symptomatic seizure (caused by acute illness such as stroke, trauma, infection), Remote symptomatic seizure (due to preexisting brain injury); Seizure associated with epileptic syndrome and other unidentified seizure.

According to the American academy of neurology practice guidelines for management of an unprovoked first seizure in adult, recurrence risk is highest within the first 2 years (21%–45%).<sup>10</sup> Though, immediate antiepileptic drug (AED) therapy is likely to reduce recurrence risk within the first 2 years but may not improve quality of life and will not improve the long-term prognosis for seizure remission. Additionally, immediate treatment exposes patients to risk of adverse events ranging from 7% to 31%.<sup>10</sup> Treatment with an antiepileptic drug is also not indicated for the prevention of epilepsy.<sup>11</sup> Decision to initiate immediate AED treatment after a first seizure needs to be individualized for each patient.

Aetiology of first seizures and treatment practices vary from place to place and not much literature is available from western India. Hence, this study was conducted with the aim to study the aetiology of first seizure in adults and to evaluate treatment practices and seizure recurrence in these patients.

## Material and Methods

This prospective observational study was conducted at the Neuro-sciences department large tertiary care hospital cum medical research institute of Northern India from April-2017 to October-2018. All adult patients of either gender, aged 18 years or above, who presented to the hospital within 15 days of new onset seizures or developed first seizure in this hospital during the study period, were included in the study. Patient with seizures on treatment, head injuries, unwitnessed seizure were excluded from the study.

Ethical clearance was obtained from Institute's ethical committee before initiation of study. Written informed consent was obtained from all patients prior to data collection. A pre-designed and semi-structured proforma was used to collect information by interviewing the patient after stabilization or attendants and from records and case sheet of the patient. Any clinical seizure manifestation that

reappeared after a minimum 24 hours period of cessation, of last seizure episode was considered as seizure recurrence. Patients were followed up for 3 months to determine recurrence rate. Status epilepticus was defined as seizure activity continuing for 5 minutes, or recurrent seizures without recovery of sensorium between attacks.<sup>12-15</sup>

## Results

A total of 114 patients of first seizure were included in the study. First seizure mostly occurred before 50 years age in most patients (65%) with males more than females. GTCS was most common type of first seizure. Most patients had single seizure (63.2%) status epilepticus occurred in 13.2% cases. Nearly 3/4 patients had provoked seizures (Table 1). Cerebrovascular aetiology was the most common followed by neuro-infections. Amongst the cerebrovascular causes infarction (ischemia) was the most common. Neurocysticercosis was the most common infection followed by Tuberculosis (Table 2).

In older age group, cerebrovascular accidents and neuro-infections were more common aetiology however in younger age group (18-29 years), neuro-infections and metabolic causes were equally common (Table 3). EEG was done in 33 patients of whom abnormalities were seen in 17 (51.5%) cases, while neuro-imaging was done in all 114 patients of whom abnormal findings were seen in 71.9% cases. Recurrence was seen in 23 (20.2%) cases during 3 months follow up. Recurrence was significantly more common in noncompliant patients and in patients with seizure cluster at initial presentation (Table 4). Various clinical, investigation, treatment and outcome characteristics in provoked and unprovoked seizures showed in table 5 & 6.

## Discussion

A total of 114 cases of new onset seizures in the adults were studied. Most patients were in younger age group with male to female ratio of 1.28:1. Chalasani and Kumar<sup>38</sup> reported a male to female ratio of 1.9:1 and 21-40 years being the most common age group. Several other studies in the past also reported a male to female ratio of more than one and higher incidence in young age group.<sup>39, 37, 35, 32, 24</sup> Generalized onset tonic clonic (GTCS) was the most common type of new onset seizure in present study (70.2%). Narayan and Murthy<sup>31</sup> found GTCS in 55% cases of new onset seizure. Other studies also reported similar findings with GTCS constituting 46 to 64% of adult new onset seizures.<sup>15-19</sup>

In present study, 63.2% patients had single seizure and 13.2% had status epilepticus. Chalasani et al.<sup>18</sup> similarly reported single seizures as most common (53.1%) and status epilepticus in 11.2% patients. Narayanan et al.<sup>20</sup> reported 79% single seizures and 6% status epilepticus. Sailaja et al.<sup>21</sup> reported status epilepticus in 8% patients. In present study vascular aetiology was most common followed by neuro-infections and systemic/metabolic causes. Similar finding were reported by various studies reporting vascular and infectious aetiology as most common with slightly varying proportion.<sup>17-19</sup> Among vascular aetiology, infarction accounted for more than half cases (54.8%) as was similarly reported by Ashwin et al.<sup>19</sup> Among neuro-infections, majority of seizures were because of neurocysticercosis as was similarly reported by Chalasani et al.<sup>18</sup> and Rao et al.<sup>22</sup>

Sailja et al.<sup>21</sup> also reported neuro-infection (34%) and vascular aetiology (29%) as most common cause of first seizures in adults. Among vascular aetiology (29 subjects), CVT (38%) and infarction 10

(34.5%) were leading causes. In present study nearly 3/4 cases had provoked seizures and 25.4% cases had unprovoked seizures. Past studies have also reported higher proportion of provoked seizures ranging from 68-89%.<sup>17, 21</sup>

In the present study, in most of younger adults (18-29 years) aetiology was not found (idiopathic 27%) followed by systemic/metabolic aetiology (24.3%) and neuro-infections (21.6%). In 30-49 years age group, cerebrovascular aetiology (37.9%) was the most common followed by neuro-infections (24.3%) and systemic/metabolic aetiology (19%). Rao et al.<sup>22</sup> reported neuro-infection as most common aetiology followed by metabolic/systemic causes in both young and middle age group. This difference could be due to time and geographical difference in study and decrease in incidence of neuro-infections. In older group (50-69 years), most common aetiology was cerebrovascular (46.3%) followed by neuro-infections (26.9%) and systemic/metabolic aetiology (19.2%) as was similarly reported by other studies.<sup>22</sup>

Abnormal discharges in EEG were found in 51.5% of the 33 patients in whom EEG was done in this study. Similar findings with abnormal EEG ranging from 43.2% to 57.3% was reported by different studies<sup>15-17</sup>, indicating that only half of the first seizure cases will have abnormal finding on EEG. In present study, abnormal neuro-imaging findings were seen in 71.9% patients. This was slightly higher to findings of past studies which have reported 44.8% to 63.8% neuro-imaging abnormalities.<sup>15-17</sup> EEG and neuro-imaging were both abnormal in 10 (30.3%) cases as was similarly reported by Singh et al.<sup>16</sup>

In present study recurrence was seen in 23 (20.2%) cases during 3 months follow up. Out of these, 64.7% cases were on regular AED treatment and 35.3% cases were not taking treatment regularly. Muralidhar et al.<sup>23</sup> found recurrence of seizures in 19.3% untreated cases and none of the cases treated with AED during 6 months follow up study. Sendil et al.<sup>17</sup> during 6 months follow up found recurrence in 19.44% due to noncompliance and all these were on two antiepileptic drugs. Kareem Al-Tameemi<sup>15</sup> reported recurrence in 17.6% patients still on AED treatment, while Narayanan and Murthy<sup>20</sup> reported recurrence in 19.7% cases in provoked seizure. Hauser et al.<sup>24</sup> found recurrence rate of 16% within one year of first unprovoked seizure 21% recurrence at 24 months and 27% at 36 months. This indicates up to 20% patients can have recurrence even on AED treatment; hence decision to start AED and number of AED needs to be individualized.

## Conclusion

Acute symptomatic seizures account for a substantial proportion of all newly occurring seizures. New onset seizures were more during middle age. Systemic/metabolic and neuro-infection are major cause in young age which are amenable to prevention or early diagnosis and management. First seizure was idiopathic in substantial number of young patients. Cerebrovascular aetiology was most common in older age. Recurrence was seen in one fifth of cases. Larger multi-centric studies with prospective design are needed to identify predictors of recurrence so that need for anti epileptic drug treatment can be individualized.

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**Conflict of Interest:** Nil

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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**Table 1: Characteristics of New Onset Seizure in Adults**

<b>Characteristics</b>		<b>N</b>	<b>%</b>
<b>Age (years)</b>	<b>18 – 29</b>	37	32.5
	<b>30 – 49</b>	37	32.5
	<b>50 – 69</b>	26	22.8
	<b>≥ 70</b>	14	12.3
<b>Gender</b>	<b>Female</b>	50	43.9
	<b>Male</b>	64	56.1
<b>Seizure Type</b>	<b>Focal Onset with Impaired Awareness</b>	5	4.4
	<b>Focal Onset with Awareness</b>	12	10.5
	<b>Focal to Bilateral Tonic Clonic</b>	17	14.9
	<b>Generalized Onset Tonic Clonic</b>	80	70.2
<b>Seizure number</b>	<b>Single Seizure</b>	72	63.2
	<b>Seizure Cluster</b>	29	25.4
	<b>Status Epilepticus</b>	15	13.2
<b>Provocation</b>	<b>Provoked Seizures</b>	85	74.6
	<b>Un-provoked Seizures</b>	29	25.4

**Table 2: Aetiology of Adult New Onset Seizures**

Aetiology		N	%
<b>Cerebrovascular (N = 42)</b>	<b>Infarction/Ischemia</b>	23	20.2
	<b>Haemorrhage</b>	8	7.3
	<b>CVT</b>	10	8.8
	<b>SAH</b>	1	0.9
<b>Neuro-infections (N = 26)</b>	<b>NCC</b>	11	9.6
	<b>Tubercular</b>	4	3.5
	<b>Other</b>	11	9.6
<b>Systemic / Metabolic (N = 21)</b>	<b>PRES</b>	9	7.9
	<b>Hyponatremia</b>	5	4.4
	<b>Alcohol Withdrawal</b>	3	2.6
	<b>Other</b>	4	3.5

CVT - Cerebral Venous Thrombosis, SAH - Sub-arachnoid Hemorrhage,  
NCC - Neurocysticercosis, PRES - Posterior Reversible Encephalopathy Syndrome

**Table 3: Etiologies of Adult New Onset Seizure in Relation with Age**

Etiologies	Age group (years)				Total
	18-29	30-49	50-69	≥ 70	
<b>Cerebrovascular</b>	7 (19%)	14 (37.9%)	12 (46.2%)	9 (64.3%)	42
<b>Neuro-infections</b>	8 (21.6%)	9 (24.3%)	7 (26.9%)	2 (14.3%)	26
<b>Systemic/Metabolic</b>	9 (24.3%)	7 (19%)	5 (19.2%)	0 (0%)	21
<b>Idiopathic</b>	10 (27%)	3 (8%)	0 (0%)	0 (0%)	13
<b>Tumour</b>	0 (0%)	2 (5.4%)	1 (3.8%)	3 (21.4%)	6
<b>Gliosis</b>	2 (5.4%)	2 (5.4%)	1 (3.8%)	0 (0%)	5
<b>Autoimmune</b>	1 (2.7%)	0 (0%)	0 (0%)	0 (0%)	1
<b>Total</b>	<b>37 (100%)</b>	<b>37 (100%)</b>	<b>26 (100%)</b>	<b>14 (100%)</b>	<b>114</b>

**Table 4: Seizure Recurrence in Relation to Treatment Compliance**

		Recurrence	No Recurrence	P value
<b>Treatment Compliance</b>	<b>Noncompliant (N = 8)</b>	8 (100%)	0	< 0.001
	<b>Compliant (N = 106)</b>	15 (14.2%)	91 (85.8%)	
<b>Seizure Type at Presentation</b>	<b>Single Seizure</b>	6 (26.1%)	64 (70.3%)	< 0.001
	<b>Seizure Cluster</b>	11 (47.8%)	18 (19.8%)	
	<b>Status Epilepticus</b>	6 (26.1%)	9 (9.9%)	

**Table 5: Study of Various Characteristics in Relation to Aetiology Groups**

Characteristics	Unprovoked		Provoked		Total 114
	Idiopathic (13)	Remote Symptomatic (16)	CNS Lesion (64)	Systemic / Metabolic (21)	
<b>Gender: Male</b>	5 (38.5%)	9 (56.3%)	41 (64.1%)	9 (42.9%)	64 (56.1%)
<b>Gender: Female</b>	8	7	23	12	50 (43.9%)
<b>Focal Onset with Impaired Awareness</b>	0 (0%)	0 (0%)	5 (7.8%)	0 (0%)	5 (4.4%)
<b>Focal Onset with Awareness</b>	0 (0%)	2 (12.5%)	10 (15.6%)	0 (0%)	12 (10.5%)
<b>Focal to Bilateral Tonic Clonic</b>	0 (0%)	5 (31.3%)	12 (18.8%)	0 (0%)	17 (14.9%)
<b>Generalized Onset Tonic Clonic</b>	13 (100%)	9 (56.3%)	37 (57.8%)	21 (100%)	80 (70.2%)
<b>Status Epilepticus</b>	0 (0%)	1 (6.3%)	13 (20.3%)	1 (4.8%)	15 (13.2%)
<b>Cluster</b>	0 (0%)	4 (25%)	20 (31.3%)	5 (23.8%)	29 (25.4%)
<b>Single</b>	13 (100%)	11 (68.7%)	32 (50%)	14 (66.7%)	70 (61.4%)
<b>Occurrence During Sleep</b>	3 (23%)	4 (25%)	8 (12.5%)	5 (23.8%)	20 (17.5%)
<b>Epileptiform EEG</b>	2 (15.4%)	3 (18.7%)	9 (14.1%)	3 (14.3%)	17 (14.9%)
<b>Abnormal Neuro-imaging</b>	0 (0%)	16 (100%)	57 (89.1%)	9 (42.9%)	82 (71.9%)
<b>Seizure Recurrence</b>	1 (7.7%)	5 (31.3%)	14 (21.9%)	3 (14.3%)	23 (20.2%)

**Table 6: Various Clinical, Investigation, Treatment and Outcome Characteristics in Provoked and Unprovoked Seizures**

Characteristics	Unprovoked Seizure		Provoked Seizure
	Idiopathic	Remote Symptomatic	
<b>Total Cases</b>	13	16	85
<b>Recurrence</b>	1 (7.7%)	5 (31.3%)	17 (20%)
<b>Recurrence in Single Seizure</b>	1/13 (7.7%)	2/11 (18.2%)	3/46 (6.5%)
<b>Recurrence in Seizure Cluster</b>	0	2/4 (50%)	9/25 (36%)
<b>Recurrence in Status Epilepticus</b>	0	1/1 (100%)	5/14 (35.7%)
<b>EEG Abnormality</b>	1	2	6
<b>Abnormal Neuro-imaging</b>	0	5/5 (100%)	14/17 (82.4%)
<b>Treated</b>	8	16	85



<b>Not Treated</b>	5 (No Recurrence)	0	0
<b>Recurrence on AED</b>	1/1 (100%)	3/5 (60%)	11/17 (64.7%)
<b>Recurrence due to Poor Compliance</b>	0	2/5 (40%)	6/17 (35.3%)
<b>Aetiology</b>	Idiopathic – 1	Post-infarct-4, Gliosis – 1	Infarct – 3 SAH - 1 CVT - 3 Tuberculoma - 1 NCC – 2 Meningoencephalitis - 3 PRES - 1 Alcohol Related - 1 Substance Abuse – 1 Autoimmune - 1