



CLINICO-ETIOLOGICAL PROFILE AND NEUROIMAGING FEATURES OF ADULTS WITH FIRST EPISODE OF SEIZURES PRESENTING TO A TERTIARY CARE CENTRE

Internal Medicine

Dr Kartik B	M.D Medicine, AHR&R, New Delhi
Col Amit Sreen	M.D (Medicine), DNB (Neurology), H.O.D Medicine & Neurologist, Department of Medicine, Military Hospital, Jalandhar, Punjab, India
Brig R K Anadure	VSM, Professor, Dept of Medicine, Army Hospital Research and Referral, Delhi Cantt
Lt Col Sumit Bhasker*	M.D (Medicine) , Trained in Geriatrics (AIIMS ,New Delhi) Department of Medicine, Military Hospital, Jalandhar, Punjab, India *Corresponding Author

ABSTRACT

Background: New onset seizures occurring in adult life require special attention regarding their etiology, as most of them occur due to a secondary cause. Physicians play an important role in providing the primary care and identifying the cause for the seizures by advising them for neuroimaging studies to arrive at an appropriate diagnosis and better outcome. **Methods:** The present observational study was undertaken with an aim to determine the clinico-etiological profile of new onset of seizures in more than 18 years age group. A total of 38 patients were included who fulfilled the inclusion criteria. **Results:** The results of the study were, the mean age was 45.3 ± 13.7 years consisting of 35 males and 3 females. The most common associated symptoms among the patients was postictal confusion noted in 91.5% patients. The most common type of seizures was GTCS type constituting 81.57%, focal seizures around 10.53% and absence seizures is 2.64%. As regards the etiologic basis, Idiopathic Seizures were most commonly noted among 52.6% followed by Alcohol withdrawal among 10.52%, Neurocysticercosis among 10.2% and Gliosis (7.9%). The EEG was normal in 33 patients constituting 86.84% and 5 patients had abnormal EEG findings i.e 13.15%. CT brain findings were normal in 76.3% and 23.68% subjects have abnormal findings. MRI Brain findings were found abnormal among 12 of 29 patients who underwent MRI brain imaging among the 38 subjects. All the study population was followed up for 3 months of duration among which 5 patients had recurrent seizures (13.16%), 24 patients (63.16%) did not have recurrence of seizures. **Conclusion:** We recommend that all patients with new onset seizures need to undergo EEG as well as neuroimaging study, initially CT should be done, if inconclusive, then MRI should be preferred modality of imaging to find the etiology of seizures. Immediate initiation of antiepileptic drugs following solitary seizure should mostly be based on each patient's risk of recurrence followed by a long follow up period.

KEYWORDS

New onset seizures, GTCS, Focal seizures, Idiopathic seizures

INTRODUCTION

Dreifuss and Penry classified seizures into generalized and partial [1]. The aim of 2001 and 2006 reports on reclassification was to identify unique diagnostic entities with etiologic, therapeutic and prognostic implications. This was done because when a syndromic diagnosis was made, then the therapy and diagnosis will be made on seizure type [2].

Seizures are a common problem in clinical practice, being responsible for about 1% of hospital admissions and 3% of emergency room visits [3]. An epileptic seizure is a transient event of signs or symptoms due to abnormally excessive & synchronous neuronal activity in the brain [4]. In contrast, a convulsion is the motor manifestation of this abnormal neuronal activity [5]. A first seizure is defined as one or multiple seizures with recovery of awareness between them within a period of ≤ 24 hours [4].

Approximately 1 of 10 people throughout their lives will present an isolated seizure [6]. The lifetime risk for epileptic seizures is between 8% to 10% and with a 2%-3% chance of developing epilepsy [7,8]. About 40% to 50% of the first seizures correspond to provoked (acute symptomatic) seizures [9,10].

It is estimated that 10% of the population will have a seizure at some point in their lifetime [11].

A first seizure in any patient may be either a symptomatic seizure, due to an acute event such as head injury, infection, electrolyte imbalance, drug intoxication, etc or could be the first manifestation of underlying epilepsy. The decision of whether or not to start anti-epileptic drug in such a patient depends upon the identification of the etiology of seizure. Usual indications for starting anti-epileptics in a patient with a single seizure include an abnormal neurological examination, neuroimaging abnormalities, abnormal EEG findings, post-ictal Todd's paresis, presentation as status epilepticus and a strong family history of seizures [13].

The first step is to distinguish the presenting episode from other paroxysmal events that can mimic seizures, which can include migraine, transient ischemic attack, and syncope [14]. The second step is to assess for provocative factors such as acute systemic disturbances

or acute insults to the brain that would predispose a patient to acute symptomatic seizures [15]. In the absence of such triggers, a comprehensive workup after a first seizure is required to establish risk of recurrence and necessity of antiepileptic treatment.

CT is generally readily available and excludes problems that require immediate attention in an acute setting [16] but MRI is the preferred imaging modality for patients with epilepsy because of its superior sensitivity for lesion detection [17]. MRI may also be superior to CT in clarifying the electro-clinical diagnosis, with an epileptogenic lesion supporting a focal seizure onset in an otherwise unclassified seizure [18]. However, a recent study of lesions detected by magnetic resonance imaging (MRI) in adults with a first seizure found that a potentially epileptogenic lesion could be identified in 28% of all patients with a seizure and in 53% patients with a focal onset seizure [19]. In another recent study, MRI showed a cause in 44% of patients who were scanned for acute seizure, half of whom were patients with a first seizure [20]. These studies showed a spectrum of potentially epileptogenic lesions similar to those seen in chronic epilepsy, including neoplasms, vascular malformations, developmental anomalies, gliosis/encephalomalacia from a variety of causes, mesial temporal sclerosis and miscellaneous other lesions [19,20]. This, in turn, greatly facilitates patient counselling and early management decisions, such as the initiation of antiepileptic drug therapy or expedited referral for surgical consideration.

At the global level, it is estimated that nearly 70 million people suffer from epilepsy. The estimated proportion of the general population with active epilepsy (i.e. continuing seizures or with the need for treatment) at a given time is between 4 and 10 per 1000 people [21-22].

Within generalized epilepsy, tonic-clonic was the commonest type [23]. Approximately 75% of epilepsy begins during childhood, suggestive of susceptibility to develop seizures in developing brain. However, a changing pattern in the age-specific occurrence of epilepsy with preponderance towards the older age group is noticed due to sociodemographic and epidemiological transition [24-26].

A fundamental change as per the new operational classification of seizures as per ILAE 2017 is that seizures may be either focal or

generalized [1,13]. Generalized seizures involve diffuse regions of the brain simultaneously. Focal seizures are those in which the seizure activity is restricted to discrete areas of the cerebral cortex. Generalized seizures may result from biochemical, cellular abnormality or structural abnormalities that have a more widespread distribution. In contrast, focal seizures are usually associated with structural abnormalities of the brain. Focal seizures arise from a neuronal network either discretely localized within one cerebral hemisphere or more broadly distributed but still within the hemisphere. The new classification system describes it as focal seizures with or without dyscognitive features [27]

Focal onset	Generalized onset	Unknown onset
- Intact/ impaired awareness - Motor or non-motor onset - Evolve from focal to bilateral tonic clonic	A] Motor - Tonic-clonic(GTCS) - Other motor(eg: atonic, myoclonic) B] Other motor (eg: absence)	- Motor - Non-motor - Unclassified

ILAE described epilepsy according to etiologies as:

Structural	Genetic	Infectious
Metabolic	Immune	Idiopathic / Unknown

Therefore, the clinical course of patients after the first seizure varies considerably, and through our study, we aim to identify the factors which may guide therapeutic decisions when the patient is seen after their first seizure

AIM AND OBJECTIVES

AIM

To study the clinical and etiological profiles and neuroimaging features of patients presenting with first episode of seizure to Army Hospital (R&R), Delhi.

OBJECTIVES

- To study the clinical profile of first-episode seizures in adults attending our hospital.
- Classifying the seizure type according to the 2017 ILAE classification.
- To ascertain the aetiology of seizures in such adults attending our hospital,
- To assess the differences in aetiology and response to treatment of first-time seizures across different age-groups and sexes.

MATERIAL AND METHODS

This was a prospective observational study

Study Area

The study was conducted among patients attending the departments of General Medicine and Neurology of Army Hospital Research and Referral, Delhi Cantt.

Study Design

Prospective observational study

Study Period

18 months (October 2020 to April 2022)

Study Population

Patients for the study were selected from the OPD and referred cases from other armed forces hospitals/primary care centres based on inclusion and exclusion criteria.

Inclusion criteria

- Patients with first episode of seizure
- Patients over the age of 18 experiencing their first seizures

Exclusion Criteria

- Known case of seizure disorder
- Patients of seizures with age of onset <18 years
- Seizure mimics like syncope
- Seizures due to recent traumatic brain injury (≤6 months)
- Post-operative seizures (including neurosurgical procedures),
- Seizures due to obstetric causes (including eclampsia) were excluded from the study.

Sample Size

The study population has been calculated by using G-power with 80% of the power and 5% of the significance level. The total sample size was determined to 95 subjects.

i. Based on previous studies sample size was calculated using formula $n = Z^2 P(1-P) / e^2$

Where (Z) = standard normal variant at Type I error ($P < 0.05$)

ii. Prevalence (P) = expected proportion in population based on previous studies i.e 1.1%

iii. Absolute error (e) – we are taking it as $2n = (1.96)^2 * 0.01 * 0.99 / (0.02)^2 = 95$

A sample size of 95 patients was kept as a convenience sample as per prevalence of disease. Due to COVID -19 Pandemic and lock down imposed by Government of India, University of Delhi advised to reduce the sample size to 20 subjects. However, this study was conducted in 38 subjects.

Study Methods

After approval from the Institutional Ethical committee, all patients were selected as per inclusion and exclusion criteria. A detailed history, complete physical examination and routine and appropriate investigations were done for all patients. The study was conducted in the department of medicine & neurology Army hospital (R&R)

Statistical analysis Plan

The data was entered into the Microsoft excel and the statistical analysis was performed by statistical software SPSS version 21.0. The Quantitative (Numerical variables) were present in the form of mean and SD and the Qualitative (Categorical variables) were present in the form of frequency and percentage. The student t-test was used for comparing the mean values between the 2 groups whereas chi-square test was applied for comparing the frequency. The p-value was considered to be significant when less than 0.05.

RESULTS

The present study was conducted in Army hospital (R&R) tertiary care centre. 38 patients were enrolled during the period from October 2020 to April 2022. following are the results

Table 1: Distribution of study population according to age

Age groups	Frequency	Percent
18-20 years	2	5.3%
21-30 years	13	34.2%
31-40 years	15	39.5%
41-50 years	1	2.6%
51-60 years	3	7.9%
Above 60 years	4	10.5%
Mean±SD (Minimum- Maximum)	45.36±13.57 (18-81)	

Table 2: Distribution of study population according to gender

Gender	Frequency	Percent
Male	35	92.1%
Female	3	7.9%
Total	38	100.0%

Table 3: Distribution of study population according to type of seizure

Type of seizure			Frequency	Percent
Generalized onset	Motor	GTCS	31	81.57%
	Non-motor	Absence seizures	1	2.64%
Focal onset	Intact awareness	Focal seizures	4	10.53%
Unknown onset	Unclassified	—	2	5.26%
	Total		38	100.0%

Table 4: Distribution of study population according to symptoms associated with seizures

Symptoms	Frequency	Percent
Headache/ Giddiness	22	57.8%
Vomiting	3	7.9%

Fever	2	5.3%
Teeth Clenching	15	39.4%
Frothing	8	21.2%
Lip Bite	3	7.9%
Tongue Bite	14	36.9%
Loss of consciousness	34	89.5%
Post Ictal Confusion	35	91.5%
Urine/Stool Incontinence	7	18.4%
Eye Rolling	22	55.3%
Aura	12	31.6%

Table 5: Distribution of study population according to etiology

Diagnosis	Frequency	Percent
Alcohol withdrawal	4	10.52%
Inflammatory granuloma	4	10.52%
Calcified Granuloma	1	2.63%
Gliosis	3	7.9%
Cerebral venous sinus thrombosis	2	5.27%
Hypertensive encephalopathy	2	5.27%
ICH	1	2.63%
Ischemic Stroke	1	2.63%
Idiopathic	20	52.63%
Total	38	100%

Table 6: Distribution of study population according to lab parameters

Parameter	Minimum	Maximum	Mean	Std. Deviation
RBS	78.00	190.00	101.60	24.62
HB	10.00	16.10	13.75	1.52
TLC/DLC	4000.00	15400.00	7848.95	2996.59
Urea	5.00	39.00	14.41	7.25
Creatinine	0.40	2.04	0.80	0.24
Sodium	130.00	148.00	138.22	3.92
Potassium	3.60	5.30	4.12	0.43
Calcium	8.40	10.20	9.05	0.46
Magnesium	1.33	2.40	2.13	0.35
Phosphorus	2.00	4.60	2.84	0.72
BIL (T/D)	0.17	1.40	0.68	0.28
ALP	20.00	207.00	58.40	45.64
GGT	10.00	1531.00	156.63	408.59

Table 7: Distribution of study population according to EEG findings

EEG	Frequency	Percent
Normal	33	86.84%
Abnormal	05	13.15%
Total	38	100%

Table 8: Distribution of study population according to CT findings

CT Scan	Frequency	Percent
Normal	29	76.3%
Calcified Granuloma	1	2.64%
Inflammatory granuloma	1	2.64%
Gliosis	2	5.25%
Focal ring enhancing lesion	3	7.89%
ICH	1	2.64%
Ischemic stroke	1	2.64%
Total	38	100%

Table 9: Distribution of study population according to MRI findings

MRI Brain	Frequency	Percent
Normal	17	44.7%
Focal ring enhancing eision (neurocysticercosis)	3	7.89%
Gliosis	3	7.89%
Calcified Granuloma	1	2.64%
Inflammatory granuloma	1	2.64%
Intracerebral hemorrhage	1	2.64%
Ischemic stroke	1	2.64%

Cerebral venous thrombosis	2	5.26%
Not available	9	23.7%
Total	38	100%

Table 10: Distribution of study population according to followup

3months followup	Frequency	Percent
Seizure recurrence	5	13.16%
No seizure	24	63.16%
Lost followup	9	23.68%
Total	38	100%

DISCUSSION

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 [28,29].

Age wise distribution

In our study, majority of the subjects belonged to 31-40 years (39.5%) and 21-30 years (34.2%) age groups. The mean age of the study population was 45.36±13.57 (18-81) years. Our results stating that patients less than 40 years of ages were prone to seizures, are in accordance to the findings of the studies done by Sheikh et al [30] who stated that the incidence rate was 40%. Sander et al [31] found the incidence rate of epilepsy to be 60.99% in patients less than 40 years of age. Similarly, Chalasani et al [32] stated 46.9% of subjects less than 40 years of age and Joshi et al as 52% less than 40 years of age to be epileptic. In our study we found that onset of epileptic seizures in age group more than 60 years as 10.5%. This finding was not in accordance to the results of 69.7% by Sinha et al [34].

Gender

In this study, there were 35 (92.1%) males and 3 (7.9%) females with a ratio of 11.67:1. In comparison with current study, Literature reported mild to moderate preponderance of males as elucidated in studies by Sendil et al [35] (1.63:1) and Hirani and Shrivastva [36] (1.17:1).

Type of Seizures

In present study, Generalized onset with Motor in nature i.e generalized tonic clonic seizure (GTCS) was the predominant (81.57%) form of seizure, Absence seizures (2.64%) and Focal onset seizures i.e focal seizure with intact awareness (10.53%). Unknown onset/unclassified type of seizures constitute 5.26%

This is in accordance with studies by Ashwin et al [2] in which the majority (57%) of the had GTCS, 31% of participants presented with focal seizures without cognitive impairment, 9.0% participants with focal seizures with secondary generalization, and 3% of participants had focal seizures with cognitive impairment. In similar studies, Sendil et al [35], and Hirani MM et al [36], GTCS was found to be the pre-dominant seizure type. However, Chalasani S et al [32] showed that partial seizure is predominant in their study accounting for 46% and GTCS accounting for 44%

Focal seizure in the studies done by Jallon et al [33]¹ was 46.2%, King et al [18] was 58% and Murthy et al [37] was 78% which is in discordance with the present study.

The reason for generalized seizure preponderance may be related to the understanding and knowledge of the disease symptoms, literacy level and attitude of the bystanders about the disease. bystanders usually consider the obvious tonic-clonic movements as seizures and other forms are not considered as seizures which could be the probable cause for high incidence of seizure type.

Associated symptoms with seizure at presentation

The most common symptom associated with seizure in current study is Post Ictal Confusion (91.5%) followed by Loss of consciousness (89.5%), Eye Rolling (55.3%), Headache/ Giddiness (57.8%), Teeth Clenching (39.4%), Tongue Bite (36.9%) and Aura (31.6%), Frothing (21.2%), Vomiting (7.9%) Lip bite (7.9%), Incontinence (18.4%) and Fever (5.3%). This corroborates with study by Ashwin et al [2] who also found that 27.0% participants had postictal confusion, 14% bladder incontinence, 20% had focal neurological deficit. Eight participants suffered from tongue bite. Benbadis et al [40] showed that tongue bite was highly specific for GTCS. A meta-analysis by Francesco Brigo [41] also found that tongue bite is more specific for seizures particularly GTCS.

Seizure type-

Our study found that the etiology of seizure was Idiopathic/unknown Seizures among 52.6% followed by Alcohol withdrawal (metabolic) among 10.52%, Inflammatory granuloma (Neurocysticercosis, NCC) (Infectious) among (10.52%), structural - Gliosis(7.9%) and Calcified granuloma(2.64%), CVT (5.3%), hypertensive encephalopathy (5.27%), ICH and ischemic stroke 2.63% each. Younger patients with seizure often show a genetic cause. New-onset seizures in elderly usually have a 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.

Ashwin *et al* [2] found that stroke was the most common cause of seizure in their study followed by infection followed by metabolic cause. This was contrast to study by *Hirani et al* [36] where seizure due to unknown cause was most common 40%. This may be because the study involved only 50 participants. However, *Sendil et al* [35] found that post stroke seizures and seizures due to unknown cause were most common and shared equal proportion. However, *Chalasani S et al* [32] in his study has shown infections were common cause of seizures in their study. Among infections Neurocysticercosis was most common. This supports our present study, in which NCC was most common cause of seizure due to infections.

EEG findings-

In current study, Abnormal EEG findings were found in 05 patients with seizure which include GTCS type in 2 cases constituting 5.26% which was showing generalized spike wave or poly spike and wave pattern. Focal epileptiform discharges seen in 3 cases constituting 7.89% showing focal slowing or spike and wave pattern. The EEG is also used for classifying seizure disorders and for the selection of anticonvulsant medications. A normal EEG implies a better prognosis, whereas profuse epileptiform activity suggests a poor outlook. Similar studies by Kanitkar *et al*. [43] & Hirtz *et al* [44] showed abnormal EEG in 42%. A study done by *Panagariya et al* [45] in Jaipur and *Hussein et al* [46] in Sudan found that EEG was abnormal in 58.9% and 64.8% epilepsy patients.

Neuroimaging Findings –

CT brain:

CT brain findings were normal in 76.3% and 23.68% subjects have abnormal findings among 38 patients. Abnormal CT findings include calcified granuloma 2.64%, inflammatory granuloma 2.64%, Gliosis of left temporal gyrus 5.26%, focal ring enhancing lesion constituting 7.89%, right frontal intracerebral haemorrhage and left MCA ischemic stroke constituting 2.64% each.

MRI Brain

findings were found abnormal among 12 of 29 patients who underwent MRI brain imaging among the 38 subjects. Abnormal MRI findings include focal ring enhancing lesion (NCC) 7.89%, Gliosis 7.89%, Calcified Granuloma. Out of 38 subjects 9 patients MRI findings were not available. MR venography suggestive of cerebral venous thrombosis constituting 5.26% of subjects.

Hirani and Shrivastva [36] reported normal CT head 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*. [34] observed that CT head was normal in 40.7% cases; in remaining patients, most frequent CT findings were infarct (22%). *Sinha et al* [34] 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%). Pannag and Ravi [47] 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%).

Seizure recurrence-

In our study all the study population was followed up for 3 months of duration among which 5 patients had recurrent seizures (13.16%), 24 patients (63.16%) did not had recurrence of seizures. 9 patients (23.68%) lost follow up. Among the 5 cases who had recurrent

episodes of seizures 4 cases found to have idiopathic cause for seizures

CONCLUSION

1. In this study of new onset seizures, the mean age of onset is 45.36 years with male predominance.
2. The most common cause of seizures being idiopathic followed by alcohol withdrawal and neurocysticercosis with most common associated symptom being postictal confusion.
3. Most common seizure is GTCS type.
4. Proper clinical diagnosis and classification of seizures is necessary to prevent the further episodes which needs neuroimaging at etiology of seizure and better management.
5. Long term follow-up and evaluation is required to look for recurrent episodes of seizures for diagnosing unknown cause of first episode of seizures.

Recommendations

1. Patient with solitary seizure should be counselled about quality of life, precautions and risk of recurrence in future.
2. All new onset seizures in young patients need to undergo EEG as well as neuroimaging study, initially CT should be done, if not arriving at diagnosis then MRI should be preferred modality of imaging to find the etiology of seizures.
3. Immediate initiation of antiepileptic drugs following solitary seizure should mostly be based on each patients risk of recurrence.
4. Every patient s preferences should be considered while prescribing antiepileptic drugs and educating them therapeutic profiles and adverse effects thereafter.
5. Long term follow-up is needed in case of idiopathic seizures.

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