

# Clinico-Etiological Profile of New Onset Seizures in Adults in Southern Odisha - An Observational Study

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## ABSTRACT

### BACKGROUND

Population based studies indicate that the incidence and prevalence of seizure disorders in adults increase with age, especially in elderly, after the age of 60 years. The underlying etiological spectrum is variable across geographies. Analysis of aetiology of seizure is essential for proper treatment to reduce the morbidity and mortality associated with it. The present study was planned to analyse the aetiology of new onset seizures in adult population (> 18 years of age).

### METHODS

The cross sectional study was carried out in the Department of Medicine of MKCG Medical College & Hospital for a period of two years. 100 consecutive cases of new onset seizures admitted in the in-patient department (indoor / ward) were included in the study as per the inclusion and exclusion criteria. The data was collected by the investigators in a pre-tested Case Record Form. Data analysis was done using Microsoft Excel and GraphPad Prism trial version 7.0. Descriptive statistics were presented as proportions for discrete variables and as mean  $\pm$  SD for continuous variables. P value of  $\leq 0.05$  was taken as statistically significant.

### RESULTS

Acute symptomatic seizures accounted for 89 % of cases. Neuro-infection was the leading aetiology in 35 % of cases, followed by cerebrovascular accidents (30 %) and metabolic causes (10 %). Neurocysticercosis was seen in 11 % cases, followed by meningitis and cerebral malaria. Among the vascular causes, stroke accounted for 20 %. Prevalence of neuro-infection was highest in the age group of 15 - 35 years. 89 % of idiopathic seizures were generalized tonic-clonic seizure (GTCS). The prevalence of status epilepticus was 8 %.

### CONCLUSIONS

Adult onset seizures have a varied spectrum of aetiology. With a thorough history, clinical examination and appropriate investigations, the aetiology can be identified. Accordingly, treatment can be instituted thus reducing the morbidity and mortality associated with it.

### KEYWORDS

Aetiology, New Seizures, Stroke, Vascular, Neuro-Infection

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**BACKGROUND**

Seizures / convulsions are very common clinical presentations for which patients seek medical advice. They are found all over the world and are frequently encountered in variety of settings. Late onset seizures, also referred to as Epilepsia tarda may be simply defined as epilepsy beginning in adult life. CNS infections like malaria, meningitis, tuberculosis, HIV, neurocysticercosis account for significant number of seizures in developing countries.<sup>1</sup> Single small enhancing CT lesions (SSECTL) (ring enhancing / disc lesions, 20 mm in size) due to dying cysticercus larva are an important cause of seizures in India.<sup>2</sup>

In post-puerperal women, cerebral venous thrombosis induced seizure is commonly seen in Indian subcontinent.<sup>3</sup> Focal onset seizures are more common but they can get secondarily generalized to a life threatening status epilepticus.<sup>4</sup> The common aetiologies of seizure in older patients are subdural haematoma, stroke, CNS infections, degenerative disorders and malignancy. Haemorrhagic strokes are more common than ischemic stroke. Systemic metabolic conditions like uraemia, hyperglycaemia, hypoglycaemia, hyponatremia, alcohol withdrawal also lead to seizures in elderly.<sup>5</sup>

Different spectrum of CNS infections as a cause of seizure varies from region to region. Etiological spectrum of acute symptomatic seizure is different in developing countries than that of developed countries. Etiological diagnosis of seizure is essential for proper treatment to reduce the morbidity and mortality associated with it. With this background this study was planned to analyse the aetiology of new onset seizures in adult population (> 18 years of age).

**METHODS**

The cross sectional study was carried out in the Department of Medicine of MKCG Medical College & Hospital – a tertiary care teaching hospital in Eastern India from October 2017 to September 2019. 100 consecutive cases of new onset seizures admitted to the In-patient department were included in the study. Patients with more than 18 years of age and presenting with new onset seizures either provoked or unprovoked were included in the study. Any patients with psychogenic seizures, eclampsia, transient ischemic attack, narcolepsy, movement disorders or hyperventilation were excluded from the study. Detailed history, physical examination, renal function tests, serum electrolytes, EEG, CT brain, MRI brain, CSF analysis, serology and other routine investigations were carried out as per standard protocol of management and to find out the aetiology.

The present study was approved by the Institutional Ethics Committee of MKCG Medical College, Berhampur, Odisha. (IEC Approval No 627) Written informed consent was obtained from the patient or the legal authorized representative / attendant after explaining them the implication of the study and assuring them that the information obtained shall be used only for the purpose of

research work and shall be kept confidential. The data was collected by the investigators in a pre-tested case record form that captured the demographic details, history, clinical features, physical examination findings and the findings of the routine and specialized investigations.

**Data Analysis**

It was done using Microsoft Excel and GraphPad Prism trial version 7.0. Descriptive statistics were presented as proportions for discrete variables and as mean ± SD for continuous variables.

**RESULTS**

Aetiology of new onset seizures varies depending on age, gender, geography and clinical setting. In this study, 55 % of patients were males and 45 % were females, with male to female ratio of 1.22. Majority of males were in 3<sup>rd</sup> decade of life and females were in 2<sup>nd</sup> decade of life. The age range was from 18 years to 80 years with a mean age of 35.2 years. Majority (25 %) of patients were in the age group of 21 - 30 years followed by 31 - 40 years (21 %). 12 % of the patients were older than 60 years. Acute symptomatic seizures, idiopathic seizures, post infarct seizures constituted 89 %, 9 % and 2 % of seizures respectively (P value ≤ 0.05). [Table 1].

Seizure Type	Occurrence N (%)
Acute symptomatic seizures	89 (89)
Idiopathic Seizures	9 (9)
Post-Infarct	2 (2)

**Table 1. Types of Seizures**

Aetiology	Occurrence N (%)
CVA	30 (30)
CNS infection	35 (35)
Traumatic Brain Injury	1 (1)
Tumour	7 (7)
Alcohol Withdrawal	3 (3)
Metabolic	10 (10)

**Table 2. Aetiology of Seizure**

Aetiology	Occurrence N (%)
Neuro-infection	35 (35)
Neurocysticercosis	11 (11)
CNS Tuberculosis	10 (10)
Vascular	30 (30)
Stroke	20 (20)
CVT	8 (8)
Others	2 (2)

**Table 3. Sub-Types of Neuro-Infections and Vascular Causes of Seizures**

Age	Aetiology	Occurrence N (%)
15 - 35 years	Neuro-infections	47 (47)
	CVA	15 (15)
35 - 64 years	Neuro-infections	32 (32)
	Stroke	23 (23)
	Idiopathic	13 (13)
	Alcohol related	3 (3)
> 65years	CVA	42 (42)
	Metabolic	28 (28)
	Neuro-infections	21 (21)

**Table 4. Age-Wise Distribution of Seizure Aetiology**

Aetiology	Occurrence N (%)
Viral Meningoencephalitis	3 (3)
Alcohol Withdrawal	1 (1)
Poisoning	1 (1)
Idiopathic	1 (1)
Metabolic	1 (1)

**Table 5. Aetiology of Status Epilepticus**

It was observed that neuro-infection was statistically significant ( $P$  value  $< 0.001$ ) and leading cause of seizure accounting for 35 % cases, followed by cerebrovascular accidents (30 %) and metabolic causes (10 %). [Table 2]. In the neuro-infection group, neurocysticercosis was found in 11 % cases, followed by meningitis (11 %) and cerebral malaria (7 %). Stroke accounted for 20 %, followed by cerebral venous thrombosis 8 %. [Table 3]

In the present study the prevalence of neuro-infection was highest in the age group of 15 - 35 years ( $P$  value  $< 0.001$ ) and 35 - 64 years ( $P$  value = 0.078), whereas about 17 % of Cerebrovascular accident (CVA) occurred between the 3<sup>rd</sup> and 5<sup>th</sup> decade. All the cases of CVA occurring in 2<sup>nd</sup> and 3<sup>rd</sup> decade were Cerebral venous thrombosis (CVT).

## DISCUSSION

The age range was from 18 years to 80 years with a mean age being 35.2 years and majority of patients were in the age group of 21 - 30 years followed by 31 - 40 years. In a study from United Kingdom by Sander et al. 25 % were below the age of 15 years, 51 % in 3<sup>rd</sup> - 4<sup>th</sup> decade and 24 % above 60 years compared to 12 % in the present study.<sup>6</sup> Another study from South India by Murthy et al. 36 % were  $> 60$  years, with mean age of 49 years. In our study, majority of patients were younger unlike western studies where many were in older age group. Mean age of presentation was lower (35 years) in our study when compared with other Indian studies.

This testifies the fact that the etiological spectrum varies from region to region. Etiological spectrum depends on age, sex, geography and medical setting. Seizures may be the manifestation of an underlying medical illness which requires specific treatment. In such cases, treatment of the seizure alone will not cure the patient, rather it may be dangerous as the underlying disease may progress and patient may get complications. The likelihood of a particular acute precipitant depends on the patient's age.<sup>7</sup> The medical setting is also pertinent. Patients in ICUs are more likely to have drug toxicity or withdrawal and metabolic abnormalities as causes for seizures.<sup>8</sup> Acute symptomatic seizure was the predominant type of seizure in adults followed by idiopathic seizures and post infarct seizures.

Acute symptomatic seizures are those where there is always an underlying neurological disease in the form of either infection, metastases, vascular or metabolic. Two epidemiologic studies, which describe the incidence of acute symptomatic seizures, needs special mention here. In Rochester, Minnesota study, the cumulative incidence of acute symptomatic seizures in patients up to 80 years of age was 3.7 %.<sup>9</sup> A community-based study in the UK also reported that 21 % of newly occurring seizures fell into the category of acute symptomatic seizures. In one south Indian study acute symptomatic seizures accounted for 22.5 % of the total patient population studied.<sup>10</sup> In present study it was observed that neuro-infection was the leading cause of seizure, followed by cerebrovascular accidents and metabolic cause. Neuro-infection occurred in 2 % of the

About 40 % of stroke occurred in patients older than 50 years. Metabolic seizure was common in 5<sup>th</sup> decade (40 %). [Table 4]

Most of neuro-infection patients presented with GTCS (61 %). 55 % of CVA patients presented with FSSG followed by GTCS (26 %) where as 50 % of metabolic seizures were GTCS. All the patients of poisoning induced seizure presented with GTCS. 89 % of idiopathic seizures were GTCS. The prevalence of status epilepticus (SE) was 8 %. One case of Epilepsia Partialis Continua due to hypocalcaemia was observed. The commonest cause of seizure was viral meningo-encephalitis (3 %) followed by alcohol withdrawal (1 %), poisoning (1 %), idiopathic (1 %), metabolic (1 %). [Table 5]

patients in a study by Sander et al. 8 % in another study by Annegers et al.<sup>11</sup> 77 % in a study by Maneesh et al.<sup>12</sup> and 32 % in a study by Murthy et al.

In the neuro-infection group, neurocysticercosis was found in 11 % cases, followed by meningitis (11 %) and cerebral malaria (7 %). Stroke accounted for 20 %, followed by cerebral venous thrombosis 11 %. Single small enhancing CT lesions (SSECTL) (ring enhancing/disc lesions, 20 mm in size) are an important cause of seizures in India.<sup>13</sup> SSECTL accounted for 50 % of seizures in a study by Murthy et al. but in our study it was found only in 5 % of cases. This may be because of regional variation. CVA occurred in 15 % of the patients in a study by Sander et al. 18 % in another study by Annegers et al. 14 % in a study by Maneesh et al. and 21 % in a study by Murthy et al. In our study CVA as a cause of seizure was found in 30 % cases. This was because of postpartum CVT which was seen in 8 % of cases, higher even when compared with other Indian studies. In a study done in the west, 16 % of acutely precipitated seizures were caused by cerebrovascular events, and this percentage increased to 40 % in the elderly.<sup>14</sup>

In another study from south India, cerebrovascular events accounted for 14 % of etiological factors and 60 % of the patients were aged over 40 years. In intracerebral haemorrhage, incidence of early seizures tends to be higher than the late onset seizures. In a study by Sander Et al. Alcohol related seizures occurred in 9 % of the patients, 11 % alcohol related seizures reported by Annegers et al. and in our study we got only 3 % alcohol related seizure. Alcohol related seizures were less common when compared with western studies. In our study seizures due to poisoning was as common as seizures due to alcohol withdrawal. Focal motor seizures, with or without secondary generalisation, were the predominant types of seizures both in early onset and late onset group.<sup>15</sup>

Seizures in elderly deserves mentioning as population-based studies indicate that seizure disorders increase in incidence and prevalence after the age of 60 years and etiological spectrum is different in developing countries when compared to developed countries.<sup>16</sup> In many older patients, an underlying cause of seizure activity is clearly identifiable. They are subdural hematoma, stroke, and CNS infection. Systemic metabolic conditions such as uraemia, hyperglycaemia, hypoglycaemia, hyponatremia, and alcohol withdrawal. Alzheimer's dementia and amyloid angiopathy are degenerative diseases associated with seizures. One of

the risk factors for tonic – clonic seizure in elderly is Alzheimer's in its late stage.<sup>10</sup> Percent of all seizures are due to Alzheimer's, particularly late in the illness. An increased prevalence of seizures also has been documented with other types of dementia. In developing countries CNS infection is the major cause of seizure in elderly whereas in developed countries cerebrovascular disease predominate.<sup>17</sup> Infections are the major causes of seizures in developing nations. Commonest infections associated with seizures are neurocysticercosis, others include cerebral malaria, tuberculosis, African trypanosomiasis, cerebral hydatidosis and congenital toxoplasmosis.<sup>18</sup> Single small enhancing CT lesions (SSECTL) defined as ring enhancing / disc lesions, < 20 mm in size are common findings on cranial CT of Indian patients presenting with acute symptomatic seizures. Etiologic possibilities earlier considered for this entity includes tuberculosis,<sup>19</sup> focal encephalitis, micro abscesses and cysticercosis. But current opinion and histopathological studies suggest single small enhancing CT lesions in majority of patients are because of dying cysticercus larva.<sup>20</sup>

Seizures are important neurological complications of bacterial meningitis, and it is often associated with poor outcomes.<sup>21</sup> 80 % of seizures usually occurs within 24 h of presentation. Seizure activity that has a focal onset is due to either focal cerebral ischemia or oedema, while generalized seizure activity and status epilepticus are due to fever, metabolic derangement, spread from a focal onset to a generalized tonic-clonic convulsion, or toxicity from antimicrobial agents.<sup>22</sup> Tuberculous meningitis is the most common type of chronic meningitis in India. In tuberculous meningitis seizures can occur at any stage of the illness and may be the presenting feature. More than 60 % of patients with intracranial tuberculoma may have seizures. In one study, 50 % of the patients with CNS tuberculosis had seizures.<sup>23</sup> Approximately 30 % of the patients who had brain tumours had seizures as the initial symptom. Slow-growing tumours, such as oligodendrogliomas and low grade astrocytoma, commonly present with seizures, whereas more aggressive tumours, such as glioblastomas, more often present with symptoms of mass effect.<sup>24</sup> Alcohol-related seizures are defined as adult-onset seizures that occur in the setting of chronic alcohol dependence. Alcohol withdrawal is the cause of seizures in a subgroup of these patients; however, concurrent risk factors including pre-existing epilepsy, structural brain lesions, and the use of illicit drugs contribute to the development of seizures in many patients.<sup>25</sup>

Most frequent causes of seizures in adulthood, particularly in the old age is stroke. Incidence of seizures after stroke varies from 4.1 % to 12.5 %. Post stroke epilepsy incidence in India is 13 %.<sup>26</sup> Metabolic abnormalities (especially hypoglycaemia, hyperglycaemia, hyponatremia and hypocalcaemia) account for 9 % of acutely triggered seizures.<sup>27</sup> Neurologic symptoms related to hyponatremia are seen much more frequently in patients with acute, rather than chronic hyponatremia. Generalized seizure may be a presenting symptom of poisoning, also it indicates a pre-terminal manifestation of serious toxicity. Overdose or toxicity of a large number of drugs and toxins, such as isoniazid (INH), carbon monoxide, theophylline, cyclic

antidepressants, and salicylates may present as seizure. Additionally, drug withdrawal states, such as from ethanol and sedative / hypnotic agents, may induce refractory seizure activity.

## CONCLUSIONS

Adult-onset seizures usually are secondary to an underlying aetiology as compared to those beginning in childhood. Childhood seizures are likely to be idiopathic. With thorough history taking and clinical examination, an aetiology may be suspected, which can be confirmed by investigations. Etiological diagnosis followed by timely and appropriate therapy will reduce the morbidity and mortality associated with this disease. Acute symptomatic seizures account for 89% of total seizures where underlying aetiology can be ascertained. Majority of seizures occurred in patients aged less than 50 years. Varied aetiology of seizures include neuro-infection, CVA, tumour, metabolic, poisoning and alcohol withdrawal. Neuro-infection and cerebrovascular accidents predominate as aetiology of seizures in all the age groups. Neurocysticercosis and bacterial meningitis are two most common neuro-infections that present as seizure. Cerebral venous thrombosis is an important cause of acute symptomatic seizures among young patients.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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