

Original Research Article

Etiological profile of adult onset seizures: a hospital based prospective study from Kashmir, India

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ABSTRACT

Background: Adult onset seizure (AOS) is considered the epilepsy that start after the age of 18 years. It is a common neurological disorder with multiple etiologies. Objective was to study the etiologies, diagnosis and treatment of AOS in Kashmiri population and to compare its different clinical and etiological profiles in different age groups.

Methods: All patients who developed seizure after the age of 18 years were recruited in the current prospective study. In total 144 subjects with AOS were included in this study. The study was done in the Neurology unit of Sher-i-Kashmir Institute of Medical Science, Srinagar- a tertiary care hospital in Kashmir, India from August 2014 to July 2016.

Results: Among the 144 recruited subjects, the 25-34 years age group was more susceptible to onset seizures. Generalized tonic-clonic seizure with a percentage of 48.8% was the most common seizure type among the studied subjects. Gender wise males were more susceptible to intracerebral hemorrhage while as cerebral venous sinus thrombosis is more common among females. Among the infection group, encephalitis was a leading causal factor in 10 (6.9%) patients and age wise younger population is more susceptible to encephalitis and central nervous system, while prion disease was more frequent in subjects with age of ≥ 55 . On comparing various cerebrovascular diseases and seizures, ICH was responsible in most number of subjects (12.5%). MRI and EEG (59.7% and 52.8% respectively) findings were abnormal in maximum number of subjects and both findings showed statistically a significant positive correlation ($r=0.73$; $p<0.01$).

Conclusions: Idiopathic factors are the main cause of AOS with EEG and MRI being the mainstay for identifying, classifying and localizing seizures among the study patients.

Keywords: Adult, Seizure, Etiology, Clinical profile, Kashmir

INTRODUCTION

Epilepsy is considered a public health priority by the World Health Organization with more than 50 million human beings affected by the disease. More than 80% of persons with epilepsy live in low and middle income countries and most of them in tropical areas.¹ Globally seizures are the most common in children.² In contrast to

the pediatric age seizures, adult onset seizures (AOS) occur in approximately 25% of patients with epilepsy will have their first seizure after the age of 18 years. The main incidence and prevalence of adult onset epilepsy (AOS) is in the age group of 25-29 and older than 60 years.^{3,4} In the United States the annual incidence of seizure is approaching 100 seizures per 100,000 in people aged ≥ 60 year.⁵ However, the true incidence of seizures might be

underestimated considering the fact that there are patients with subclinical or non-convulsive seizures. A number of factors including cerebrovascular diseases (CVD), intracerebral hemorrhage (ICH), hypertensive encephalopathy (HE), central nervous system (CNS) tuberculosis, prion diseases, cerebrovascular accidents, head trauma, brain tumors, drugs, infections and different metabolic factors have been associated with AOS.⁶ The individuals with AOS need a special attention with regard to etiology. Brain tumors are one of several causes that may be suspected.^{7,8} One of its most important causes is brain tumors, which has an incidence of epilepsy reaching approximately 30%.^{7,9} Patients with slowly growing chronic lesions are more likely to have seizure disorder.¹⁰ Another important cause of AOS is CVD, seizures related to intracerebral hemorrhage and ischemic stroke. However, the geographical variations determine the common causes in a particular region and hence etiology of AOS is variable from one nation to another and even from one place to another in the same nation.¹¹

India in general and Kashmir in particular lack any well designed and conclusive studies regarding the etiology of neurological disorders. Although, a number of hospital based studies are available but results are mixed and inconclusive.^{12,13} Similar to the studies from developing countries, most of studies from India done so far have focused on epilepsy and clinical seizure types in children. Therefore, the study was aimed to find out the role of different clinical and etiological characteristics among Kashmiri subjects admitted with seizure disorder.

METHODS

This was a prospective study of a cohort of patients admitted to Sher-i- Kashmir Institute of Medical Sciences (SKIMS) Kashmir, India, a tertiary care hospital located at Kashmir, North India. The subjects with a diagnosis of seizure were recruited between August 2014 to July 2016 from outpatient department and indoor departments particularly from neurology unit of the institute. Approval was obtained from the hospital ethics committee and informed consent of the patients was taken. All patients with age 25 years or more who were admitted in Neurology ward of SKIMS, Srinagar formed the subjects of the study. The consent of all patients was taken and the study was done in accordance to guidelines of Institutional Ethics Committee SKIMS. In total, 144 patients with AOS who had developed seizure were enrolled in this prospective study.

All patients with first time seizure during a period of two years formed the subjects of the study. We have included more than 25 years of age because some idiopathic epileptic syndromes of childhood can present up to 25 years of age. Cases of seizures in patients below age of 25 years, patients with past history of seizures, insufficient clinical data for seizure diagnosis or subjects with pseudo-seizures were excluded from the study.

A prospective analysis of all participating subjects with new onset seizures was performed. Detailed history and clinical examination was done on all patients. Routine investigations like complete blood count and biochemistry were done on all patients. CSF analysis, electrocardiograph, X-ray- chest (PA), serum anti cysticercal antibodies, Mantoux, serum anti tubercular antibodies were also done where ever indicated. Magnetic resonance imaging (MRI) and electroencephalography (EEG) were done in all studied subjects. The diagnostic probability was based on clinical data -obtained from the patient charts and the results of the EEG and/or MRI scans. In all cases the seizure type is classified according to International League Against Epilepsy (ILAE) 1981 classification in to generalized and partial (simple, complex and partial with secondary generalization) based on description of seizures by patient and/patient attendants.¹⁴

The etiology of seizures was determined on the basis of medical history, neurologic examination, the EEG recording, and the MRI scan. We used the classification of risk factors by following the guidelines proposed by the Commission of Epidemiology and Prognosis of the International League Against Epilepsy.^{14,15} The categorization of seizures is based on the presence or absence of a presumed acute precipitating insult, which permits distinction into provoked (acute symptomatic seizures) and unprovoked seizures. Unprovoked seizures may belong to two categories: remote symptomatic and seizures or epilepsies of unknown cause (idiopathic and cryptogenic). Seizure frequency was classified according to definitions by ILAE Commission Report [14-18] into, single seizure, *status epilepticus* and seizure cluster (cluster of seizures that occur within a short period of time but do not meet the criteria for diagnosis of status).

Statistical analysis

All the statistical analysis were done using Stata software, version 12 (Stata Corp., College Station, TX, USA). The data collected are presented as percentage incidence or mean±standard deviation. The data association and difference in means were analyzed using Pearson's Chi-square. P-values<0.05 were considered as statistically significant.

RESULTS

In total 144 patients were recruited in the study. Age wise younger age group (25-34 years) and gender wise males showed higher incidence (Table 1). Among the participating subjects, GTCS were the most common type of seizures (48.8%) followed by complex partial seizure (CPS) (14.6%). Epilepsy seems to be a multi-etiological with almost similar distribution of etiological factors like idiopathic (12.5%), ICH (12.5%), hypertensive encephalopathy (HE) (10.4%), tumours (7.6%) etc. Gender wise males were more susceptible to ICH followed by idiopathic cause. While in female patients,

CVST, ICH and idiopathic cause was found in 7 patients each (Table 2). Although, there was no apparent cause which was dominant in either group, but CVST was mainly found in female patients (7/11). Encephalitis was a leading causal factor in 10 (6.9%) patients, followed by CNS tuberculosis in 8 (5.6%), Prion diseases (CJD) in 5 and NCC in 2 patients. CJD was diagnosed empirically on the basis of history followed by EEG and MRI findings. Age wise younger population is more susceptible to Encephalitis and CNS Tuberculosis, while Prion disease was more frequent in subjects with age of 55 or more. (Table 2).

On comparing various cerebrovascular diseases and seizures, ICH was responsible in 12.5% of studied subjects followed by CVST in 7.6% and Arterial infarct in 5.6%. In present study ICH was more common as compared to some other studies, the reason being that we mainly encounter haemorrhagic stroke than ischemic strokes. Age wise cerebrovascular causes were common in patients who had attained age of 65 years or more, followed by age group of 25-35 years (Table 2). However, gender wise males showed more predominance however, in CVST, females were more in number (7 out of 11 patients) (Table 2).

Table 1: General characteristics of subjects with adult onset seizures.

Variable	N (%)
Age (years)	
Mean (SD)	48.4 (\pm 1.33)
Gender	
Male	83 (57.6)
Female	61 (42.4)
Seizure type	
Generalized tonic-clonic seizure	70 (48.61)
Complex partial seizure	21 (14.58)
Secondary generalized seizures	19 (13.19)
Secondary partial seizure	15 (10.42)
Status epilepticus	12 (8.33)
Myoclonic	7 (4.96)
Etiological factor	
Cerebrovascular diseases	70 (48.6)
Infectious brain diseases	27 (18.7)
Tumours	18 (12.5)
Metabolic disorders	15 (10.4)
Drugs/chemicals	13 (9.1)
Degenerative brain diseases	01 (0.7)

SD=Standard deviation.

MRI findings presented abnormal findings in 59.7% of the patients and EEG findings were abnormal in 52.8% of the subjects (Table 2). On comparing EEG and MRI findings, it was observed that there is highest percentage of subjects with both these findings abnormal (59%) (Table 3).

DISCUSSION

Epilepsy is a symptom of numerous disorders, but in the majority of sufferers the cause remains unclear despite careful examination, investigation and history taking. Although, the age of onset of epilepsy can give a clue to the causation but, etiology of epilepsy after the age of 18 are variable in both types and frequencies. The vast variability depends on many factors which could be environmental, genetic and to some extent the level of living.

In the current study, we observed 25-34-year age group is at increased risk of seizures. Males are comparatively at higher risk, however CVST is majorly affecting women subjects. GTCS showed maximum representation as compared to other seizure types. Abnormal findings of MRI and EEG were the mainstay for identifying, classifying and localizing seizures among the study patients though, MRV was preferred in women subjects suffering from CVST.

In agreement with our study, a study from eastern India reported that 40% of cases fall in the age group of 20-40 years.¹⁹ Similarly, other studies reported higher percentage of cases in the age group of <40 years.^{20,21} Although studies from developed world also showed a bimodal distribution in the incidence of seizures. The first peak of seizures being more frequent in the first few years of life while a second and more pronounced peak among subjects with age more than 65 years.^{22,23} This variation in the current study from developed world could be due to major population falling within age-group of 25-40 years as compared to elderly population. The other factor could be that in elderly people, seizures are neglected as compared to young population.

Another possible factor is that idiopathic epilepsy and epilepsy due to cerebral infections like encephalitis and CNS tuberculosis were more common in that age group. Similarly, CVST was more common in age less than 40 years. The higher incidence of seizure in males in our study (male: female ratio=1.4:1) is comparable to other studies which reported a mild to moderate male preponderance.²⁴ In a study done in Bordeaux, France, age adjusted incidence of acute symptomatic seizures were considerably higher in men than in women.²⁵

The most common type of seizures like generalized seizure (53.5%) and SE type in our study is completely in agreement with observations of Larner et al.²⁵ Similarly, a study from India replicated the same results and noted GTCS as the major type among the studied population.²⁶ However, this finding is in contrary to other studies in past which shows partial seizure to be most common presentation.²⁴ This variation might be due to lack of reliable witnesses to the events or due to improper recall of events. Status epilepticus was also found in a few patients; majority of which was generalized status epilepticus.

Table 2: Gender wise distribution of different characteristics of patients with adult onset seizures.

Variable	Number (%)	Male (%)	Female (%)	Chi-square test (P-value)
Age group (years)				
≤30	20 (13.9)	09 (10.8)	11 (18.1)	1.981 (0.852)
31-45	35 (24.3)	21 (25.3)	14 (22.9)	
46-60	22 (15.3)	12 (14.5)	10 (16.4)	
61-75	21 (14.6)	13 (15.7)	08 (13.1)	
76-80	37 (25.7)	22 (26.5)	15 (24.6)	
>80	09 (6.2)	06 (7.2)	03 (4.9)	
Etiological type				
Cerebrovascular diseases	70 (48.6)	39 (47.0)	31 (50.8)	5.340 (0.376)
Infectious brain diseases	27 (18.7)	19 (22.9)	08 (13.1)	
Tumours	18 (12.5)	11 (13.2)	07 (11.5)	
Metabolic disorders	15 (10.4)	09 (10.8)	06 (9.8)	
Drugs/chemicals	13 (9.1)	05 (6.0)	08 (13.1)	
Degenerative brain diseases	01 (0.7)	0 (0.0)	01 (1.6)	
Cerebrovascular diseases				
Intracerebral hemorrhage	18 (48.6)	11 (61.1)	07 (38.9)	5.340 (0.376)
Cerebral venous Sinus thrombosis	11 (29.7)	04 (36.4)	07 (63.6)	
Arterial infract	08 (21.6)	05 (62.5)	03 (37.5)	
Seizure type				
Generalized tonic-clonic seizure	70 (48.61)	39 (55.7)	31 (44.3)	6.785 (0.237)
Complex partial seizure	21 (14.58)	12 (57.1)	09 (42.9)	
Secondary generalized seizures	19 (13.19)	11 (57.9)	08 (42.1)	
Secondary partial seizure	15 (10.42)	11 (73.3)	04 (26.7)	
Status epilepticus	12 (8.33)	04 (33.3)	08 (66.7)	
Myoclonic	7 (4.96)	06 (85.7)	01 (14.3)	
MRI findings				
Normal	58 (40.3)	32 (55.17)	26 (44.83)	0.242 (0.623)
Abnormal	86 (59.7)	51 (59.30)	35 (40.70)	
EEG findings				
Normal	68 (47.22)	36 (52.94)	32 (47.06)	1.164 (0.281)
Abnormal	76 (52.78)	47 (61.84)	29 (38.16)	

ICH=intracerebral hemorrhage; CVST=cerebral venous sinus thrombosis; HE=hypertensive encephalopathy; EEG=electroencephalography; MRI=Magnetic resonance imaging. *P-values were calculated using Pearson's chi-square test for categorical variables.

Table 3: Showing EEG and MRI findings among subjects with seizures and their correlation.

EEG Findings	MRI Normal	MRI Abnormal	Total	Correlation (P value)
EEG Normal	53 (36.8)	15 (10.4)	68 (47.2)	0.7264 (<0.001)
EEG Abnormal	05 (3.5)	71 (49.3)	76 (52.8)	
Total	58 (40.3)	86 (59.7)	144 (100.0)	

For pairwise relations the Bonferroni correlation method was applied; P-value <0.05 is statistically significant.

Similar to our observations, many studies have reported that the most common cause of seizures in the elderly is cerebrovascular disease (34.1-39.3%).²⁷⁻²⁹ A cerebrovascular basis for the AOS is supported by observation that it is more common in the presence of conventional risk factors for CVD such as hypertension, even without clinically evident stroke.^{16,17} The association between AOS and occult CVD is of crucial significance because such seizure could alert the physician to the like hood of elevated stroke risk, and

prompt consideration of treatment of vascular risk factors in patient where this opportunity may otherwise not present itself.²⁰ Our result regarding cases of seizure due to CVD was similar to the above results and it was 52% of cases, but in case of brain tumors it was registered in only 33% of them. Other reports about types of seizure in different types of causes of AOS were so variable. Lastly therapeutic responses of most patients with CVD, inflammatory and the group with unknown cases was very good, but the control of epilepsy in patients with brain tumors and post traumatic was poor and this result

is a well-known fact. Routine EEG was positive in 53% of cases and this result is in agreement with many previous reports.³⁰⁻³² MRI was conclusive in 60% of cases, this result indicate that MRI is the investigation of choice in AOS.³³ This high yield of MRI in this study is apparently due to high percent of CVD, brain tumors, inflammatory and post traumatic cases in comparison to other studies where degenerative, alcohol withdrawal and unknown cases are the most frequent causes and obviously the last causes are usually not detected by this investigation.

Post stroke seizure is harmful and requires treatment with anti-epileptic drugs. Post traumatic epilepsy is a well-known fact that has been investigated thoroughly but as a cause of AOS, there are only few reports regarding this issue and these reports mentioned that trauma could be a major cause of AOS in some countries and a minor cause in other places. In this study most individuals with newly diagnosed epilepsy responded well to treatment with AED. In fact, more than 90% of our patients were seizure free on medication. A previous study showed that seizures in elderly patients respond well to treatment and that AEDs effectively control seizures in approximately 80-86% of the elderly population.^{34,35} In accordance with our study, a study noted that about 75% needed single AED for treating seizures in the elderly and more than 20% required either two or three AEDs.³⁶

The rare occurrence of brain tumours in the current study is in agreement with previous reports.²⁴ In Rochester, acute symptomatic seizures associated with primary or secondary brain tumours occurred at all ages but were rare in persons younger than 45 years of age. Unlike most other acute symptomatic seizures, seizures associated with neoplasm were equally common in men and women. In present study tumours were responsible in all age groups, 6 patients were less than 40 years and were having primary brain tumours and 4 patients were elder than 60 years and had secondaries to brain. Brain tumors, either primary or secondary, account for 5-20% of cases of seizures occurring for the first time in adult.^{7,8,37} Seizure is the first symptom in 30% of brain tumors. In adult, a first seizure, particularly if focal should be evaluated by MRI for an occult brain tumor.

CONCLUSION

The study suggests that 25-34 years age group and males are at increased risk. Among the various seizure types, GTCS were presented by most of the participating subjects. Abnormal findings of MRI and EEG were the mainstay for identifying, classifying and localizing seizures among the study patients though, MRV was preferred in women subjects suffering from CVST.

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