

**CLINICAL AND ETIOLOGICAL PROFILE OF ELDERLY SEIZURES: A HOSPITAL
BASED PROSPECTIVE STUDY FROM NORTHERN STATE OF INDIA**Sheikh Nawaz Ahmad^{1,2}, Gulzar Ahmad Bhat³ and Dr. Mushtaq Ahmad Wani^{1*}¹Department of Neurology, Sheri-Kashmir Institute of Medical Sciences-Srinagar.²J&K Health Department, Srinagar Kashmir.³Department of Clinical Biochemistry, Sher-i-Kashmir Institute of Medical Sciences, Srinagar.***Corresponding Author: Dr. Mushtaq Ahmad Wani**

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ABSTRACT

Background: Elderly seizure is one of the most common neurological disorder among aged people all over the globe with multiple etiologies. The current study was aimed to study the etiologies and diagnosis of Elderly seizure in Kashmiri population and to compare its different clinical and etiological profile among different age group males and females. **Patients & Methods:** All patients who developed seizure after the age of 40 years were recruited in the current prospective study. In total 109 subjects with Elderly seizure were included in this study. The study was executed in the Neurology unit of Sher-i-Kashmir Institute of Medical Science, Srinagar- a tertiary care hospital in Kashmir from August 2014 to July 2016. **Results:** Among the 109 recruited subjects, the 71-80 years age group was more susceptible to seizures. Generalized tonic-clonic seizure with a percentage of 45.87% was the most common seizure type among the studied subjects. Among etiological factors, almost 50% of the study subjects presented with cerebrovascular diseases. Males were more susceptible to intracerebral hemorrhage and cerebral venous sinus thrombosis. MRI/CT and EEG findings were abnormal in maximum number of subjects (61.5% and 53.2% respectively) and both findings showed statistically a significant positive correlation in determining the seizure among study subjects ($r=0.93$; $p<0.001$). 78.82% subjects presented with abnormal Cerebrospinal fluid analysis values. **Conclusion:** Idiopathic factors are the main cause of Elderly Seizures with EEG and MRI being the mainstay for identifying, classifying and localizing seizures among the study patients.

KEYWORDS: Elderly, Seizure, etiology, clinical profile, Kashmir.**INTRODUCTION**

Seizure is one of the main public health issues among all age groups. The World Health Organization (WHO) has put forth this disease as one of the main priorities with millions of people affected by this disease globally. The main representation of the people with this disease is from very low and underdeveloped countries.^[1] The seizures though found in 25% in pediatric age group, are very common among elderly aged people as well.^[2,3,4] 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 due to recall bias, considering the fact that there are patients with subclinical or non-convulsive seizures. The disease seems to be multietiological with various 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 hypothesized to be associated with the disease.^[6,7,8]

Brain tumours alone are considered to be one of its most important causes, 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] However, the geographical variations determine the common causes in a particular region.^[11] and hence etiology of seizures is variable from one geographical region to another and even from one place to another in the same geographical region.

Neurological disorders in general and epilepsy in particular are not conclusively reported in India as well as in study population (Kashmir). A number of hospital based studies are available but results are mixed rather than conclusive.^[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 adults and children only. Therefore, the current study was aimed to find out the role of different clinical and etiological characteristics among Kashmiri elderly subjects admitted with seizure disorder.

MATERIAL AND 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 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 >40years or more who were admitted in Neurology ward of SKIMS, Srinagar. The consent of all patients was taken and the study was done in accordance to guidelines of Institutional Ethics Committee SKIMS. In total, 109 patients with elderly seizures 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. Cases of seizures in patients below age of 40yrs, 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. Well designed questionnaire was framed to collect the detailed history and clinical examination was done on all patients. Base line investigations (BLI) like complete blood count (CBC) and biochemistry as well as cerebro spinal fluid (CSF) analysis were done on all patients. X-ray – Chest, Computed Tomography (CT), 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 CT/MRI scans. In all cases the seizure type is classified according to International League Against Epilepsy (ILAE) 1981 Classification.^[14] into Generalized and Partial (simple, complex & partial with secondary generalization) based on description of seizures by patient and/ patient attendants. The etiology of seizures was determined as explained elsewhere (ref), briefly etiology depends on the basis of medical history, neurologic examination, the EEG recording, and the CT/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 & 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 13 (Stata Corp., College Station, TX, USA). The data collected are presented as percentage incidence or mean \pm 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 109 patients were recruited in the study. The main age of the study subjects was 64.5 (\pm 5.33years). 71– 80year age group subjects were comparatively higher than other groups. (Table 1). There was a slight higher representation of males than females. Among the participating subjects, GTCS were the most common type of seizures (46%) followed by secondary generalized seizures (16.5%). The disease seems to be a multi-etiological with almost half (48.62%) of the diseased subjects presented with cerebrovascular diseases. Similarly distribution of etiological factors like infectious brain diseases (18.35%) and metabolic disorders (14.68%) were some of the factors associated with seizures among elderly people (Table 1). MRI/CT findings presented abnormal findings in 61.47% of the patients and EEG findings were abnormal in 53.2% of the subjects. Maximum number of cases (78.52%) were with abnormal CSF analysis.

Gender wise females were slightly more susceptible to cerebrovascular diseases followed by idiopathic cause. While in male patients, infectious brain diseases, tumours, and metabolic disorders were slightly higher when compared to female seizure patient (Table 2). Although, there was no apparent cause which was dominant in either group, but CVST was mainly found in female patients. Encephalitis, CNS and tuberculosis was a leading causal factor in 20 (18.35%) patients (Table 2).

The subjects were diagnosed empirically on the basis of history followed by EEG and MRI/CT findings. 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 our 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 65years 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). The most common Seizure type was GTC's in ICH followed by secondary Generalized Seizures (SGS) (Table 2).

Abnormal MRI/CT and EEG were documented in 53.21% of the subjects. These two radio diagnostic

finding showed appositive correlation in determining elderly seizure (Table 3).

Table 1: General characteristics of subjects with Elderly Seizures.

| Variable | N(%age) |
|-------------------------------------|--------------------|
| Age (years) | |
| Mean (*SD) | 64.5 (\pm 5.33) |
| Age group (years) | |
| 41 – 50 | 19 (17.43) |
| 51 – 60 | 26 (23.85) |
| 61 – 70 | 26 (23.85) |
| 71 - 80 | 29 (26.60) |
| >80 | 09 (8.26) |
| Gender | |
| Male | 61 (55.96) |
| Female | 48 (44.04) |
| Seizure Type | |
| Generalized tonic-clonic seizure | 50 (45.87) |
| Complex partial seizure | 15 (13.76) |
| Secondary generalized seizures | 18 (16.51) |
| Secondary partial seizure | 13 (11.93) |
| Status epilepticus | 08 (07.34) |
| Myoclonic | 05 (4.59) |
| Etiological factor | |
| Cerebrovascular diseases | 53 (48.62) |
| Infectious brain diseases | 20 (18.35) |
| Tumours | 09 (8.26) |
| Metabolic disorders | 16 (14.68) |
| Drugs/chemicals | 08 (7.34) |
| Degenerative brain diseases | 03 (2.75) |
| MRI/CT Findings | |
| Normal | 42 (38.53) |
| Abnormal | 67 (61.47) |
| EEG Findings | |
| Normal | 51 (46.79) |
| Abnormal | 58 (53.21) |
| Cerebrospinal Fluid analysis | |
| Normal | 22 (20.18) |
| Abnormal | 87 (78.82) |

*SD= Standard deviation

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

| Variable | Total Number (%age) | Male (%age) | Female (%age) | Chi-square test (P value) |
|-----------------------------|---------------------|-------------|---------------|---------------------------|
| Age group (years) | | | | |
| 41 - 50 | 19 (17.43) | 09 (8.26) | 10 (9.17) | 0.451 (0.115) |
| 51 - 60 | 26 (23.85) | 15 (13.76) | 11 (10.09) | |
| 61 - 70 | 26 (23.85) | 13 (11.93) | 13 (11.93) | |
| 71 - 80 | 29 (26.60) | 18 (16.51) | 11 (10.09) | |
| >80 | 09 (8.26) | 05 (4.59) | 04 (3.67) | |
| Etiological type | | | | |
| Cerebrovascular diseases | 53 (48.62) | 25 (22.9) | 28 (25.69) | 0.097 (0.376) |
| Infectious brain diseases | 20 (18.35) | 12 (11.01) | 08 (7.33) | |
| Tumours | 09 (8.26) | 06 (5.5) | 03 (2.75) | |
| Metabolic disorders | 16 (14.68) | 09 (8.26) | 07 (6.42) | |
| Drugs/chemicals | 08 (7.34) | 03 (2.75) | 05 (4.59) | |
| Degenerative brain diseases | 03 (2.75) | 02 (1.83) | 01 (0.92) | |

| Seizure Type | | | | |
|----------------------------------|------------|------------|------------|---------------|
| Generalized tonic-clonic seizure | 50 (45.87) | 28 (25.69) | 22 (20.18) | 2.285 (0.170) |
| Complex partial seizure | 15 (13.76) | 09 (8.26) | 06 (5.5) | |
| Secondary generalized seizures | 18 (16.51) | 12 (11.01) | 08 (7.33) | |
| Secondary partial seizure | 13 (11.93) | 09 (8.26) | 04 (3.67) | |
| Status epilepticus | 08 (07.34) | 03 (2.75) | 05 (4.59) | |
| Myoclonic | 05 (4.59) | 04 (3.67) | 01 (0.92) | |

* P-values were calculated using Pearson's chi-square test for categorical variables.

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

| EEG Findings | MRI/CT Normal | MRI/CT Abnormal | Total | Correlation (P value) |
|--------------|-------------------|-------------------|--------------------|-----------------------|
| EEG Normal | 40 (36.70) | 11 (10.10) | 51 (46.79) | 0.935(<0.001) |
| EEG Abnormal | 04 (3.67) | 54 (49.54) | 58 (53.21) | |
| Total | 44 (40.37) | 65 (59.63) | 109 (100.0) | |

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

DISCUSSION

Seizure disorder remains as one of the disorders with unclear symptoms despite careful investigation, examination, and history taking. Although, the age of onset of epilepsy can give a clue to the causation but, etiology of elderly epilepsy are variable in both types and frequencies. The vast variability depends on many factors which could be environmental, genetic, both in combined form and to some extent the level of living.

In the current study we observed 71-80 year age group is at increased risk of seizures. GTCS showed maximum representation as compared to other seizure types. Abnormal findings of CT/MRI and EEG were the mainstay for identifying, classifying and localizing seizures among the study patients.

In agreement with our study, few studies reported increased frequency of seizures among subject with age more than 65 years,^[22,23] while a few studies including studies from India reported 40% of seizures fall in the age group of 20-40 years.^[19,20,21] This variation in the current study could be due to major population falling within age-group of 25-40 years as compared to elderly 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 almost equal prevalence of seizure in males in our study is comparable to other studies which reported a mild to moderate male preponderance.^[24,25]

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 recall bias i.e. 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.

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 elderly seizure 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 seizure and occult CVD is of crucial significance because such seizure could alert the physician to the likelihood 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 elderly seizures were so changeable. 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 abnormality was conclusive in 78% of cases, this result indicates that MRI is the investigation of choice in elderly seizures.^[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.

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 elderly seizures, there are only few reports regarding this issue and these reports mentioned that trauma could be a major cause of elderly seizures in some countries and a minor cause in other places. In current 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 our 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 71 -80 year age group are at increased risk among elderly subjects. Among the various seizure types, GTCS were presented by most of the participating subjects. Abnormal findings of MRI and EEG with abnormal cerebrospinal fluid analysis were the mainstay for identifying, classifying and localizing seizures among the study patients though, MRV could be a preferred tool in women subjects suffering from CVST.

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Ethical approval: Approved by IEC SKIMS.

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