ORIGINAL RESEARCH

Analysis of metabolic etiologies of seizure in elderly patients in tertiary care hospital in north-eastern up

Ajay Kumar[1], Sudheer Yadav[2], Niraj Kumar Chaudhary[3], Vivek Kumar Pandey[4]

[1]Associate Professor, [2,3]Assistant Professor, [4]Senior Resident, Department of Medicine, BRD Medical College, Gorakhpur, U P, India

Correspondence:
SudheerYadav
Assistant Professor, Department of Medicine, BRD Medical College, Gorakhpur, U P, India
Email:drsudheer05@gmail.com

ABSTRACT
Background: Seizures are widespread illnesses that have been recognised since antiquity and are commonly encountered in medical practice. The purpose of this study was to determine the most often seen etiologies of seizures in elderly patients.
Methods: The present cross-sectional study include105 cases of Seizure in patients aged 50 years and above of either gender who were admitted between January 2020 and December 2020 to the Medicine Department of the BRD Medical College in north-east UP. Each patient's data were obtained using a custom-designed proforma that included a complete history, clinical characteristics, past medical history, physical examination, liver function test, renal function test, serum electrolytes, CSF analysis, EEG,CT Head, MRI brain(if required).
Results: Seizures were more common in males (57.14%) when compared to females (42.86%), with a male to female ratio of 1.44:1. The most common cause of Seizure (26.67 %) was vascular (infarct) followed by Metabolic. Among metabolic causes, Hyponatremia (22.86%) was the most frequent followed by Hyperglycemia (20 %) and Hypoglycemia (5.71 %). The most prevalent type of Seizure (92.38 %) was generalised(GTCS), followed by focal (7.62 %).
Conclusions: Seizures in the elderly deserve special attention in terms of aetiology, as most are due to some underlying cause. Primary care physicians are crucial in identifying individuals with elderly onset seizures and arranging biochemical testing and imaging to provide a correct etiological diagnosis. However, additional large multicentric studies will be necessary to increase the study's generalizability.
Keywords; CSF-Cerebrospinal fluid,EEG-Electric Encephalography, GTCS-Generalised tonic clonic seizure, ICH-Intracranial Hemorrhage, SAH- Subarachnoid Hemorrhage

BACKGROUND
Seizures are one of the most prevalent neurological disorders, affecting around 10% of the population at some point in their lives [1]. A seizure is a transient occurrence in the brain caused by abnormally high or synchronised neuronal activity.Determining the type of Seizure occurred is critical for limiting the diagnostic approach to specific etiologies, selecting the proper therapy, and providing potentially critical prognostic information [2].
Cerebrovascular disease, neurocysticercosis, drug and alcohol withdrawal, traumatic brain injury, and CNS malignancies are the primary etiologies in adults [3]. In some situations, diagnosing and treating seizures will be straightforward; it may be a continuous difficulty in

others. To differentiate a seizure from other paroxysmal episodes, questions should focus on symptoms preceding, during, and following the episode. Routine blood tests are recommended to rule out more common metabolic causes of seizures, such as electrolyte, glucose, calcium, magnesium problems or hepatic or renal illness. Diagnosing a seizure in a patient is critical for determining the cause and managing the condition. Concerns about the cost of these inquiries are always present in resource-scarce underdeveloped countries [3].

Misdiagnosis carries the risk of legal complications, increases family concern, results in an extended hospital stay, and may result in life-threatening incidents. Modern radiological studies such as magnetic resonance imaging (MRI) and computed tomography (CT) scans are quite beneficial in determining the cause. The EEG can be used to make a diagnosis based on clinical observations. Almost all patients experiencing new-onset seizures should undergo a brain imaging test to ascertain whether an underlying structural problem is causing the seizures.

However, these imaging procedures are not widely available in developing nations such as India. Seizures may usually be recognised from other disorders by paying close attention to the patient's history and pertinent laboratory studies. There is currently no proven method of preventing epilepsy. Proper nutrition,sleep and abstinence from illegal drugs and alcohol may help people avoid seizures. This can help reduce the risk of a brain injury that results in seizures or epilepsy. A methodical strategy to confirm the diagnosis, establish the aetiology, and estimate the likelihood of recurrence will assist the doctor in providing the best therapy possible [5].

METHODS
The present cross-sectional study consists of 105 cases of Seizure admitted between January 2020- December 2020 in the Medicine Department of the BRD Medical College, Gorakhpur,UP. All patients were evaluated on a predesigned proforma after ethical approval and informed consent.

INCLUSION CRITERIA
1. Age ≥50 years
2. New onset seizure

EXCLUSION CRITERIA
1. Age <50 years
2. Previous history of seizure

The data of each patient was collected on a proforma specially designed for this study and included detailed history, clinical features, past medical history, physical examination, liver function test, renal function test, CSF analysis, CT brain, MRI brain, EEG, serum electrolytes and other routine investigations.

STATISTICAL ANALYSIS
The SPSS (Version 15.0) program was used for statistical analysis. Descriptive statistics were presented as mean, frequency and ratios. The Chi-square test was used to compare the variables between the groups. At a 95% Confidence Interval, significance was evaluated at a p-value <0.05.

RESULTS
The present study was carried out in the Department of Medicine,BRD Medical College, Gorakhpur,UP including a total of 105 patients. While observing, the age category with maximum frequency was 60-69 (37.14%), followed by 70-79 (32.38%), then after 50-59

(23.81%), and lastly, the category with minimum frequency was 80-89 (6.67%). The males (57.14%) were more frequent than the females (42.86%).

While cosidering the etiology, maximum frequency was Vascular(Infarct) (26.67%), followed by Hyponatremia (22.86%), Hyperglycemia (20.00%), Vascular (ICH) (16.19%), Hypoglycemia (5.71%) & Unidentified (4.76%), Hyperglycemia+ Hyponatremia(Mixed metabolic) (2.86%) & Vascular (SAH) (0.95%) [Table-1].

Table-1: Tabular presentation of patient's distribution according to Etiology

Etiology	Number Of Patients	Percentage (%)
Vascular(Infarct)	28	26.67%
Hyponatremia	24	22.86%
Hyperglycemia	21	20.00%
Vascular(ICH)	17	16.19%
Hypoglycemia	6	5.71%
Unidentified	5	4.76%
Hyperglycemia+Hyponatremia (Mixed Metabolic)	3	2.86%
Vascular (SAH)	1	0.95%
Grand Total	**105**	**100.00%**

Most affecting type of Seizure is GTCS with the 92.38% population, then the Focal affecting 7.62% population respectively.

As per association of aetiology of disease with gender was concerned, majority were male (57.14%) than female (42.86%, with the significant difference (p=0.0096*). In males, the maximum patients were of Vascular (Infarct) (17.14%), and the minimum wereof subarachnoid hemorrhage (0.95%). Similarly, in the females, the maximum were of Hyperglycemia (11.43%), and the minimum were of Unidentified (1.90%) &Hypoglycemia (1.90%), respectively [Table-2].

Table-2: Tabular presentation of patient's frequency and Association of Etiology with Gender.

Etiology	Number Of Patients	Percentage (%)	P value
Female	**45**	**42.86%**	
Hyperglycemia	12	11.43%	
Hyperglycemia+Hyponatremia (Mixed Metabolic)	3	2.86%	
Hypoglycemia	2	1.90%	χ=16.91 **p=0.0096***
Hyponatremia	11	10.48%	
Unidentified	2	1.90%	
Vascular(ICH)	5	4.76%	
Vascular(INFARCT)	10	9.52%	
Male	**60**	**57.14%**	
Hyperglycemia	9	8.57%	
Hypoglycemia	4	3.81%	
Hyponatremia	13	12.38%	
Unidentified	3	2.86%	
Vascular (SAH)	1	0.95%	
Vascular(ICH)	12	11.43%	
Vascular(INFARCT)	18	17.14%	
Grand Total	**105**	**100.00%**	

As per association of aetiology with the type of Seizure was concerned, Majority were of GTCS (92.38%) than Focal (7.62%), with a statistically significant difference (p=0.0054*). In the Focal type, the majority of the patients were of Hyperglycemia (4.76%), and the minimum were of Hyperglycemia+ Hyponatremia (0.95%). Similarly, in the GTCS type, majority were of Vascular(Infarct) (24.76%) and minimum were of Unidentified (1.90%) & SAH(0.95%) respectively [Table-3].

Table-3: Tabular presentation of patient's frequency and Association of Etiology with Type of Seizures.

Etiology	Number Of Patients	Percentage (%)	P value
Focal	**8**	**7.62%**	
Hyperglycemia	5	4.76%	
Hyperglycemia+Hyponatremia (Mixed Metabolic)	1	0.95%	
Vascular(INFARCT)	2	1.90%	χ=20.09 p=0.0054*
GTCS	**97**	**92.38%**	
Hyperglycemia	16	15.24%	
Hyperglycemia+Hyponatremia	2	1.90%	
Hypoglycemia	6	5.71%	
Hyponatremia	24	22.86%	
Unidentified	5	4.76%	
Vascular (SAH)	1	0.95%	
Vascular(ICH)	17	16.19%	
Vascular(INFARCT)	26	24.76%	
Grand Total	**105**	**100.00%**	

As per association of aetiology of the disease affecting the metabolic (51.43%) and non-metabolic (48.57%) type of patients for different age categories,we found that in metabolic patients, the aetiology & age categoryassociation with the maximum number of patients was Hyponatremiaie. 22.86% along with different aged categories 50-59 (3.81%), 60-69 (9.52%), 70-79 (8.57%) and for 80-89 (0.95%) respectively. However, the aetiology associated with the minimum number of patients were ofHyperglycemia+ Hyponatremia, ie.2.86%, along with the single age category of 60-69 (2.86%).Similarly, in non-metabolic patients the etiology& age category-association with maximum number of patients were VascularInfarct ie. 26.67% along with different agedcategories 50-59 (4.76%), 60-69 (7.62%), 70-79 (10.48%) and for 80-89 (3.81%) respectively. However, the aetiology-category association with the minimum number of patients were of Vascular (SAH), ie. 0.95%, along with the single age category of 50-59 (0.95%) [Table-4].

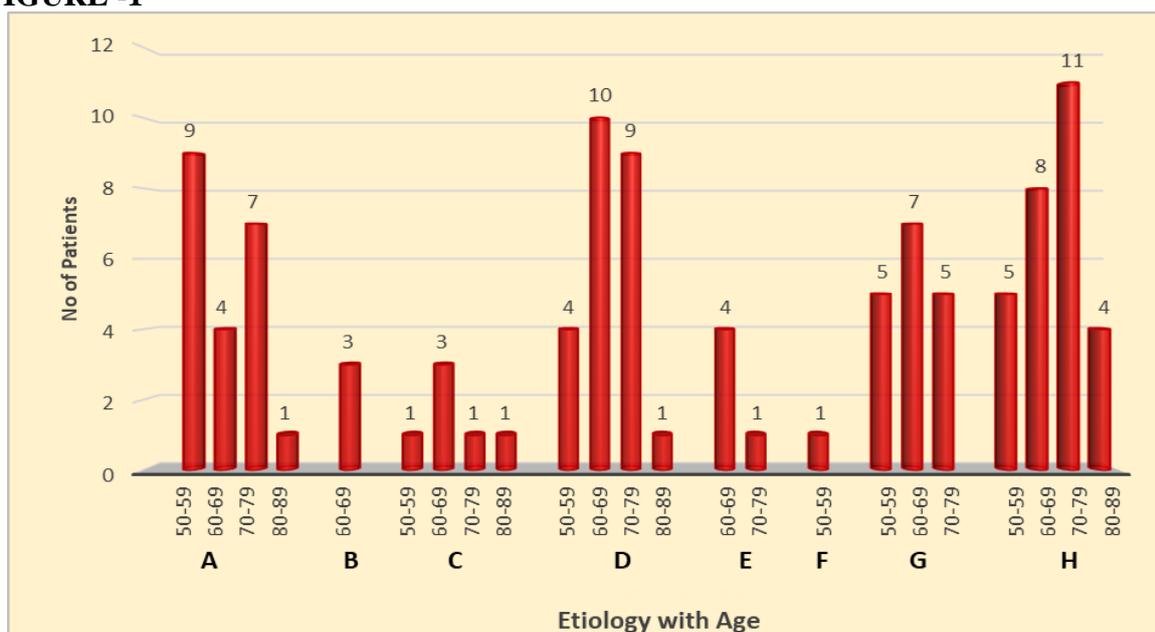**Table-4: Tabular presentation of Metabolic/Non-Metabolic patient's frequency and Association of Etiology with Gender.**

Metabolic/Non-Metabolic Etiology With Gender	Number Of Patients	Percentage (%)
Metabolic	**54**	**51.43%**
Hyperglycemia	**21**	**20.00%**
Female	12	11.43%
Male	9	8.57%
Hyperglycemia+Hyponatremia (Mixed Metabolic)	**3**	**2.86%**
Female	3	2.86%
Hypoglycemia	**6**	**5.71%**
Female	2	1.90%

Male	4	3.81%
Hyponatremia	**24**	**22.86%**
Female	11	10.48%
Male	13	12.38%
Nonmetabolic	**51**	**48.57%**
Unidentified	**5**	**4.76%**
Female	2	1.90%
Male	3	2.86%
Vascular (SAH)	**1**	**0.95%**
Male	1	0.95%
Vascular(ICH)	**17**	**16.19%**
Female	5	4.76%
Male	12	11.43%
Vascular(INFARCT)	**28**	**26.67%**
Female	10	9.52%
Male	18	17.14%
Grand Total	**105**	**100.00%**

As per association of type of Seizure affecting the number of patients for different age categories, we found that in the Focal category (7.62%) maximum were of 60-69 (2.86%), and minimum were of 80-89 (0.95%). Similarly, in the GTCS category (92.38%) maximum were of 60-69 (34.29%), and minimum were of 80-89 (5.71%), respectively. The difference among both the categories was statistically non-significant (p=0.8980).

As per association of type of Seizure affecting the number of patients for Male/Female categories, we found that in the Focal category (7.62%)maximum were of female (4.76%), and minimum were of male (2.86%). Similarly, in the GTCS category (92.38%), maximumwere of male (54.29%), and minimum were of female (38.10%), respectively. The difference among both the categories was statistically non-significant (p=0.2428).
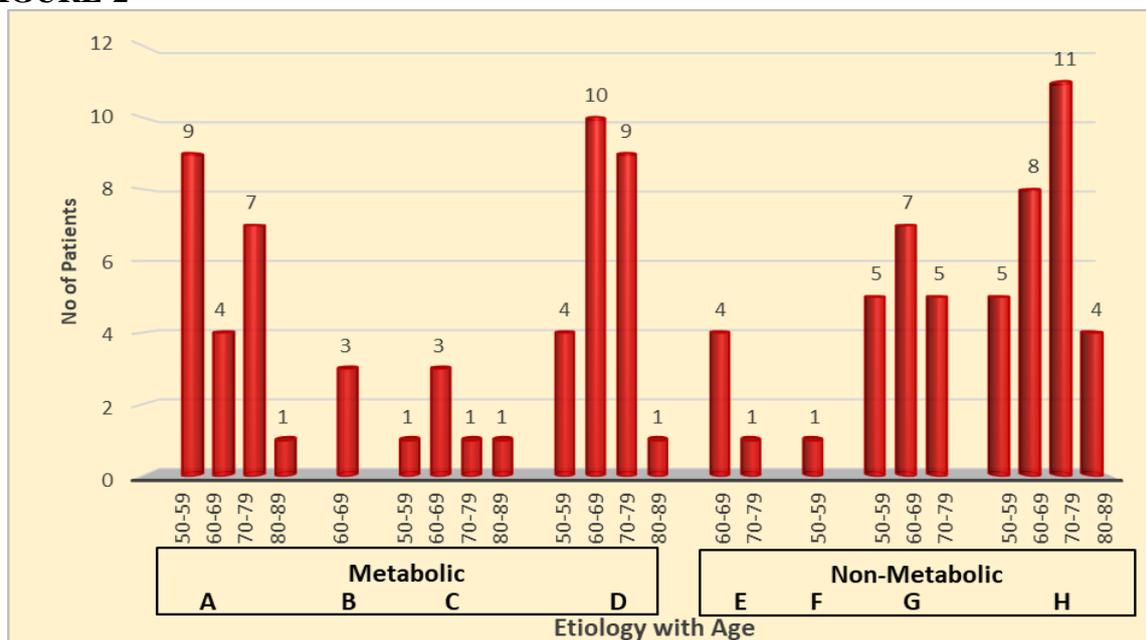
FIGURE -1

Graphical representation of Age-based Patient's Frequency and Association of Etiology.A- HYPERGLYCEMIA; B-HYPERGLYCEMIA+HYPONATREMIA (Mixed

Metabolic); C- HYPOGLYCEMIA; D- HYPONATREMIA E- UNIDENTIFIED; F-VASCULAR (SAH); G- VASCULAR(ICH); H- VASCULAR(INFARCT)

FIGURE-2

Graphical presentation of Metabolic/Non-Metabolic patient's frequency and Association of Etiology with Age.A- HYPERGLYCEMIA; B-HYPERGLYCEMIA+ HYPONATREMIA (Mixed Metabolic); C- HYPOGLYCEMIA; D- HYPONATREMIA E- UNIDENTIFIED; F- VASCULAR (SAH); G- VASCULAR(ICH); H-VASCULAR(INFARCT)

DISCUSSION

A cross sectional study was conducted among elderly patients ≥50 years, comprised of 105 elderly patients with the first episode of Seizure occurring at or above 50 years of age. The seizure type was established based on the International League against Epilepsy (ILAE) classification system of seizures. In this era, proper history, clinical examination, appropriate investigations and analysis of aetiology are required to reduce associated morbidity and mortality in elderly new-onset seizures and its association with different causes.

In the present study, we found that the age category with maximum frequency was 60-69 (37.14%), followed by 70-79 (32.38%), then after 50-59 (23.81%), and lastly, the category with minimum frequency was 80-89 (6.67%). A study conducted by Wallace et al. [5] showed that the seizure incidence increases with increase in age 65-80 years age group. In the present study, we found that among 105 patients with new-onset seizures, 57.14% were males while 42.86% were females. In our study, males were predominant, and this was similar to results reported by Muralidhar and Venugopal [6]Hirani and Shrivastav [7], and Sendiletal.[8].Steroid hormones might be the potential mechanism of gender differences in epilepsy [9]. However, we have not found the specific biological basis of sex disparity in seizure in the previous literature [9], which needs further studying.

While analyzing the etiological profile of seizure patients, we found that the maximum frequency were of Vascular(Infarct) (26.67%), followed by Hyponatremia (22.86%), then Hyperglycemia (20.00%), then after Vascular(ICH) (16.19%), further Hypoglycemia (5.71%), Unidentified (4.76%), Mixed Metabolic (Hyperglycemia+Hyponatremia) (2.86%), & Vascular (SAH) (0.95%) respectively. These results were comparable to study done by Kanitkar et al., [10] Reddy etal[11] and Pandey et al[12].Ours results were contrasted with

the studies conducted by Jiménez et al. [13] and Hirani and Shrivastava [14], which showed the most common underlying aetiology was idiopathic.

In the association of aetiology of the disease affecting the metabolic (51.43%) and non-metabolic (48.57%) type of patients for different age categories, we found that in metabolic patients, the aetiology & age category-association with the maximum number of patients was Hyponatremia, ie. 22.86% along with different aged categories 50-59 (3.81%), 60-69 (9.52%), 70-79 (8.57%) and for 80-89 (0.95%) respectively. Similarly, in non-metabolic maximum number of patients was Vascular(Infarct) ie. 26.67% along with different aged categories 50-59 (4.76%), 60-69 (7.62%), 70-79 (10.48%) and for 80-89 (3.81%) respectively. The difference was found statistically significant (<0.0001*).In the study by Kaur et al. [15] the most common metabolic causes were found to be alcohol withdrawal and Hyponatremia (25 % each).

While analyzing the type of Seizure, in this study, we found the most common type of Seizure was GTCS with 92.38% population, then FOCAL affecting 7.62% population . The present study was similar to Reddy et al. [11],Sudhir et al. [16] ,Narayan and Murthy [17]where GTCS was most common type of Seizure.

The association of etiology of disease with type of Seizure, maximum patients were of GTCS (92.38%). In GTCS category maximum frequency were of Vascular Infarct (24.76%) however,in Focal category, maximum were of Hyperglycemia (4.76%). While analyzing the association of type of Seizure for different age categories, in the GTCS category (92.38%), maximum were of 60-69 year (34.29%),while in Focal category (7.62%), maximum were of between 60-69 (2.86%). The difference among both the categories was statistically non-significant (p=0.8980).

 As per Type of Seizure with gender was concerned, in GTCS category (92.38%), maximum were males (54.29%) patients, while in Focal (7.62%), the maximum were of females (4.76%). The difference among both the categories was statistically non-significant (p=0.2428). However, the small sample size and the single centric study was the limitations of this study. A further large multicentric study will be required to increase the generalizability of the study.

CONCLUSION

Seizure being a medical emergency, its etiological determination is quite important in expediting the management and helping in the prevention of seizures. Seizures were more common in males than females. Most common etiology of Seizure was Vascularinfarct followed by Hyponatremia. In metabolic causes, Hyponatremia was most common cause, followed by Hyperglycemia&Hypoglycemia respectively. Most common seizure type was generalizedfollowed by focal. Elderly-onset seizures require particular care in terms of aetiology, since most of them are secondary to an underlying cause. Primary care physicians play a critical role in detecting patients with elderly onset seizures and can enable these patients to undergo biochemical testing and imaging in order to arrive at an accurate etiological diagnosis.

REFERENCES

1. Berg AT, Shinnar S. the risk of seizure recurrence following a first unprovoked seizure: a quantitative review. Neurology 1991; 41(7):965-972.
2. Annegers JF, Hauser WA, Lee JR, Rocca WA. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935-1984. Epilepsia 1995;36(4):327-333.
3. Loiseau J, Loiseau P, Guyot M, Duche B, Dartigues JF, Aublet B. Survey of seizure disorders in the French southwest. I. Incidence of epileptic syndromes. Epilepsia 1990;31(4):391-396.

4. De Boer HM, Mula M, Sander JW. (2008) The global burden and stigma of epilepsy. Epilepsy Behav 12:540-546.

5. Wallace H, Shorvon S, Tallis R. Age-specific incidence and prevalence rates of treated epilepsy in an unselected population of 2 052 922 and age-specific fertility rates of women with epilepsy. Lancet 1998;352:1790-3.

6. Muralidhar V, Venugopal K. New onset seizures: Etiology and co-relation of clinical features with computerized tomography and electroencephalography. J Sci Soc. 2015;42:82–7. [Google Scholar].

7. Hirani MM, Shrivastva S. Clinical profile of new onset seizures in adults. Indian J Appl Res. 2015;5:19–21. [Google Scholar].

8. Sendil G, Kumar AN, Kumar MV. Late onset shake-etiology at stake – A prospective study. Int J Sci Stud. 2014;2:20–4. [Google ScholarYang, PJ, Poul EB, Michael EC, Patncia KD. Computed tomography and childhood seizure disorders. Neurology 1979; 29: 108-88.

9. Reddy DS. The neuroendocrine basis of sex differences in epilepsy. PharmacolBiochemBehav. (2017) 152:97–104. doi: 10.1016/j.pbb.2016.07.002

10. Kanitkar SA, Gaikwad AN, Kalyan M, Aarwal R, Krunal K, Tamakuwala KK, et al. Study of seizure disorder in elderly: Etiology, types, EEG and image findings. Transworld Med J. 2013;1:24–5. [Google Scholar].

11. Reddy, G. R.Vishvanayak, V. Clinico-Etiological Profile of New Onset Seizures in Gaeriatric Patients at a Tertiary Care Hospital. Academia Journal of Medicine, 2019, 2(2): 195-199.

12. Ravi PrakashPandey, AnuragChaurasia, Sunil Ahuja, PanchalingppaBetageri, ManojIndurka. A Study of Clinical Profile of Seizure Disorder in Geriatric Population, Sch. J. App. Med. Sci., 2017;5:237-243.

13. Jiménez Jiménez FJ, Molina Arjona JA, Zancada F, Santos J, RoldánMontaud A, Fernández Ballesteros A. Etiology of late-onset epilepsy.A prospective study in an area of rural health care. Med Clin (Barc) 1990;94:521–4.

14. Hirani MM, Shrivastva S. Clinical profile of new onset seizures in adults. Indian J Appl Res. 2015;5:19–21.

15. SarabjotKaur, RavinderGarg, SimmiAggarwal, Sumit Pal Singh Chawla, and Ranabir Pal. Adultonset seizures: Clinical, etiological, and radiological profile. J Family Med Prim Care. 2018 Jan-Feb; 7(1): 191–197.

16. Sudhir, U., Kumar, A. T., Srinivasan, G., Kumar, R. V., &Punith, K. (2013). Aetiology of seizures in elderly. Journal of the Indian Medical Association, 111(10), 686–688, 691.

17. Narayanan T, Murthy JM. New onset acute symptomatic seizures in a neurological Intensive Care Unit. Neurol India. 2007;55:136–40.