New Onset Seizure in the Elderly: Classification, Etiology, and Impact on Quality of Life and Caregiver Burden

Naresh Maitan[2]   Neetu Choudhary[1]   Parampreet S. Kharbanda[1]   Sameer Vyas[3]   Ashish Aggarwal[4]
Prashant Panda[5]   Jitupam Baishya[1]

[1] Department of Neurology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[2] Department of Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[3] Department of Radiodiagnosis, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[4] Department of Neurosurgery, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[5] Department of Cardiology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence Jitupam Baishya, MD, DM, Department of Neurology, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh 160012, India (e-mail: jtpm1999asm@gmail.com).

Abstract

Objective   The incidence of seizures is highest in the elderly, and their management is challenging in view of atypical presentation and comorbidities. The aims of this analysis were to study the classification, etiology, and risk factors in new onset seizures in the elderly ($>$60 years) and their impact on the quality of life (QOL) and caregiver burden.

Materials and Methods   All the elderly presenting to neurology, neurosurgery and emergency medicine OPD with new onset seizures after the age of 60 years were included. QOL and caregiver burden were assessed at least 6 months after the first seizure. The QOL was assessed with the World Health Organization Quality of Life OLD (WHOQOL-OLD) and was compared with age-matched controls. Caregiver burden was assessed with the Zarit Burden Interview.

Result   Eighty patients fulfilling the inclusion criteria and 80 age-matched controls were recruited. There was no difference in age (68.30 ± 6.22 vs. 69.09 ± 6.07 years; $p = 0.39$) and gender (M:F = 50:30 vs. 48:32; $p = 0.74$) among the cases and controls. Forty-four (55%) patients had focal seizure. Hypertension was the commonest risk factor (61.3%), followed by ethanol intake (40%) and diabetes (38.8%). Cerebrovascular disease was the commonest etiology (37.5%), followed by infection (15%). Thirteen (16.2%) patients died during hospital stay and 20 (25%) died after discharge from the hospital. Cases scored significantly low on all domains of WHOQOL-OLD at 6 months of follow-up. In all, 54.1% caregivers reported mild to moderate burden.

Conclusion   Focal seizure is the commonest seizure type of new onset seizure in the elderly. Hypertension is the commonest risk factor and cerebrovascular disease is the commonest etiology. New onset seizures in the elderly have a significant impact on both QOL and caregiver burden.

Keywords
► late onset seizures
► new onset seizures in the elderly
► quality of life
► caregiver burden

Introduction

Epilepsy is the third most common neurological disorder in the elderly after stroke and dementia.[1] The incidence of new onset seizure is highest among the elderly and with an increasing aging population, prevalence of epilepsy in the elderly is also increasing.[2] Due to comorbidities, different presentations, and physiological changes with age, management of seizures in the elderly becomes challenging. Also, care of the elderly poses a challenge to family members and caregivers mentally, physically, and financially.

Studies addressing quality of life (QOL) compared with their age-matched healthy counterparts and caregiver burden are sparse, more so from this part of the world. In this study, we attempted to classify new onset seizures in the elderly as per the International League Against Epilepsy (ILAE) 2017 classification and study their etiology, risk factors, and impact on QOL and caregiver burden.

Materials and Methods

This prospective, longitudinal observational study was conducted in a tertiary care academic hospital of national importance in India. All the patients with new onset seizure after the age of 60 years who presented to emergency services and neurology outpatient department (OPD) from January 1 to December 31, 2021 were included. Patients with definite or doubtful history of seizure before the age of 60 years were excluded. Seizures were classified based on the narration of the accompanying person who has witnessed the seizure and/or any video recording of the event if available. Necessary metabolic and infective workup in blood and cerebrospinal fluid (CSF), imaging studies (computed tomography [CT] of the head and/or magnetic resonance imaging [MRI]), and electroencephalogram (EEG) were done as per the treating clinician's discretion to arrive at a diagnosis. Electrocardiogram (ECG), echocardiography, and detailed examination by a cardiologist were done when required to rule out seizure mimics. The patients were followed up telephonically for QOL and caregiver burden assessment at least after 6 months of recruitment.

Quality-of-Life Instrument

The World Health Organization Quality of Life OLD (WHO-QOL-OLD),[3] a specially designed tool to assess QOL in the elderly that encompasses six domains, was used in this study. QOL assessment was done at least 6 months after their first visit to the hospital. Equal number of age-matched participants was recruited as controls to compare the QOL. Controls were individuals older than 60 years, without history of seizure, coronary artery disease (CAD), chronic kidney disease (CKD) on dialysis, and without significant disability (modified Rankin scale [mRS] <3). Controls were chosen randomly from the internal medicine OPD who visited the OPD due to other problems and who consented for the study.

Caregiver Burden Assessment

The Zarit Burden Interview[4,5] was administered to the primary caregiver at least after 6 months of enrollment in the study. The study questionnaire was administered telephonically by one of the authors (N.M. and N.C.).

Statistical Analysis

All the data were entered in Microsoft Excel sheet. The mean and standard deviation (SD) were calculated for normally distributed variables. For categorical variables (type of seizure, risk factors, QOL), percentage and frequencies were calculated. Independent t-test was applied to compare normally distributed quantitative variables between the two study groups. For skewed data, the Mann–Whitney U test was applied. A two-tailed p-value of less than 0.05 was considered statistically significant with 95% confidence interval.

Data statement: Relevant data can be obtained from the corresponding author on reasonable request.

Results

Eighty patients with new onset seizures after the age of 60 years and equal number of controls were included in the study. There was no significant difference in the mean age between the two groups (68.3 vs. 69.09 years, $p = 0.39$). Among cases, 50 (62.5%) were males and 30 (37.5%) were females. There was no difference in gender distribution among the cases and controls ($p = 0.74$). Clinical characteristics of the cases are shown in ►**Table 1**. Forty-four cases (55%) presented with focal seizures and 57 (71.2%) had altered sensorium at the time of presentation. Stroke was the most common etiology (37.5%; most of which were ischemic—28.7%), followed by neuro-infection, tumor, and metabolic derangement (►**Table 2**). Among infectious causes, 1 had neurocysticercosis, 2 had tubercular meningo-encephalitis, 1 had pyogenic meningitis, 1 had rhinocerebral mucormycosis (had past history of COVID; COVID negative at the time of seizure). In the remaining seven patients, though infection was evident based on CSF findings or definite infectious foci like urosepsis and respiratory sepsis, no definite organism could be detected despite all necessary workup. Among various risk factors in the cases, hypertension was the commonest (61.3%), followed by alcohol (40%), diabetes (38.8%), and smoking (36.2%). Only 5% of cases had mRS score of less than 3 at the time of presentation. EEG was done in 49 patients, out of which 23 were abnormal. Focal slowing was the commonest EEG abnormality. None of them had electrographic seizure (►**Supplementary Table S1**, available in the online version only). Out of 80 cases, 33 died at 6 months of follow-up, out of which 13 died during the initial hospitalization itself. The etiologies of seizure in patients who died at 6 months of follow-up are shown in ►**Supplementary Table S2** (available in the online version only). At 6 months of follow-up, 36% cases had mRS score of less than 3 (►**Supplementary Fig. S1**, available in the online version only). Ten cases were lost to follow-up at 6 months. Out of 37 alive patients at follow-up, only 2 continued to have seizure at least once a month and the remaining 26 were

Table 1 Clinical characteristics of the cases

Characteristics	Number (%)
Time of initial seizure episode ($N = 80$)	
<1 wk	69 (86.2%)
1 wk–1 mo	6 (7.5%)
>1 mo	5 (6.2%)
Number of seizures till the time of enrolment ($N = 80$)	
Single episode	31 (38.8%)
2–5 episodes	24 (30.0%)
Multiple episodes	25 (31.2%)
Seizure duration ($N = 80$)	
<1 min	5 (6.2%)
1–2 min	57 (71.2%)
>2 min	18 (22.5%)
Type of seizures ($N = 80$)	
Generalized	34 (42.5%)
Focal	44 (55%)
Unclassified	2 (2.5%)
Sensorium at admission ($N = 80$)	
Normal	23 (28.8%)
Abnormal	57 (71.2%)
Neuroimaging ($N = 80$)	
Normal	30 (37.5%)
Abnormal	50 (62.5%)
EEG ($N = 49$)	
Normal	26 (53.1%)
Abnormal	23 (46.9%)
Outcome ($N = 80$)	
Alive at the time of follow-up	47 (58.75%)[a]
Died after discharge from hospital	20 (25%)
Died during hospital stay	13 (16.25%)

Abbreviation: EEG, electroencephalogram.
[a]Out of 47 patients, 10 were lost to follow-up.

Table 2 Etiology

Etiology	N (%)
Stroke	30 (37.5%)
Infection	12 (15.0%)
Tumor	11 (13.8%)
Metabolic	10 (12.5%)
Degenerative	8 (10.0%)
Unknown	7 (8.8%)
Trauma	2 (2.5%)

patients older than 60 years.[6,7] With advancement for medical science and consequent increase in longevity, epilepsy in the elderly has a significant impact on their QOL and burden on caregiver. In this report, we tried to assess the QOL of new onset seizure patients and caregiver burden at least 6 months after the incident event.

Forty-four (55%) patients had focal seizure and 34 (42,5%) had generalized seizures, which was in keeping with classical teaching that generalized seizures are less frequent in the elderly. Studies by Green et al[8] and Kar et al[9] also showed similar seizure classification as this cohort. However, another study by McAreavey et al[10] contradicts our findings, which could be due to a different study setting. More than 70% of the patients had abnormal sensorium at presentation, more than 80% presented within 7 days of the first seizure, and approximately 40% presented to the hospital with history of a single episode of seizure. Age and gender distribution of the cases in this study was similar to that of previous studies.[11]

Cerebrovascular disease was the commonest etiology (37.5%), followed by neuro-infection. Other studies[1,9,12] have also reported a similar trend in etiology, except neuro-infection, which was more common in this study, which is likely due to the higher prevalence of infectious diseases in this part of the world. Hypertension and diabetes are the commonest lifestyle comorbidities of the modern era, and hypertension was the commonest risk factor in our study as well. The risk factor profile of the cases was not different from that of published studies.[8,11]

At follow-up, 33 subjects died, out of which 9 had a stroke as the cause of seizure. Another clue suggests that comorbidities play a large role in mortality. Out of 33, twenty subjects die after discharge from the hospital which can be due to sepsis, aspiration, etc. Although patients who completed the follow-up had a significant improvement in their mRS scores, they had significantly lower score in all domains of WHOQOL-OLD compared with the age-matched controls. The difference was highest in the autonomy and social perception domains. Although only two patients continued to have seizure at follow-up and a good number of cases were off ASM, the reason behind the poor score in all domains of QOL, more so in the autonomy and social perception domains, could be social stigma and uncertainty of seizure recurrence people with epilepsy (PWE) suffer from. The recent ILAE task force report[11] on epilepsy on the elderly has also highlighted the poor QOL in all domains in the
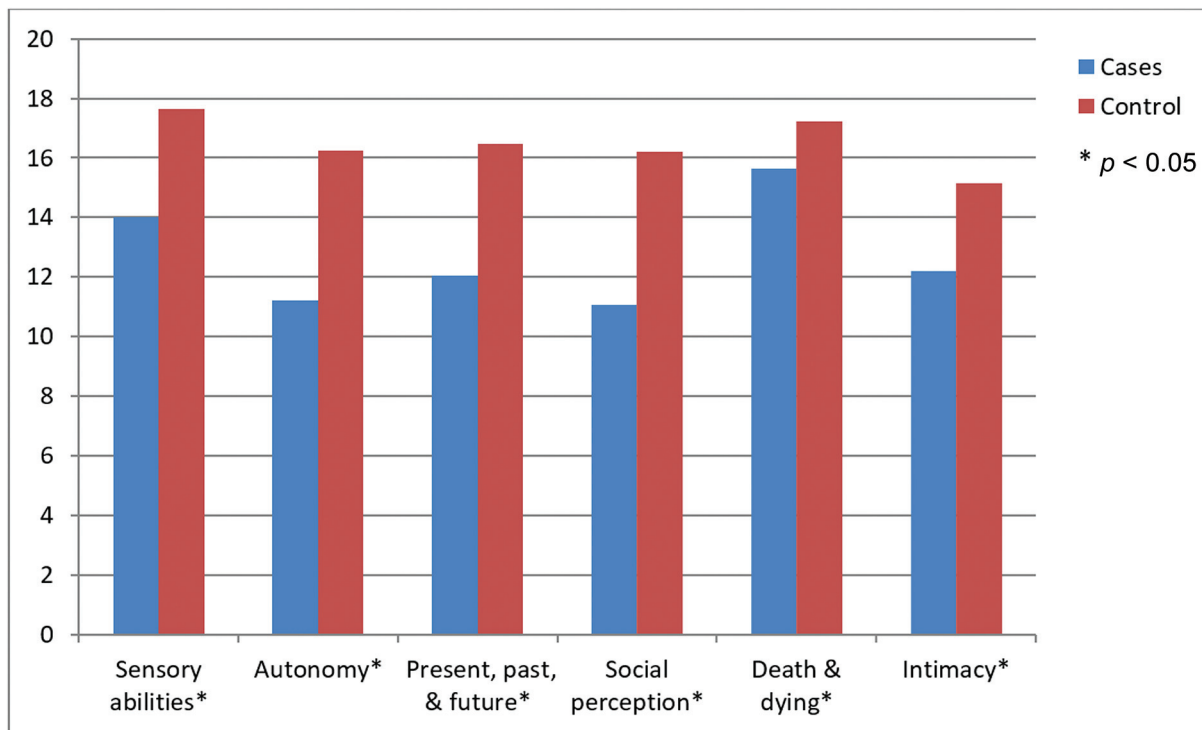
seizure free for a minimum of the last 3 months. Out of the 37 patients at follow-up, 12 were on regular antiseizure medications (ASMs), 10 were off ASM, and 15 failed to share the medication details.

The patients scored significantly low in all five domains of WHOQOL-Old at 6 months of follow-up compared with controls (►**Fig. 1**). The mean age of the primary caregiver was 48.08 ± 15.9 years. The spouse was the primary caregiver in 15 cases, children in 13, son/daughter-in-law in 7, and others in 2 cases. More than 50% caregivers reported mild to moderate burden at 6 months of follow-up (►**Fig. 2**).

Discussion

The incidence of new onset seizure is highest in the elderly population and more than 20% of new onset seizures occur in

Fig. 1 World Health Organization Quality of Life OLD (WHOQOL-OLD) score of cases and controls.
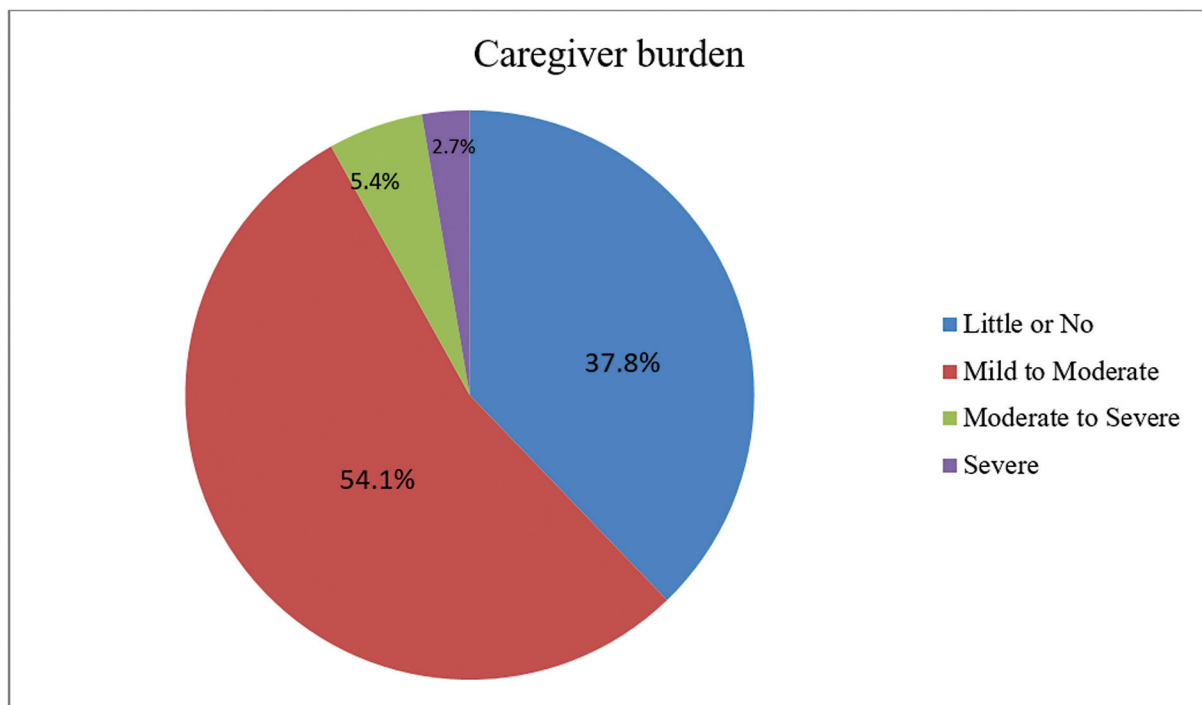

Fig. 2 Zarit burden score.

elderly with epilepsy. This study is different from previous studies. In previous studies QOL was compared with young people with epilepsy and most of them utilized epilepsy specific QOL inventories like quality of life in epilepsy -31 (QOLIE-31), whereas in this analysis, we had an age matches control group and the QOL questionnaire used was not epilepsy specific. More than half of the caregivers reported mild to moderate burden in providing optimal care to the patient, which is often neglected. The ILAE task force has advocated for an integrated approach involving family

members, community organizations, and physicians with an aim of providing adequate information and education regarding epilepsy and care, which may be helpful. Although some nations have started community programs for elderly patients, its actual impact on their QOL and improvement in health status is yet to be established.[13]

The study had few limitations. The most important limitation of the study is referral bias. The cohort may not be a true representation of the community, and as the study was conducted in a tertiary referral center due to referral bias, the mortality and etiology of the cohort need to be interpreted with caution. Although seizure was an important contributor, the effect of underlying conditions like stroke, sequel of neuro-infections, etc., toward QOL cannot be quantified. However, given the significant improvement in mRS scores, it is possible that seizures contributed the most to poor QOL. A similar study with a larger sample size would be more conclusive.

Conclusion

Stroke is the most common etiology of new onset seizure in the elderly and hypertension is the commonest risk factor. Despite significant improvement in functional status and seizure freedom, QOL remains poor. A comprehensive and integrated approach involving community organizations is necessary to address caregiver burden and for improving the QOL.

Highlights

- Cerebrovascular disease is the commonest etiology and hypertension is the commonest risk factor of new onset seizures in the elderly.
- Although there has significant improvement in the functional status and seizure control, they continue to have poor QOL.
- More than half of the caregivers have mild to moderate burden in providing optimal care.

Authors' Contribution
N.M. contributed to the design and conceptualization of the study, data collection and analysis, and drafting of the manuscript. N.C. contributed to acquisition of data and revision of the manuscript for intellectual content. P.S.K., S.V., A.A., and P.P. contributed to the design of the study and revision of the manuscript for intellectual content. J.B. contributed to the design and conceptualization of the study, data collection and analysis, and drafting and revision of the manuscript for intellectual content.

Note
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References

1 Lee SK. Epilepsy in the elderly: treatment and consideration of comorbid diseases. J Epilepsy Res 2019;9(01):27–35
2 Hauser WA, Hesdorffer DC. Epilepsy: Frequency, Causes and Consequences. New York, NY: Demos; 1990:275
3 World Health Organization. WHOQOL-OLD Manual. European Office, Copenhagen,. WHO:Geneva;2022
4 Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. Gerontologist 1980;20 (06):649–655
5 Bachner YG, O'Rourke N. Reliability generalization of responses by care providers to the Zarit Burden Interview. Aging Ment Health 2007;11(06):678–685
6 Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935-1984. Epilepsia 1993;34(03):453–468
7 Sander JW, Hart YM, Johnson AL, Shorvon SD. National General Practice Study of Epilepsy: newly diagnosed epileptic seizures in a general population. Lancet 1990;336(8726):1267–1271
8 Green SF, Loefflad N, Heaney DC, Rajakulendran S. New-onset seizures in older people: clinical features, course and outcomes. J Neurol Sci 2021;429:118065
9 Kar A, Hoysalakumar DP, Rathor PK. Clinical and etiological study of new-onset seizure in elderly people. Int J Med Rev Case Rep. 2022;6(16):65–69
10 McAreavey MJ, Ballinger BR, Fenton GW. Epileptic seizures in elderly patients with dementia. Epilepsia 1992;33(04):657–660
11 Subota A, Jetté N, Josephson CB, et al. Risk factors for dementia development, frailty, and mortality in older adults with epilepsy: a population-based analysis. Epilepsy Behav 2021;120:108006
12 Thomas SV, Pradeep KS, Rajmohan SJ. First ever seizures in the elderly: a seven-year follow-up study. Seizure 1997;6(02):107–110
13 Epilepsy Foundation. Epilepsy and aged care resources. 2022. Accessed June 17, 2021 at: https://epilepsyfoundation.org. au/managing-epilepsy/later-years-and-epilepsy/epilepsy-and-aged-care-resources/