Original Article
Journal of Epilepsy Research
pISSN 2233-6249 / eISSN 2233-6257

Clinical Profile and Predictors of In-Hospital Mortality in *De Novo* Convulsive Status Epilepticus in the Elderly Populace

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Background and Purpose: *De novo* status epilepticus (SE) had worse outcome in comparison to the patients with SE who had previous history of epilepsy. The aim of the present study was to identify clinical features of *de novo* convulsive status epilepticus (CSE) and the predictors of in-hospital mortality.

Methods: Seventy-seven elderly (≥60 years of age) hospitalized patients with *de novo* CSE were evaluated for clinical profile, aetiologies and predictors of in-hospital mortality.

Results: The average age of the participants in the study was 65.96±6.72 years. In *de novo* CSE, the most common aetiologies were acute symptomatic in 68.8% of cases, followed by remote symptomatic in 24.7%. In-hospital mortality in the *de novo* CSE in the elderly was 30 (38.9%) in our series. Stroke was the leading cause of death among them (acute stroke in 23 cases and old infarct in 1 case), followed by post-traumatic (n=4) and CNS infection (n=2). On multivariate analysis, it was found that variables significantly related to mortality in *de novo* CSE were low Glasgow coma scale (GCS) (adjusted odds ratio [AOR], 53.5; 95% confidence interval [CI], 5.17-555.14; p=0.001) and lack of response to first line treatment (AOR, 0.06; 95% CI, 0.01-0.50; p=0.01).

Conclusions: In-hospital mortality in *de novo* CSE patients was linked to a low GCS and a lack of response to first-line therapy. The most efficient strategy to prevent in-hospital mortality in the elderly is to treat *de novo* CSE promptly and aggressively in the setting of stroke. **(2022;12:48-52)**

Key words: *De novo* CSE, Elderly, Hospital mortality, Outcome

Received April 6, 2022
Revised July 25, 2022
Accepted August 14, 2022

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Introduction

Status epilepticus (SE) is a neurological emergency associated with a high rate of mortality and morbidity. There is a first peak in the incidence and prevalence rate of SE in infant and a second peak in the elderly subjects, which is often defined as 60 years.[1,2] Elderly constitutes the largest and fastest-growing segment among the patients with SE. In major research conducted in Richmond, Virginia; SE was their first seizure for more than 70% of the elderly patients in this cohort.[2] Various studies revealed 40-60% of SE patients have no previous history of epilepsy (*de novo* SE).[3-5] Stroke, central nervous system (CNS) infection, systemic infection, or metabolic disorders were the most common etiologies of *de novo* SE in elderly population, followed by head injury, alcohol or drug intoxication, hypoxia, brain tumour, CNS lupus, and idiopathic/cryptogenic.[6]

In comparison to the patients with SE who had previous history of epilepsy, *de novo* SE had poorer prognosis. Poorer prognosis in patients with *de novo* SE is attributed to their advanced age at onset and the presence of potentially fatal brain illnesses such as hypoxic-ischemic encephalopathy or severe stroke, as well as infection of the CNS.[6,7] There is a paucity of research on predictors of risk factors for poorer outcome in *de novo* SE, particularly in the elderly patients.[8] The current study was aimed to find the clinical characteristics of *de novo* convulsive status epilepticus (CSE) and the predictors of in-hospital mortality.

Methods

A hospital-based, cross-sectional study on *de novo* CSE in the elderly (≥60 years of age) patients was conducted from July 2017 to September 2019. The institutional ethical committee approval was taken. Patients with pseudo seizures, non-CSE, and history of epi-

Table 1. Distribution of patients according to their general characteristics (n=77)

Characteristic	Improved	Death	Total	*p*-value
Age				0.111
60-70 years	40 (85.1)	21 (79.2)	61 (79.2)	
>70 years	7 (14.9)	9 (20.8)	16 (20.8)	
Gender				0.111
Male	40 (85.1)	21 (70.0)	61 (79.2)	
Female	7 (14.9)	9 (30.0)	16 (20.8)	
Etiology				
CNS infections*	7 (77.8)	2 (22.2)	9 (11.7)	0.273
Acute vascular events†	12 (34.3)	23 (65.7)	35 (45.5)	0.000¶
Metabolic‡	9 (100.0)	0 (0.0)	9 (11.7)	0.164
Remote§	14 (73.7)	5 (26.3)	19 (24.7)	0.193
Cryptogenic	5 (10.6)	0 (0.0)	5 (6.5)	0.070
CSE type				0.052
Tonic-clonic	23 (48.9)	8 (26.7)	31 (40.3)	
Focal with B/L convulsive seizures	24 (51.1)	22 (73.3)	46 (59.7)	
Duration of CSE				0.147
<12 hours	45 (95.7)	26 (86.7)	71 (92.2)	
>12 hours	2 (4.3)	4 (13.3)	6 (7.8)	
Response to 1st line drug treatment				0.002‖
Responder	45 (95.7)	21 (70.0)	66 (85.7)	
Non-responder	2 (4.3)	9 (30.0)	11 (14.3)	
GCS				0.000¶
<8	23 (48.9)	30 (100.0)	53 (68.8)	
>8	24 (51.1)	0 (0.0)	24 (31.2)	
Co-morbidities				
Hypertension	10 (21.3)	11 (36.7)	21 (27.3)	0.139
Diabetes mellitus	7 (14.9)	5 (16.7)	12 (15.6)	0.834
Dyslipidaemia	0 (0.0)	1 (3.3)	1 (1.3)	0.208
CAD	0 (0.0)	2 (6.7)	2 (2.6)	0.073
None	1 (2.1)	0 (0.0)	1 (1.3)	0.421
Duration of hospital stay				0.198
1-4 days	21 (44.7)	9 (30.0)	30 (39.0)	
>4 days	26 (55.3)	21 (70.0)	47 (61.0)	
EMSE				0.001
>40	16 (42.1)	22 (57.9)	38 (49.4)	
≤40	31 (79.5)	8 (20.5)	39 (50.6)	

Values are presented as number (%).
CNS, central nervous system; CSE, convulsive status epilepticus; B/L, bilateral; GCS, Glasgow coma scale; CAD, coronary artery diseases; EMSE, epidemiology-based mortality score in status epilepticus.
*CNS infections (neurocysticercosis, meningoencephalitis, tuberculoma).
†Acute vascular events (infract, hemorrhage, cerebral venosinus).
‡Metabolic (hypoglycemia, hyperglycaemia, hyponatremia, slcohol).
§Remote (post trauma, old infract, old haemorrhage, tumors, small calcific lesion, dementia).
‖*p*-value <0.05 (significant).
¶*p*-value <0.001 (highly significant).

lepsy or epileptic seizures before the age of 60 were excluded from the study. During this period, 122 elderly individuals with CSE were admitted, out of which 77 patients with *de novo* CSE met the inclusion criteria. CSE is defined as continuous seizure or intermittent seizures from which there is incomplete recovery of consciousness lasting ≥5 minutes.[9]

Patients' age, gender, seizure semiology, duration and aetiology of CSE, neurological findings, treatment and length of hospital stay, and initial Glasgow coma scale (GCS) at the time of admission were all recorded. Routine investigations including blood gas analysis, blood glucose, electrolyte levels, liver and renal function tests were all performed. Patients were subjected to chest X-ray, ultrasound of the abdomen, echocardiogram, and cerebrospinal fluid examination if they were deemed necessary. Neuroimaging (computed tomography or magnetic resonance imaging) were done depending upon clinical indication. Within 12 hours of the termination of CSE, the 30-minute electroencephalogram (EEG) was recorded using the 10-20 electrode placement technique.

All CSE patients were given intravenous (IV) antiepileptic drugs, lorazepam and phenytoin as per the standard protocol (IV lorazepam [0.1 mg/kg], followed by the IV loading of phenytoin [20 mg/kg] as the first-line drugs). Second-line medications were given as an IV loading dose of valproate or levetiracetam in unresponsive cases and if CSE continued, patients were given general anaesthesia (coma induction). Patients also received mechanical ventilatory assistance if necessary as well as appropriate management of underlying disease.

Statistical analysis

Data were entered in Microsoft Excel sheet and analysed using the Statistical Package for Social Sciences software version 24.0 (SPSS, Armonk, NY, USA). The chi-square test and Fisher exact test were used to analyse categorical variables, while the unpaired *t*-test was used to assess quantitative ones. The odds ratio (OR) and 95% confidence interval (CI) were used to create the mortality risk factor using univariate and multivariate logistic regression. Covariates for multivariate logistic regression were gender, duration of CSE, GCS, and response to first line of treatment. The *p*-value of less than 0.05 was considered statistically significant.

Results

A total of seventy-seven elderly patients with *de novo* CSE were recruited. Out of which 61 cases (79.2%) were male and the mean age of the study population were 65.96±6.72 years (range, 60-90). The main seizure type was focal with bilateral convulsive seizure in 59.7% of cases. *De novo* CSE was well controlled with the first-line drugs in 85.7% of cases. In *de novo* CSE, the most common aetiologies were acute symptomatic in 68.8% of cases, followed by remote symptomatic in 24.7%, and unknown in 6.5% of cases. The clinical characteristics of the patients are shown in Table 1. In-hospital mortality in the CSE in the elderly was 30 (38.9%) in our series. Immediate cause of death in 18 cases (16.4%) was due to underlying diseases and in 12 cases (9.8%) the cause of death was CSE.

Table 2. Multiple binary logistic regression for the assessment of risk factors for mortality in patients with *de novo* (n=77)

Factor	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	*p*-value*
Gender			0.130
Male	Reference	Reference	
Female	0.53 (0.31-0.89)	0.37 (0.11-1.33)	
Duration of CSE			
<12 hours	Reference	Reference	
>12 hours	0.58 (0.36-0.94)	0.56 (0.09-3.60)	0.540
GCS			0.001‡
<8	1.25 (0.73-2.14)	53.5 (5.17-555.14)	
>8	Reference	Reference	
Response to 1st line drug treatment			
Responder	Reference	Reference	0.010†
Non-responder	0.47 (0.28-0.78)	0.06 (0.01-0.50)	

OR, odds ratio; CI, confidence interval; CSE, convulsive status epilepticus; GCS, Glasgow coma scale.
*For adjusted OR.
†*p*-value <0.05 (significant).
‡*p*-value <0.001 (highly significant).

Amongst them, stroke was the most common cause of mortality (acute stroke in 23 cases, old infarct 1 case), followed by post-traumatic (n=4) and CNS infection (n=2). On multivariate analysis, it was found that the factors related with poorer prognosis were; GCS less than 8 with an adjusted OR (AOR) of 53.5; 95% CI, 5.15-555.14 and lack of response to first line treatment AOR of 0.06; 95% CI, 0.01-0.50 (Table 2).

Discussion

Through our study, it was observed that in-hospital mortality in *de novo* CSE in the elderly was 38.9%. According to a retrospective investigation on factors that predict outcome in individuals with *de novo* SE, 36% died in hospital, 29% developed post-SE symptomatic epilepsy, and 8.43% had recurrent SE.[6] Another retrospective study on patients hospitalized for reasons unrelated to epilepsy or recent seizures found that an overall mortality rate is 61%, with just 20% recovering to baseline and leaving the hospital.[8]

The level of consciousness at the time of presentation is a significant prognosis factor for outcome following SE,[10] which is also a significant predictive element in our series. In our study, stroke was the most common cause of *de novo* CSE in the elderly, accounting for 59.7% of cases, and was also associated with higher mortality. Stroke is a common cause of SE in the elderly, especially in people who have never had a seizure before, according to epidemiological studies of SE. Long-term mortality in patients with a first episode of stroke-related SE was 57% in a population-based study from Germany, compared to 48% in patients with acute stroke without SE. Multivariate analysis showed that cases with SE of stroke origin had a significantly higher long-term fatality rate with a hazard ratio of 2.12, compared to acute stroke patients without seizure.[11]

We also found that mortality in *de novo* SE in the elderly was also linked to a lack of response to first-line therapy. Refractory SE is a dangerous and life-threatening condition that necessitates long-term, high-level intensive care and is frequently linked to poor functional outcomes.[12,13] Tsai et al.[6] reported that about one-fifth of *de novo* SE patients were resistant to first-line anticonvulsants, which was also related with a poor prognosis.

Limitations of study

Only CSE cases were included in this study due to the lack of supplementary testing such as continuous video EEG monitoring, and being a single-centre, hospital-based study, it does not represent the general population at large.

In our series, the predictors of in-hospital mortality in *de novo* CSE in the elderly were related to the extent of consciousness impairment, stroke, and lack of responsiveness to first-line treatment. The results of this study signify that treating *de novo* CSE in the elderly promptly and aggressively in the setting of stroke is the most effective way to avoid in-hospital mortality.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Acknowledgements

The study is in accordance with the ethical standards of the institution. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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