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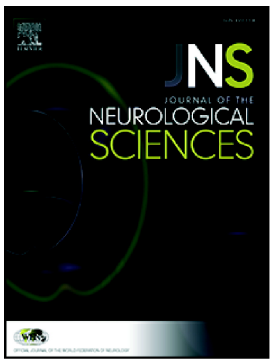

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Review Article

Prevalence and clinical correlates of non-convulsive status epilepticus in elderly patients with acute confusional state: A systematic literature review

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Abstract

Non-convulsive status epilepticus (NCSE) is a potentially treatable condition that poses considerable diagnostic challenges. NCSE is thought to be more common in the elderly than in the general population, however additional diagnostic challenges complicate its recognition in older patients, because of the wide differential diagnosis with common underlying causes of acute confusional state in this age group. We set out to review the existing evidence on the clinical correlates of NCSE in the elderly population. A systematic literature review was conducted according to the methodological standards outlined in the PRISMA statement to assess the clinical correlates of NCSE in patients aged 60 or older. Our literature search identified 11 relevant studies, which confirmed that the incidence of NCSE increases with age, in particular with regard to focal forms with impairment of consciousness. Female gender, history of epilepsy (or a recently witnessed seizure with motor features), and abnormal ocular movements appeared to correlate with the diagnosis of NCSE in the elderly, prompting prioritization of electroencephalography tests for diagnostic confirmation. Epidemiological data in the elderly vary widely because of the heterogeneity of definitions and diagnostic criteria applied across different studies. Based on our findings, it is recommended to keep a low threshold for requesting electroencephalography tests to confirm the diagnosis of NCSE in elderly patients with acute confusional state, even in the presence of a presumed symptomatic cause.

Keywords: Non-convulsive status epilepticus; elderly; acute confusional state; electroencephalography.

1. Introduction

Non-convulsive status epilepticus (NCSE) is a challenging, albeit potentially treatable, neurological condition with a number of mimics and chameleons complicating its diagnostic work-up [1]. The proposed clinical definitions of NCSE share two key features: non-convulsive clinical manifestations with alterations in the conscious state ranging from mild confusion to coma, and abnormal brain electrical activity (as recorded by electroencephalography, EEG) [2,3]. It has been suggested that response to treatment should be included as an additional diagnostic criterion, thus excluding forms of NCSE associated with coma and extensive structural damage, where abnormal EEG activity is likely to represent an epiphenomenon without relevant prognostic implications [4]. However this approach has been challenged based on the argument that refractory forms of NCSE should be included in its definition [5]. Further complications in the diagnostic process are the lack of evidence-based EEG criteria for NCSE and the uncertainties about the exact pathophysiological meaning of characteristic EEG patterns, such as generalized and lateralized periodic discharges.

Following an extensive review of abnormal epileptic discharges on EEG recordings [6], in 2013 the Salzburg consensus statement promoted the use of a unified EEG terminology and proposed working diagnostic criteria for NCSE [7-12]. The Salzburg criteria draw largely on the revised terminology for rhythmic and periodic EEG patterns in critically ill patients with coma/stupor of the American Clinical Neurophysiology Society [13,14]. Moreover, there is uncertainty about the timeframe after which non-convulsive seizures should be considered as manifestations of NCSE and treated as such [15,16]. In 2015, the International League Against Epilepsy proposed a new definition and classification system, emphasising the

importance of operational timeframes for early recognition and prompt treatment of status epilepticus to avoid permanent neuronal injury and medical refractoriness [17]. Based on available clinical and experimental data, the proposed timeframes for abnormally prolonged non-convulsive seizures were set at 10 minutes and 10-15 minutes for focal seizures with impaired awareness and generalized non-convulsive seizures (absence seizures), respectively.

The recognition of NCSE in the elderly can be particularly challenging, as a wide range of differential diagnoses need to be considered in this population [18]. Acute confusional state (ACS) in the elderly may be the main clinical manifestation of NCSE, although ACS is more often related to common underlying causes of delirium, including pain, infection, nutrition, constipation, hydration, medications, and environmental factors. NCSE is thought to have a higher prevalence in the elderly than in the general population [19], and is known to share clinical features with conditions that are frequently diagnosed in later life, such as delirium [20] and dementia [21]. Clinical boundaries in the elderly can be blurred, since the underlying causes of delirium may be responsible for NCSE [22-24] and NCSE may occur in the context of underlying neurodegenerative brain disorders [25].

The difficulties surrounding the diagnosis of NCSE in the elderly population highlight a need for the identification of clinical features (or clues from the medical history and clinical examination) that predict EEG findings suggestive of NCSE in elderly patients with ACS. It would be particularly important to evaluate the available evidence on the stratification of risk of patients having NCSE in clinical scenarios characterized by limited access to neurophysiological investigations, as a stepping stone ultimately leading to the development of guidance on EEG prioritization among emergent EEG requests. We therefore set out to

conduct a systematic literature review to assess the prevalence and clinical correlates of NCSE in the elderly.

2. Methods

We carried out a systematic review of the available literature according to the methodological standards outlined in the PRISMA statement [26]. The following inclusion criteria were adopted: 1) original studies on elderly individuals, defined for the purpose of this review as aged 60 or older; 2) studies on elderly patients with ACS or similar clinical conditions presenting with altered consciousness and/or behavior; 3) studies with focus on the prevalence and clinical correlates of NCSE in elderly patients with ACS; 4) studies published in English language. Exclusion criteria were as follows: 1) studies on patients diagnosed with coma; 2) studies on patients with focal status epilepticus without impairment of consciousness; 3) studies published as single case reports. Three scientific databases (MEDLINE, EMBASE, PsycInfo) were searched using the terms "NCSE", "elderly", "EEG", "diagnosis", "epidemiology", "aetiology", "confusion", as well as their derivations. In order to ensure that no relevant studies were missed out, an additional search for NCSE and EEG regardless of age limits was undertaken. Finally, the reference lists of the articles retrieved through the outlined search strategy were manually screened and the Google Scholar database was searched for grey literature meeting the above criteria.

3. Results

Our literature search identified 11 relevant studies: their characteristics and main findings are summarized in **Table 1**.

[PLEASE INSERT TABLE 1 HERE]

Labar et al. [27] found 10 elderly patients with NCSE out of 674 adult admissions over the course of one year: three with complex partial status epilepticus and seven with complex partial status epilepticus and secondary generalization. The authors reported data on the specific outcome of NCSE in the elderly from their sample: five patients were discharged with new neurological deficits, four had medical complications, three died due to sepsis, and two recovered. The authors concluded that NCSE in the elderly is associated with higher mortality, as outcomes correlate with underlying causes of NCSE: primary NCSE or NCSE developing in the context of epilepsy is more common in younger individuals and appears to be associated with better response to treatment and better outcome, whereas NCSE in the elderly is often symptomatic of underlying structural or metabolic causes and its prognosis is linked to the management of the underlying conditions.

Fernandez-Torre et al. [28] described four cases of NCSE, thought to be representative of the possible spectrum of NCSE in the elderly: absence status in a patient with pre-existing idiopathic generalized epilepsy; late-onset de novo absence status precipitated by benzodiazepine withdrawal; complex partial status in a patient with focal brain lesion (dyscognitive status according to current terminology); subtle generalized status representing the final phase of convulsive status epilepticus. The last category is accompanied by coma and often requires admission to ICU, hence falling out of the scope of the present review. The first three categories are clinically indistinguishable and careful history taking and evaluation of the EEG features play important roles in the differential diagnosis. Importantly, cases of absence status are characterized by a more favourable outcome. Intravenous benzodiazepines can be successful in resolving de novo absence status, which is usually related to sudden discontinuation of psychotropic drugs, and for which no prophylactic antiepileptic treatment is advocated. Absence status in the context of previous idiopathic generalized epilepsy is also characterized by a good prognosis and can be treated by

reinstating previously discontinued antiepileptic drugs or by adjusting/changing antiepileptic drugs already in use but no longer effective.

Sheth et al. [29] described the clinical characteristics of 22 elderly outpatients presenting with ACS and showing an ictal epileptic substrate. These authors reported diagnostic delays of up to 5 days, with earlier diagnosis associated to previous episodes of ictal confusion. The patients had impaired attention and concentration, problems with goal-directed actions, speech reduction, subtle ictal manifestations including subtle gaze preference and low-amplitude focal myoclonic jerks, typically affecting the face, eyelids or hands, as well as automatisms and, occasionally, contralateral apraxia.

Bottaro et al. [30] described 19 consecutive elderly patients (mean age 83 years) presenting with NCSE and compared them with 34 age-matched elderly patients with altered mental status, but no EEG evidence of NCSE. The authors found a more frequent history of epilepsy and tramadol use in the NCSE group, which was also characterized by longer hospital stays and worse outcomes, but failed to identify any statistical differences in other clinical variables (including cognitive impairment), neuroimaging findings, laboratory abnormalities or use of antibiotics. According to the authors, the diagnosis of NCSE could have been missed without the EEG data and the association between NCSE and poorer outcomes could have been related to the presence of underlying pathologies.

Korn-Lubetzki et al. [31] reported that two out of seven patients diagnosed with NCSE in a large cohort of elderly with ACS had seizures with motor manifestations prior to the onset of confusion. The authors of thus report highlighted that most of the patients with NCSE had also presented with anorexia.

Veran et al. [32] studied a population of 44 patients aged over 60 years with confusion of unexplained origin and reported that acute onset of symptoms, female gender, and lack of clinical response to simple commands were significantly more frequent in the seven patients found to be in NCSE. Differences in prevalence rates of other clinical features commonly

encountered in patients with NCSE (such as myoclonia, eyelid myoclonia, tachycardia, or agitation) did not reach statistical significance.

Shavit et al. [33] identified 14 patients out of 15,359 elderly patients admitted to acute general geriatric wards during a period of 7 years, with unexplained changes in mental, cognitive or behavioral status or confusion causing hospitalization or occurring during hospitalization. Patients had multiple co-morbidities, but history of epilepsy was relatively overrepresented. In this study, improvement in cognition following anticonvulsant therapy was a mandatory requirement for the diagnosis of NCSE. This approach could have led to the exclusion of refractory forms of NCSE, as well as to an over-representation of cases of ictal delirium, in which the ictal activity is predominantly, if not exclusively, responsible for the altered cognition.

Naeije et al. [34] found that a history of cognitive impairment, use of antibiotics, and hypernatremia were significantly associated with the presence of possible NCSE in 11 patients aged 65 years or above. However these authors concluded that no clinical parameters could be reliably used to differentiate between elderly people in whom delirium has an ictal basis and those with delirium caused by other factors. Based on their use of continuous EEG monitoring, the authors also noted that elderly patients with delirium and EEG consistent with NCSE had higher mortality rates and longer hospital stays.

Ali et al. [35] found that hyponatraemia was the leading cause of seizure activity responsible for ACS in 60 patients over the age of 65, in line with the findings of Bottaro et al. [30]. Symptomatic causes, such as cerebrovascular disease, were confirmed to be frequent. Patients with normal neuroimaging findings and metabolic profiles improved with antiepileptic treatment, suggesting the existence of a subgroup of patients in whom pure ictal activity may be entirely responsible for the confusional state.

Delgado et al. [36] described the clinical characteristics and outcomes of 31 patients with NCSE with a mean age of 79 years (age range 65-90 years). These authors found that a

diagnosis of NCSE was hypothesized before EEG confirmation in only 23% of cases, because the clinical presentation was mostly attributed to underlying dementia or encephalopathy due to medical causes. NCSE was deemed to play a causative role in the alterations of behavior and/or consciousness in patients previously presenting with isolated seizures with motor features. The authors concluded that witnessed seizures with motor manifestations, as well as the presence of lesions with cortical involvement, should alert to the possibility of subsequent NCSE.

More recently, Canas et al. [37] identified and characterized a cohort of 40 elderly patients (aged above 60 years; mean age 77 years) fulfilling EEG diagnostic criteria for NCSE admitted at their institution in a 3-year period. After an extensive review of video-EEG data, the authors found that dyscognitive NCSE associated with epileptiform discharges above 2.5 Hz was the most frequent electroclinical phenotype. However the clinical presentations were quite heterogeneous, ranging from patients with afoa continua to patients in coma, associated with frequent epileptiform discharges or rhythmic slow activities. Acute symptomatic (45%) and multifactorial (28%) etiologies were the most common causes of NCSE, and were associated with the worst prognosis. Despite a trend to use newer antiepileptic drugs in the early steps of NCSE treatment, mortality was high (23%) and was predicted by higher status epilepticus severity scores. The authors concluded that in the elderly NCSE has heterogeneous electroclinical phenotypes and etiologies, and advocated more aggressive treatment approaches to reduce mortality in patients with high status epilepticus severity scores.

4. Discussion

The heterogeneity of definitions and diagnostic criteria applied across different studies is reflected in variable figures of incidence and prevalence of NCSE, including in the elderly population [38,39]. The incidence of all types of status epilepticus is estimated to be 10-41 per 100,000, with higher rates (55-86 per 100,000) in people over the age of 60 years [40,41]. NCSE accounts for a substantial proportion (5% to 49%) of all cases of status epilepticus [41]. Shorvon [42] estimated an incidence of NCSE of 10-20 cases per 100,000. Over time, different estimates of the proportion of patients with NCSE have been proposed, with suggestions that NCSE may account for one quarter of all cases of SE [43-45]. In patients aged 60 or older seen in the emergency department with confusion or altered mental status, approximately 16% have been found to have NCSE [38]. The incidence has been estimated to increase with age: 15.5/100,000 in the 60-69 age group, 21.5/100,000 in the 70-79 age group, and 25.9/100,000 in patients aged 80 and older [38]. Mortality appears to be age-dependent (lowest in the younger elderly and highest in the oldest) and those over 80 years of age have a mortality of approximately 50% [38].

Based on the critical appraisal of clinical research [41,44,46-48], it has been suggested that the results of epidemiological studies may underestimate the prevalence of NCSE for multiple reasons [45]. Epidemiological studies tend to be hospital-based, and fail to account for cases of NCSE that do not reach a specialist setting: referral bias could lead to the exclusion of a potentially large proportion of patients with mild and/or self-limiting conditions who might not seek medical attention or might be treated in the community. Although the EEG is an essential criterion for the diagnosis, access to neurophysiology investigations is often unavailable and it is therefore possible that cases of NCSE developed

out of hours may be missed. Moreover, patients whose status duration is not recorded or whose seizures are terminated within 30 minutes tend to be excluded from epidemiological studies, as well as cases of SE evolving in NCSE and cases of NCSE with coma. Overall, NCSE is not a homogeneous clinical entity, but can have different presentations. The report of the ILAE Task force on Classification of Status Epilepticus distinguishes four axes: semiology, aetiology, EEG correlates, and age [17]. According to Axis 1, NCSE can be further subcategorized into NCSE with coma and without, and the latter is further distinguished into generalized and focal forms. The generalized forms encompass typical and atypical absences, whereas the focal forms are further categorized according to the assessment of consciousness, which has been shown to be particularly challenging in focal seizures [49-52].

Despite these limitations, it appears undisputable that the incidence of status epilepticus increases with age and with it the proportion of cases of NCSE, in particular of focal forms with impairment of consciousness. This is thought to reflect the experimental and clinical observation that focal epileptic discharges tend to spread less often with old age [1,53,54]. The reviewed literature confirms the high prevalence of dyscognitive status among cases of NCSE in the elderly, whereas *de novo* absence status epilepticus is reported in about 10% of elderly patients with protracted ictal confusion [29]. Absence status may occur *de novo* in later life as a situation-related event, attributable to toxic or metabolic precipitating factors with no previous history of epilepsy, and there may be psychiatric co-morbidities in patients taking multiple psychotropic drugs. For instance, *de novo* absence status has been described as an uncommon complication of benzodiazepine withdrawal. In this context, absence status represents an acute symptomatic phenomenon and is amenable to treatment without long-term use of antiepileptic drugs if the triggering factors can be controlled or corrected. For

example, Thomas et al. [55] reported 11 cases of late onset absence status, showing that in eight of them the onset coincided with acute benzodiazepine withdrawal: in these patients, there was no recurrence without chronic antiepileptic treatment. Moreover, absence status in the elderly may represent a late complication of idiopathic generalized epilepsy [56]: this second peak of idiopathic generalized epilepsy with absence seizures, at least in women, may be the result of hormonal influences in the context of a genetic background [57].

Although it has been established that NCSE has a relatively higher frequency in elderly patients and may account for a sizeable quota of patients with ACS, the available evidence fails to capture the exact scale of the problem. Specifically, the reviewed evidence on the clinical characteristics predicting EEG patterns compatible with NCSE in confused elderly patients is scarce and contradictory. There are grey areas represented by elderly persons with confusion, encephalopathy, and electrical discharges that do not fit the criteria for NCSE: in these individuals, abnormal electrical abnormality may not be ictal, but reflect underlying structural or metabolic changes, although the demarcation of these states is still controversial. Finally, no unequivocal clinical features allow for a stratification of risk in order to prioritize urgent EEG in elderly persons with ACS that may be attributable to NCSE, although some features seem to be more suggestive, such as female gender, history of seizure disorders, and abnormal ocular movements (**Figure 1**). Therefore, the clinical features that have been reported to be more frequently associated with NCSE can reinforce a clinical suspicion and all cases of unexplained and rapid altered mental status remain equally worth investigating for NCSE, with a low threshold for requesting an EEG.

[PLEASE INSERT FIGURE 1 HERE]

The literature on clinical features predictive of NCSE in patients with ACS and altered mental status regardless of age is somewhat more copious and consistent with the findings of the present review. Despite the small numbers, the observation that female gender may be associated with NCSE is quite interesting and replicates the results of a previous case report and review of the literature focusing on late-life absence status [58]. The findings of this review showed a significant female dominance in 15 out of 16 studies on absence status, suggesting that social, genetic, and/or pharmacological factors may be responsible for this gender predisposition. Longer longevity, a tendency to seek medical attention more frequently that the opposite sex, and non-specified biological factors have been proposed to be at the origin of the gender difference, whereas the influence of hormonal factors has been deemed to be non-contributory. It has to be noted, however, that the reviewed case reports and studies focused on younger patients (below 60 years of age) and therefore these findings might not be fully relevant to the more restricted age group of elderly persons with absence status.

A history of seizure disorder may alert to the possibility of NCSE in the elderly with ACS, but does not exhaust the list of possible clinical indicators of an underlying ictal delirium. An early report by Privitera et al. [59] suggested that prior generalized tonic-clonic seizures, long-standing psychiatric disorders treated with psychotropic drugs, and underlying medical problems such as vascular disease and metabolic disorders might act as precipitating factors for NCSE. Although other groups argued that no clinical features are helpful in identifying patients at risk of NCSE [60], the overall literature on NCSE across the lifespan indicates that

certain clinical features are more likely to be found in patients with NCSE and should prompt the referral for an urgent EEG [61]: severely impaired mental states and ocular movement abnormalities [62], pre-existing epilepsy and vascular pathology [63], seizures in the acute setting, ocular movements (nystagmus and/or gaze deviation), and ongoing central nervous system infection [64], previous history of chronic epilepsy [65], younger age and previous history of seizures [66].

5. Conclusions

The reviewed literature has a number of intrinsic limitations, that should be taken into account when interpreting its findings. The studies on NCSE in the elderly population are heterogeneous in their plan and design, and include patients with acute changes in mental, cognitive, behavioral states or confusion which are labeled as ACS, a term that encompasses a range of sudden and at times subtle changes in cognition, behaviour, emotion, and consciousness. Moreover, clinicians working in acute settings do not always have access to baseline cognitive parameters of the patients they are dealing with and NCSE can complicate neurodegenerative diseases that have already eroded cognitive domains. Clinical assessments are often dependent on the information provided by care-givers, which may be inaccurate or may underestimate certain aspects of the medical history, and cannot be replaced by a more objective quantitative evaluation. Overall, it is difficult to make comparisons among the reviewed studies because of the heterogeneity of definitions of ACS. In only one of the studies [32], the diagnosis of patients presenting with confusion of unknown origin was confirmed with a semi-quantitative tool, the Confusion Assessment Method. The high heterogeneity of the reviewed studies could also be responsible for the divergent conclusions about the impact of NCSE on patients' prognosis: it has not been possible to rule out that, in some cases, NCSE might simply represent a severity marker of underlying conditions determining the clinical outcome.

Despite these limitations, the results of our systematic literature review confirm that the incidence of NCSE increases with age, in particular with regard to focal forms with impairment of consciousness. Female gender, history of epilepsy (or a recently witnessed seizure with motor features), and abnormal ocular movements appear to correlate with the

diagnosis of NCSE in the elderly. Clinicians should be aware that this condition can complicate a range of neurological disorders, encompassing ischaemic damage, encephalopathy, and septic processes. Based on these findings, it is recommended to keep a low threshold for requesting further investigations to confirm the diagnosis of NCSE in elderly patients presenting with ACS, even in the presence of a presumed symptomatic cause. Future research should be conducted on the neurophysiological strategies that can improve the diagnostic process of NCSE in the elderly, including extended EEG [67] and, in selected patients, video-ambulatory EEG [68]. This latter has been shown to be particularly useful in complex clinical scenarios, such as the diagnosis of epileptic and non-epileptic seizures [69,70]. Further studies are also needed to better characterize the clinical presentations of patient subgroups presenting with ACS and to identify those at higher risk of developing NCSE.

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TABLE

Table 1. Summary of clinical studies on non-convulsive status epilepticus in elderly patients with acute confusional state.

Study	Design	Age (range / mean±sd / lower limit)	Total number of patients	Number of patients with NCSE	Clinical variables associated with NCSE	Clinical variables not associated with NCSE	Aetiology and other distinctive features
Labar et al. 1998 [27]	Prospective observational study	>65	674	10	N/A	N/A	Cerebrovascular disease as leading cause of NCSE (n=4), followed by metabolic derangement (n=2), brain neoplasia (n=1), head injury (n=1), electroconvulsive therapy (n=1), hyponatraemia (n=1), pre-existing epilepsy (n=1); poorer prognosis in the elderly, because of underlying causative processes and medical complications
Fernandez-Torre et al. 2004 [28]	Retrospective observational study	74-81	4	4	History of idiopathic generalised epilepsy, recurrent aphasia, recurrent generalized tonic-clonic seizures and subtle clonic twitching in the facial and cervical muscles	Automatisms and myoclonic jerks (not observed in one case)	Four subtypes of NCSE: 1. absence status in the context of idiopathic generalized epilepsy 2. de novo absence status related to acute discontinuation of long-term use of benzodiazepines 3. dyscognitive status 4. subtle status following recurrent generalized tonic-clonic seizures
Sheth et al. 2006 [29]	Prospective observational study on consecutive outpatients with acute ictal confusion	70±8.5	22	22	Ictal neglect and reduced mood, impaired attention and concentration, reduced speech, subtle gaze preference, low amplitude fragmentary myoclonic jerks (typically in face, eyelids or hands), hand automatism, contralateral apraxia, lack of persistence of motor activity	N/A	Failure to recognize ictal activity underlying confusion for up to 5 days; previous episodes of protracted ictal confusion in 15 patients
Bottaro et al. 2007 [30]	Retrospective case-control study comparing 19 consecutive elderly patients with NCSE and 34 elderly patients with altered mental status without electroencephalographic evidence of NCSE	>75	53	19	History of epilepsy, tramadol use	No statistically significant differences between patients with and without NCSE	Association between NCSE and longer hospitalization / unfavourable outcome; NCSE caused by acute medical disorders (n=14), epilepsy (n=2), cryptogenic (n=4)
Korn-Lubetzki et al. 2007 [31]	Prospective observational study on consecutive patients with acute unexplained change in mental, cognitive or behavioral status / confusion before or during hospitalization	73-90	307	7	Anorexia, seizure 2-5 days prior to onset of confusion	N/A	Renal failure as leading cause of NCSE (n=3), followed by epilepsy, dementia, hypothermia, sepsis and dementia (all n=1)

Veran et al. 2010 [32]	Prospective case-control study comparing patients with confusion of unknown origin with and without subsequent diagnosis of NCSE	>60	44	7	Acute onset (<24 h), female gender (100% among patients with NCSE), lack of response to simple commands	No statistically significant differences between patients with NCSE and others for age, drugs, presence of myoclonia, eyelid myoclonia, tachycardia, or agitation	N/A
Shavit et al. 2012 [33]	Prospective observational study on patients admitted to acute geriatric ward with acute unexplained change in mental, cognitive or behavioral status / confusion before or during hospitalization	81±7	15,359	14	Confusion, stupor, coma	N/A	Prevalence of medical conditions: systemic hypertension (n=10), cardiovascular disease (n=8), cerebrovascular disease (n=8), urinary tract infection (n=8), dementia (n=7), history of epilepsy (n=6), diabetes mellitus (n=4); medical therapy: antiepileptic drugs (n=5), antipsychotic drugs (n=2), narcotic drugs (n=1)
Naeije et al. 2014 [34]	Prospective case-control study comparing patients with delirium with and without possible NCSE (epileptic discharges)	≥65	64	11	History of cognitiv impairment, use of antibiotics, hypernatremia	N/A	Association between NCSE and higher mortality rates / longer hospital stays
Ali et al. 2015 [35]	Retrospective observational study	>65	60	60	N/A	N/A	Hyponatraemia as leading cause of NCSE, followed by acute stroke, nonketotic hyperglycemia, previous stroke, neurodegenerative disorders; improvement with antiepileptic treatment in 20 patients with normal neuroimaging and no metabolic abnormalities
Delgado et al. 2015 [36]	Retrospective observational study	>65	31	31	Previous seizure with motor components, remote symptomatic brain lesion with cortical involvement	N/A	Metabolic / infectious diseases as leading cause of NCSE (74%, a third of whom presenting remote structural damage in neuroimaging studies), followed by diagnosis of dementia / motor deficits prior to admission (55%), history of epilepsy (29%)
Canas et al. 2018 [37]	Retrospective observational study	>60	40	40	Dyscognitive features, clinical presentations ranging from aura continua to coma	N/A	Acute symptomatic etiologies (45%), followed by multifactorial etiologies (28%), as leading causes of NCSE, associated with the worst prognosis

Abbreviations. NCSE, non-convulsive status epilepticus; N/A, not available.

FIGURE

Figure 1. Factors potentially associated with non-convulsive status epilepticus (NCSE) in elderly with acute confusional state.

Review Article

Prevalence and clinical correlates of non-convulsive status epilepticus in elderly patients with acute confusional state: A systematic literature review

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Highlights

Non-convulsive status epilepticus (NCSE) poses considerable diagnostic challenges.

NCSE is more common in the elderly than in the general population.

Female gender correlates with the diagnosis of NCSE in the elderly.

A history of epilepsy correlates with the diagnosis of NCSE in the elderly.

Abnormal ocular movements correlate with the diagnosis of NCSE in the elderly.