

Acute confusional state/delirium: An etiological and prognostic evaluation

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Abstract

Introduction: Acute confusional state/delirium is a frequent cause of hospital admission, in the elderly. It is characterized by an acute fluctuating impairment of cognitive functions and inattention. Recognition and prompt treatment is crucial to decrease the morbidity and mortality associated with it. **Materials and Methods:** In this retrospective study, we determined the etiology and prognostic factors of an acute confusional state. A total of 52 patients of acute confusional state were clinically evaluated. All patients were also subjected to a battery blood biochemical examination, cerebrospinal fluid analysis and neuroimaging. Disability was assessed by using modified Barthel index (MBI). Patients were followed-up for 3 months. **Results:** The mean age of our cohort was 65.04 ± 10.6 years. 32 (61.5%) patients were male. In 33 patients, we were able to identify possible precipitating cause of an acute confusional state. In the rest of the patients results of all the tests were normal. Leukocytosis and hyponatremia were frequent factors associated with delirium. The mean duration of the hospital stay was 10.73 ± 3.6 days (range 5-21 days). Patients with an abnormal work-up (possible precipitating cause) had significantly lower mortality, less duration of hospital stay and less severe disability after 3 months. Age, underlying illness, serum creatinine, abnormal neuroimaging and MBI were identified as a significant prognostic indicator. 18 (34.6%) of our patients died, of these in 10 patients we could not find a precipitating cause. **Conclusion:** Patients, in whom a cause was found out, had better prognosis in terms of lesser mortality and the duration of hospital stay.

Key Words

Acute confusional state, confusion assessment method, delirium index, modified Barthel index

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Introduction

Acute confusional state or delirium is a clinical syndrome characterized by disturbed consciousness, cognitive function, or perception. The delirium usually develops over a short period of time (usually hours to days) and it has a tendency to fluctuate during the course of the day. It is often associated with serious adverse outcomes such as death, dementia, and the need for long-term patient care.^[1,2] Incidence of an acute confusional state ranges from 6% to 56% in hospitalized patients and nearly 80% in intensive care unit.^[3] Delirium is a common

cause of mortality and morbidity in the older population. It adds an extra burden to the care givers and family members.

Delirium may be the result of a variety of systemic or cerebral disease or to drug intoxication or withdrawal. The key to the management of cases of an acute confusional state lies in recognizing a cause or other contributing illness and alleviating it.^[4] We evaluated the patients of acute confusional state with the objective of identifying the possible causes of acute confusional state along with the evaluation of its prognostic importance.

Materials and Methods

We conducted this retrospective follow-up study on patients with an acute confusional state. These patients were admitted in the Department of Neurology at King George Medical University Uttar Pradesh, Lucknow. Study period was from January 2011 to December 2011. approval from the Institutional Research Ethics Committee was obtained. A written informed consent was taken from the relatives.

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Inclusion criteria

We included patients with acute confusional state/delirium of less than 7 days duration. The enrolled patients fulfilled the diagnostic criteria of an acute confusional state, according to the confusion assessment method. The confusion assessment method diagnostic algorithm included the following criteria: (1) An acute onset and fluctuating course; (2) inattention; (3) disorganized thinking; and (4) altered level of consciousness. The diagnosis of delirium by confusion assessment method needed the presence of features 1 and 2 and either 3 or 4.^[5] Patients with preexisting illnesses, such as dementia, cerebrovascular accidents, a known psychiatric illnesses and recurrent seizures, were excluded.

Evaluation

All patients were subjected to a detailed history, neurological and systemic examinations. Information about the drug and alcohol intake was recorded. Cognitive evaluation was performed using the Mini-Mental State Examination (MMSE). All the patients were subjected to routine biochemistry (serum sodium, potassium levels and blood sugar), complete hemogram, liver, renal and thyroid functions, arterial blood gas analysis, chest X-ray, ultrasound abdomen, cranial computed tomography and cerebrospinal fluid (CSF) analysis. Patients were categorized into two groups. One group included those patients in whom we were able to establish a possible precipitating cause for an acute confusional state and other group included those patients in whom we could not identify the possible precipitating cause. Clinical, biochemical and neuroimaging parameters of two groups were compared.

Severity of confusion was assessed by delirium index (DI). DI is a clinical instrument to measure the severity of delirium symptoms. In this scoring system, inattention, disorganized thinking, altered level of consciousness, disorientation to time and place, memory impairment, perceptual disturbances and psychomotor agitation or retardation were taken into account and scored 0-3 points each, according to the severity.^[6] All the patients were classified into one of the 3 types of delirium (hypo-active, hyperactive and mixed). Hyperactive delirium was diagnosed if patient was hyperactive, combative and uncooperative. Hypoactive delirium was diagnosed if patient appeared sluggish, lethargic and stuporosed. Patients with mixed-type delirium fluctuated between hyperactive and hypoactive types.

The treatment of an acute confusional state and delirium was directed toward identifying and correcting precipitating medical conditions. Low-dose antipsychotics were used to decrease psychomotor agitation if indicated. They were followed-up for 3 months. Disability was assessed by using modified Barthel index (MBI), which includes the degree of dependence for bowel and bladder, grooming, toilet use, transfer, mobility, dressing, feeding, use of stairs and bathing. For each activity, a score of 0 indicates a complete dependence and a score of 2 or 3 indicates that the patient can do that particular activity independently. A score of <12 indicates poor functional status and a score of ≥ 12 indicates good functional status.^[7]

Statistical analysis

Data were analyzed using the statistical software package, statistical package for the social sciences (Version 16.0, SPSS

Inc, 444 N. Michigan Avenue, Chicago, IL, USA) and Microsoft Excel. The difference between two values was considered to be significant only if P value was found to be <0.05 . Two sample t -test was used to see the difference between the mean of two delirium groups. If data was not normally distributed, a non-parametric equivalent of two sample t -test, two sample Wilcoxon rank-sum (Mann-Whitney) test was used. Chi-square or fisher exact test was used for qualitative data. A multivariate analysis was subsequently carried out using a logistic regression model.

Results

During the study period, 84 patients of acute confusional state were screened. 32 patients did not meet the inclusion criteria [Figure 1]. Our study cohort, thus, comprised of 52 patients. The mean age of patients was 65.04 ± 10.6 years. 32 (61.5%) patients were male. 25 (48.1%) patients had a presence of a co-morbid medical condition. Hypertension was the most common ($n = 14$, 26.92%) associated condition. Four patients, with cerebrovascular accidents, had multiple infarcts. In this study, 33 (66.5%) patients had a possible precipitating factor and in remaining patients a precipitating cause of acute confusional state was not established [Figure 2]. The mean duration of hospital stay was 10.73 ± 3.6 days (range 5-21 days). 18 (34.6%) of our patients died, of these in 10 patients we could not find a precipitating cause.

Details of other precipitating factors, observed in our study, have been mentioned in the Table 1. Leukocytosis and hyponatremia were frequent contributing factor for delirium. In our study, the cause for acute confusional state could be identified more frequently in male patients ($P = 0.02$). The frequency of hyperactive and mixed type of delirium was significantly higher in the group with an identified precipitating condition for acute confusional state [Figure 3].

We observed that the mortality rate was higher ($P = 0.03$) and hospital stay was prolonged ($P = 0.002$) among patients, in whom the cause for delirium could not be ascertained [Figure 4]. We found a significant correlation between age,

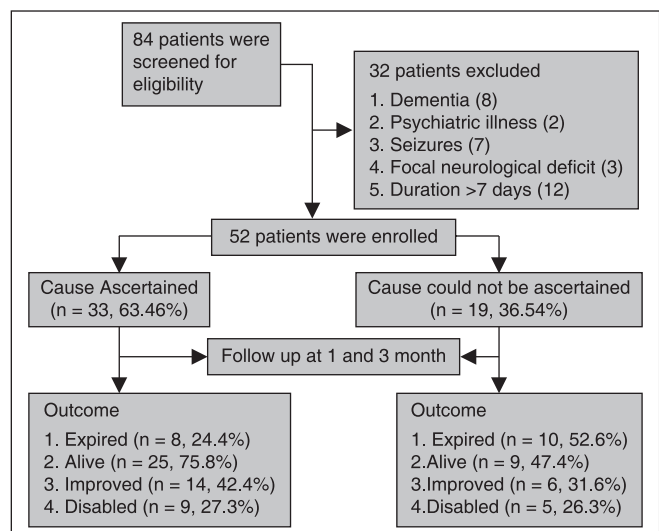


Figure 1: Flow diagram of the study

Table 1: Base line characteristics of patients

Characteristics	Cause ascertained (n = 33, 63.5%)	Cause could not be ascertained (n = 19, 36.5%)	P value
Age (in years)	64.42 (±11.8)	66.11 (±8.5)	0.68
Sex			
Male	24 (72.7)	8 (42.1)	0.02
Female	9 (37.3)	11 (57.9)	
Underlying illness (DM, HTN, CVA, CAD, CKD, COPD and TB)			
None	15 (45.5)	12 (63.2)	0.11
Single	11 (33.3)	6 (31.6)	
Multiple	7 (21.2)	1 (5.1)	
GCS	13.18 (±1.3)	12.79 (±1.0)	0.06
Meningeal signs	4 (12.1)	0	0.11
Hemoglobin (g/dl)	11.36 (±1.6)	11.31 (±1.4)	0.68
≥11	22 (66.7)	14 (73.7)	0.58
<11	11 (33.3)	5 (26.3)	
Total leukocyte count (/μl)	9200.3 (±3884.2)	8067.8 (±1418.9)	0.96
>11000	7 (31.2)	0	0.03
≤11000	26 (78.8)	19 (100)	
RBS (mg/dl)	102.06 (±26.2)	114.63 (±38.9)	0.23
≥55	32 (96.7)	19 (100)	0.44
<55	1 (3.3)	0	
Serum sodium (meq/L)	134.24 (±9.5)	140.37 (±6.2)	0.02
≥135	24 (72.7)	19 (100)	0.01
<135	9 (37.3)	0	
Serum potassium (meq/L)	3.96 (±0.4)	4.20 (±0.2)	0.06
Blood urea (mg/dl)	41.24 (±16.1)	36.97 (±18.0)	0.28
≤40	22 (66.7)	14 (73.7)	0.59
>40	11 (33.3)	5 (36.3)	
Serum creatinine (mg/dl)	1.09 (±0.5)	0.87 (±0.3)	0.24
≤1.5	5 (15.2)	1 (5.3)	0.28
>1.5	28 (84.8)	18 (94.7)	
Liver function test			
Normal	31 (93.9)	19 (100)	0.27
Abnormal	2 (6.1)	0	
Thyroid function test			
Normal	31 (93.9)	19 (100)	0.27
Abnormal	2 (6.1)	0	
Chest X-ray			
Normal	25 (75.8)	18 (94.7)	0.08
Abnormal	8 (24.2)	1 (5.3)	
CNS imaging			
Normal	12 (36.4)	6 (31.6)	0.727
Abnormal	21 (63.6)	13 (68.4)	
CSF analysis			
Normal	20 (60.6)	18 (94.7)	0.15
Abnormal	5 (39.4)	1 (5.3)	
MBI at admission	5.39 (±4.4)	4.74 (±1.9)	0.88
MBI at 3 rd month	15.80 (±5.3)	15.44 (±4.4)	0.10
DI at admission	14.61 (±2.9)	16.05 (±2.0)	0.05
DI at 3 rd month	3.28 (±3.4)	3.44 (±1.3)	0.22
Type of delirium			
Hypoactive	15 (45.5)	15 (78.9)	0.03
Hyperactive	13 (39.4)	4 (21.1)	
Mixed	5 (15.2)	0	
Hospital stay (in days)	9.61 (±3.1)	12.68 (±3.6)	0.002
Outcome			
Expired	8 (24.4)	10 (52.6)	0.03
Alive	25 (75.8)	9 (47.4)	
Disabled (MBI<12)	9 (27.3)	5 (26.3)	0.57
Improved (MBI≥12)	14 (42.4)	6 (31.6)	

DM = Diabetes mellitus, HTN = Hypertension, CVA = Cerebrovascular accident, CAD = Coronary artery disease, CKD = Chronic kidney disease, COPD = Chronic obstructive pulmonary disease, TB = Tuberculosis, CNS = Central nervous system, DI = Delirium index, MBI = Modified Barthel index, GCS = Glasgow coma scale, CSF = Cerebrospinal fluid, RBS = Random blood sugar

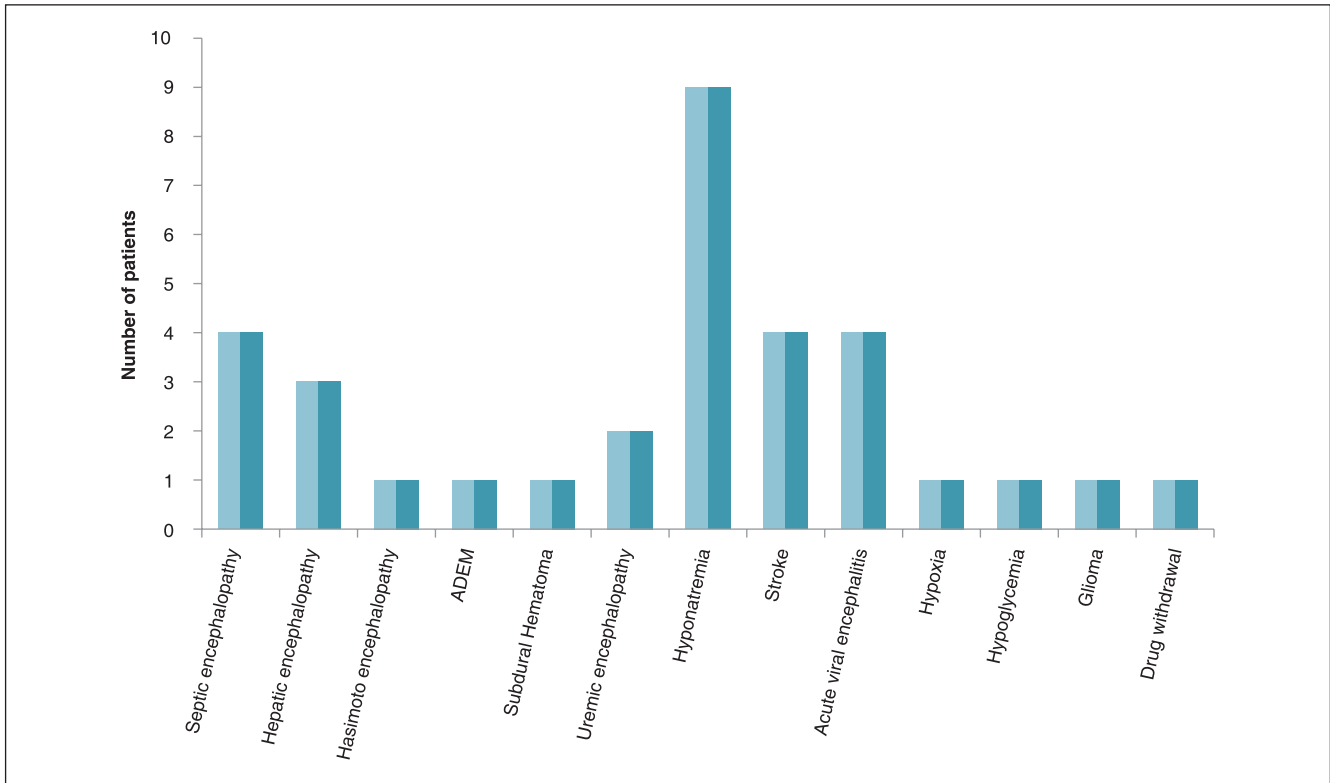


Figure 2: Bar diagram showing the various causes of acute confusional state found during the study

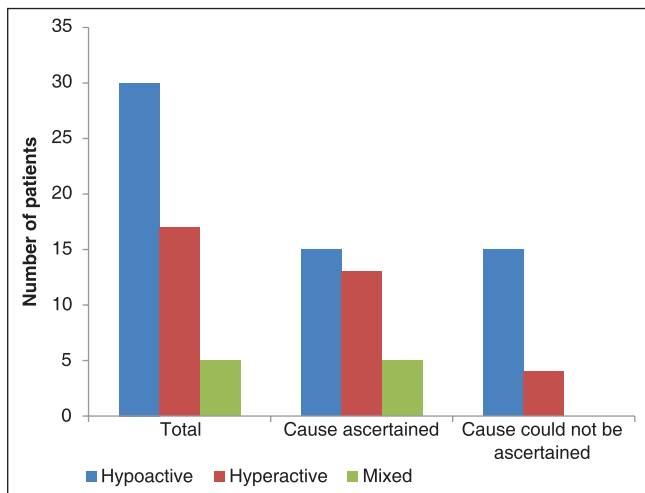


Figure 3: Bar diagram showing the frequency of type of delirium

underlying illness, serum creatinine, abnormal neuroimaging and MBI with a disability of the patients [Table 2]. However, baseline characteristic such as age, sex, underlying illnesses, Glasgow coma scale, leukocyte count, serum sodium, blood urea, serum creatinine, abnormal CSF analysis, liver function, thyroid function, baseline DI and MBI did not significantly influence the mortality and duration of hospital stay.

Discussion

We observed that identifying the precipitating factor is important because treatment of precipitating factors influenced the overall

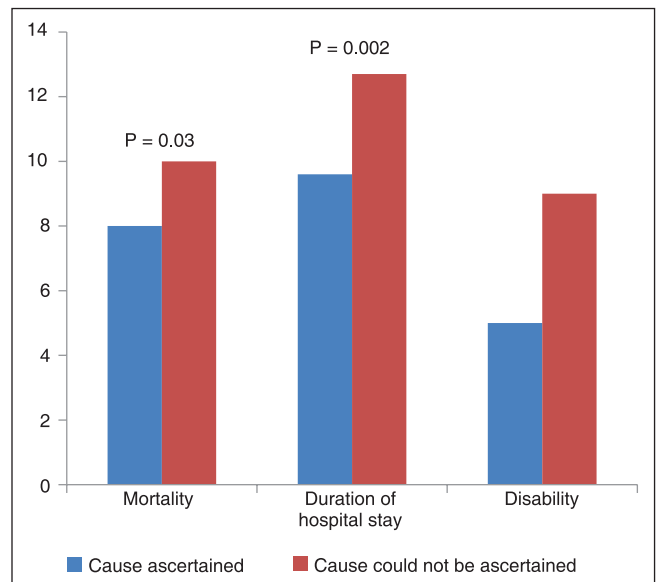


Figure 4: Bar diagram showing mortality, duration of hospital stay and disability differences between patients with established precipitating factor and the group without established etiology

outcome in patients with acute confusional state. Both number of deaths and duration of hospital stay were longer, if, a precipitating factor was not identified. Occurrence of delirium, in fact, reflects an underlying brain dysfunction, which almost invariably results following a systemic or brain disorder or to drug intoxication or drug withdrawal. Delirium often has an adverse prognostic impact on functional and cognitive outcome, as well as on morbidity

Table 2: Significant predictors of disability at the end of follow-up

Variable	Disability (P value)
Age	0.049
Underlying illness	0.005
Serum creatinine	0.011
Abnormal CNS imaging	0.002
MBI	0.008

CNS = Central nervous system, MBI = Modified Barthel index

and mortality.^[8,9] Kiely *et al.* examined the association between persistent delirium and 1-year mortality in 412 newly admitted patients. Approximately, one-third of subjects remained delirious at 6 months. Cumulative 1-year mortality was 39%. Patients with persistent delirium were 2.9 times as likely to die during the 1-year follow-up, in comparison to whose delirium resolved. In addition, when delirium resolved, the risk of death diminished thereafter.^[10]

In a study, predominant primary etiologies for delirium were infections (58%), following by metabolic abnormalities (36%) and adverse drug effects (18%). Complete resolution of the delirium was found in 33% (30/92), with persistence in 12% (11/92), and no change in 8% (7/92) of the patients. 48 percent (44/92) of the patients died. Most deaths (50%) were in the 1st month. The main cause of death was infection related (70%), of which bronchopneumonia was predominant (39%), followed by sepsis (32%). Independent predictors of death were infection, advanced age, low plasma albumin level, dehydration and heart failure.^[11] In our study, a definite cause for acute confusional state was found in 66.5% of the all included patients. Hyponatremia was a dominant precipitating metabolic factor. Similar to our observation, Chrispal *et al.*, in study of 81 patients with hip fractures, observed that approximately 21% of patients developed post-operative delirium. On multivariate analysis, the underlying dementia, duration of surgery >2.5 h and pre-operative packed cell volume <25 were independent predisposing risk factors for the development of post-operative delirium. In several patients, a precipitating factor was not identified.^[12] We made an important observation that mortality and duration of the hospital stay were significantly lower among those patients in whom a possible precipitating cause was found. A correct identification of possible etiological factor is important because reversal of that cause will help in early resolution of delirium.

Drugs are a significant risk factor for delirium; they are one of the most easily reversible precipitants. Drugs commonly associated with delirium include anticholinergic agents, benzodiazepines and opiates. Though, we have not included any toxic screen or alcohol level estimation in your work-up, but a thorough medication history was obtained. In one of our patient delirium resulted following opium withdrawal.

Stroke patients with the development of delirium have unfavorable outcomes, particularly higher mortality, longer hospitalizations and a greater degree of dependence after discharge. In a meta-analysis, it was observed that stroke patients with delirium had higher inpatient mortality and mortality at 12 months compared with non-delirious patients. Patients with delirium also tended to stay longer in hospital

compared with those who did not have delirium and were more likely to be discharged to nursing homes or other institutions.^[13] Though, we had excluded patients of pre-existing stroke; however, four patients had multiple infarcts on neuroimaging.

Several studies have suggested that delirium is associated with risk of dementia and also acceleration of decline in existing dementia. Davis *et al.*, recently, noted that delirium was associated with general cognitive decline, with an 8-fold increase in incident dementia and accelerated decline in MMSE scores.^[14] Early recognition and prompt treatment are essential to prevent future cognitive decline in these patients.

Conclusion

Patients, in whom a cause was found out, had better prognosis in terms of lesser mortality and lesser duration of hospital stay.

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