

Original Research Article

A study of etiological profile of acute confusional state

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ABSTRACT

Background: ACS (Acute confusional states) are on the rise taking the shape of an epidemic. These states are common among the elderly, but young individuals are also not spared. Prompt diagnosis and management of these states can decrease the associated morbidity and mortality.

Methods: In this prospective observational study, etiological profile of ACS was evaluated in a total 100 patients, selected over a period of one year, after they fulfilled the CAM (Confusion Assessment Method) criteria.

Results: Among 100 patients of ACS, mean age was 54.77 ± 18.50 years, males were 66% and 34% were females. The most common diagnosis provisionally made on the basis of history and clinical examination was metabolic encephalopathy in 37% patients, meningoencephalitis (24%), CVA (Cerebrovascular accident) (18%), seizures (9%), sepsis (6%), poisoning (6%). Whereas the final diagnosis made after subjecting the patients to relevant investigations, was metabolic encephalopathy in 37% of patients, meningoencephalitis (20%), CVA (18%), sepsis (12%), unprovoked seizures (6%), poisoning (6%) and undetermined in 1%. The final diagnosis matched the provisional diagnosis in most of the patients except sepsis as a provisional diagnosis was underdiagnosed. The mean duration of hospital stay was 7.6 ± 3.67 days and the hospital stay was most commonly complicated by aspiration pneumonia and acute kidney injury.

Conclusions: This study emphasizes that the ACS is an emergency medical situation, where prompt identification, workup and treatment should be done parallelly and urgently to prevent the morbidity and mortality.

Keywords: Acute confusional state, Confusion assessment method, Metabolic encephalopathy, Meningoencephalitis, Septic encephalopathy

INTRODUCTION

ACS (Acute confusional state), synonymous with acute brain failure, acute organic reaction, delirium and post-operative psychosis is defined as a transient disorder of cognition and attention accompanied by disturbances of the sleep - wake cycle and psychomotor behaviour.¹ It is a mental and behavioural state of reduced comprehension, coherence and capacity to reason.²

It is often associated with serious adverse outcomes such as death, dementia and the need for long term patient care.³ Incidence of ACS state ranges from 6% to 56% in

hospitalized patients and nearly 80% in intensive care unit.⁴

METHODS

Total 100 patients of ACS fulfilling the diagnostic criteria i.e. CAM (Confusion Assessment Method) criteria were enrolled with an aim to evaluate the causes of these states and to study the clinical correlates of various causes of these states. After the patients fulfilled the diagnostic criteria, an informed consent was obtained from patients' attendants before their final inclusion for participation in the study.

Inclusion criteria

A patient was deemed to have an ACS if patients fulfilled the CAM criteria, where atleast 3 score was required to make the diagnosis (Table 1).

Table 1: The Confusion Assessment Method (CAM) diagnostic algorithm.

The Confusion Assessment Method (CAM) Diagnostic Algorithm ⁵
Feature 1: Acute Onset or Fluctuating Course This feature is usually obtained from a family member or nurse and is shown by positive responses to the following questions: Is there evidence of an acute change in mental status from the patient’s baseline? Did the (abnormal) behavior fluctuate during the day, that is, tend to come and go, or increase and decrease in severity?
Feature 2: Inattention This feature is shown by a positive response to the following question: Did the patient have difficulty focusing attention, for example, being easily distractible, or having difficulty keeping track of what was being said?
Feature 3: Disorganized thinking This feature is shown by a positive response to the following question: Was the patient’s thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
Feature 4: Altered Level of consciousness This feature is shown by any answer other than “alert” to the following question: Overall, how would you rate this patient’s level of consciousness? (alert [normal]), vigilant [hyperalert], lethargic [drowsy, easily aroused], stupor [difficult to arouse], or coma [unarousable])

The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4.

Exclusion criteria

- Age less than 18
- Psychiatric disease
- Any head trauma

After enrolling the patients in the study, a thorough collateral history was taken usually from the attendants, and clinical examination was done and patients were provisionally broadly categorised into two group of ACS, one with neurological causes of ACS and the other with non-neurological causes of ACS.

Then these patients were subjected to relevant investigations including the complete hemogram, renal and liver function tests, serum electrolytes, arterial blood gas analysis, blood sugar levels, Xray chest and ultrasonography of the abdomen. Few investigations like brain imaging, CSF (Cerebrospinal fluid) studies, EEG(Electroencephalography), urine toxicology

screening were done when required. These patients were followed daily till their discharge or death.

The results obtained from the study were statistically analysed using SPSS Statistics -19.0 version. The observations were tabulated in the form of mean±standard deviation (SD). The continuous variables were analysed using analysis of variance (ANOVA). In parametric data, student- t test was applied. Quantitative variables were correlated using chi-square test and coefficient of correlation.

RESULTS

Among a total of 100 patients of ACS, most of the patients were in the age group of 61-80 years. Males were 66% and females 34%, with a male to female ratio of 1.94:1.

Hypertension and diabetes were the most common risk factors observed in 19% and 17% of the patients of ACS respectively, whereas no risk factor was seen in only 15% of the patients.

The presentation of the ACS was quite varied with symptoms ranging from decreased responsiveness in 79% of the patients to agitation in 18%, seizure activity in 8%.

According to the psychomotor activity, 79% patients had hypoactive type of ACS (lethargy/slowing) , 18% patients had hyperactive type of ACS (agitation/hyper talkativeness) while rest of the 3% patients had mixed type of ACS where patients had the features of both the major types (Figure 1).

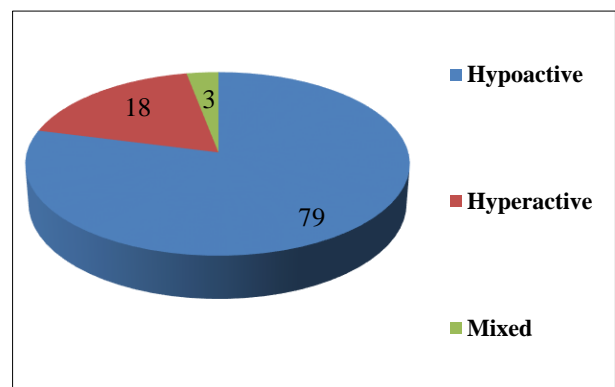


Figure 1: Distribution of patients with various types of Acute Confusional States (ACS).

The diagnosis of ACS was made clinically by the CAM criteria where 30% of the patients had score 3 and 70% of the patients had score 4.

The mean GCS (Glasgow coma score) was 11.53±2.92. Majority of the patients (72%) had a GCS of 12-15, GCS <8 was seen in 15% of the patients. GCS 8-11 was present in 13% of the patients.

The various clinical signs noted were asterix in 46% of the patients, meningeal signs in 24%, hemiparesis in 18%, aphasia in 15% and cerebellar signs in 2% of the patients of ACS.

After detailed history taking and clinical examination, patients were broadly divided into those with neurological cause of ACS (51%) and those with non-neurological cause of ACS (49%) (Table 2).

Table 2: Broad categories of provisional diagnosis of patients with ACS.

Diagnosis	n	%
Neurological	51	51.0
Non neurological	49	49.0
Total	100	100.0

Among the patients with neurological causes of ACS (51%), 24% had clinical signs of meningoencephalitis, 18% had clinical signs suggestive CVA and 9% had seizures. Among the patients with non-neurological cause of ACS (49%), 37% of total had clinical findings suggestive of metabolic encephalopathy, 6% had clinical evidence of sepsis, and 6% were provisionally diagnosed with poisoning as the cause of ACS.

All these patients of ACS were subjected to a set of investigations, where hyponatremia was found to be the commonest electrolyte abnormality (25%).

The patients with neurological cause of ACS were subjected to the brain imaging which revealed meningeal enhancement in 24% of the patients, acute non haemorrhagic infarct in 14%, intracerebral haemorrhage in 2%, acute haemorrhagic infarct in 2% and ICSOL in 2% of the patients.

Patients with seizure activity (n=9) were then subjected to EEG studies among them generalized spike and slow wave pattern was most common.

Patients with meningeal signs (n=24) were then subjected to CSF studies which were abnormal in all the patients, findings suggestive of viral meningitis were seen most commonly among them (13%), followed by pyogenic meningitis in 9% of the patients. 1% patient had tubercular and cryptococcal meningitis each.

Patients with provisional diagnosis of poisoning (n=6), were subjected to urine toxicology screening, where opiates were positive in 3% of the patients, 1% of the patients had amphetamines, barbiturates and benzodiazepines each.

After relevant investigations, final diagnosis were made. The majority of patients (37%) were found to have metabolic encephalopathy, followed by meningoencephalitis in 20% of patients, 18% patients

were CVA, 12% had sepsis, 6% had unprovoked seizures and poisoning each. However, the cause in 1% patient was undetermined (Figure 2).

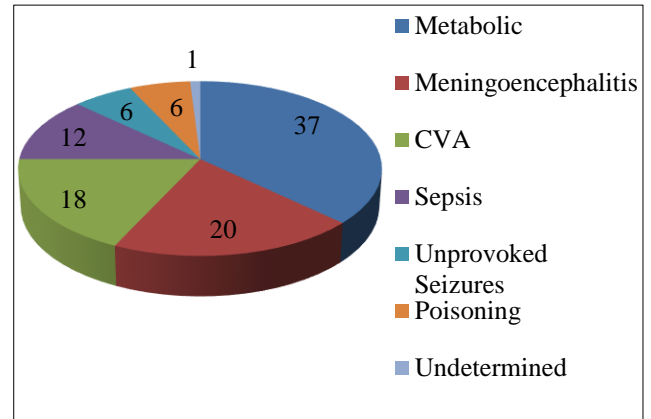


Figure 2: Final diagnosis of patients of Acute Confusional State (n=100).

Among the patients with metabolic cause of ACS, electrolyte imbalance was the most common metabolic cause present in 32% of the total patients of ACS, these patients also had other metabolic abnormalities present like hepatic encephalopathy in 12% of total, uremic encephalopathy in 8% of total, hypoglycaemia in 3%, respiratory in 2% and hypothyroid in 1% of the total patients.

Among the patients with sepsis (n=12), the most common was meningoencephalitis fulfilling the criteria of SIRS (Systemic Inflammatory Response Syndrome) in 4% of the total, UTI (Urinary tract infection) /pyelonephritis in 3%, pneumonia in 3%, foot gangrene in 1% and acute gastroenteritis in 1% of the total patients.

It was observed that the hospital stays in 43% of the patients was complicated, most commonly by aspiration pneumonia in 14% of the patients, electrolyte disturbances in 12% and acute kidney injury in 7% of the patients. Overall mortality in the study group was 28%.

Most of the cases of metabolic encephalopathy (n=16) (43.2%), 50% of the patients with sepsis (n=6), 50% of the patients with unprovoked seizures (n=3) and 45% of the patients with meningoencephalitis (n=9) occurred in the age group of 41-60 years. Poisoning was more common (66.6%) in younger patients in 21-40 years of age group (n=4). CVA was more commonly observed in elderly (83.3%) in the age group of 61-80 years (n=15). (p value= 0.04) (Figure 3).

Among males, metabolic encephalopathy was the leading cause in 39.4% of the patients. Sepsis was more common in females (23.5%). Unprovoked seizures, CVA, poisoning were common in males with 21.2%, 7.6%, 9.1% respectively. (p value =0.032)

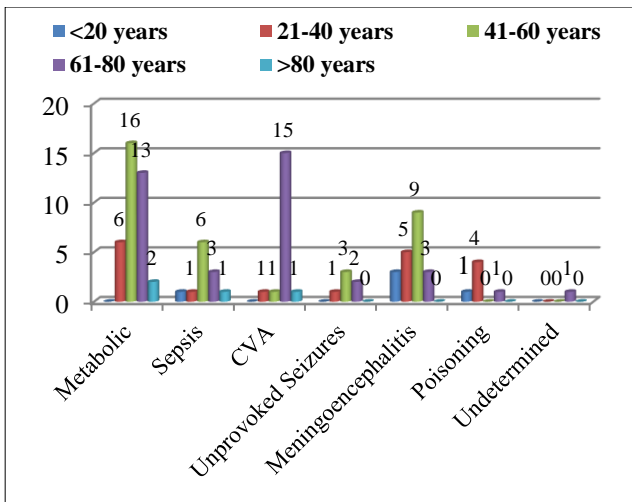


Figure 3: Age distribution of patients according to final diagnosis.

Majority of the patients had one or the other risk factors. Among the patients with metabolic abnormality, 29.7% of the patients had CLD (Chronic liver disease) as the risk factors, 2.7% had hypertension and CKD (chronic kidney disease). In patients with sepsis, majority of the patients had Diabetes (58.3%), in patients with CVA 83.3% patients had hypertension. Patients with meningoencephalitis had diabetes as the major risk factor (p value=0.00).

Outcome in metabolic group was poorer, as there were 32.1% deaths observed in this group(n=9). Followed by 28.6% mortality in sepsis(n=8), 8% mortality in CVA(n=7), 10.7% mortality in meningoencephalitis (n=3) and 3.6% mortality in undetermined(n=1). Unprovoked seizures and poisoning had no mortality (Figure 4).

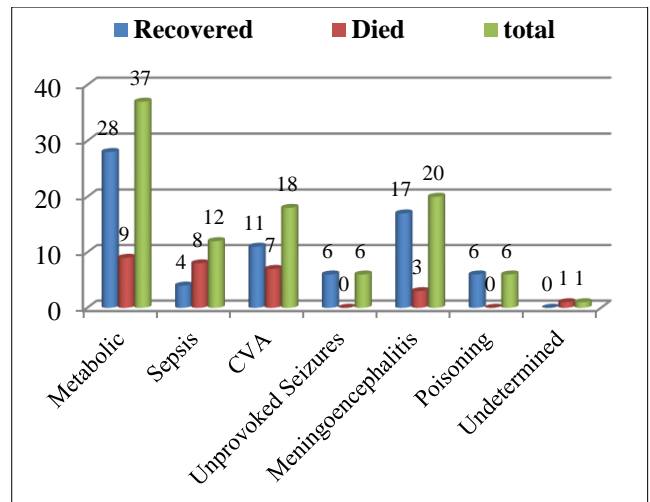


Figure 4: Mortality outcome in each diagnostic group.

Highest mortality (50%) was observed in age group of 61-80 years. And lowest mortality (3.5%) was observed in <20 years of age (p value=0.191).

The mortality outcome correlated well with various biochemical parameters like Hb (p value=0.000), TLC (p value=0.015), BUN(p value=0.000), creatinine(p value=0.000), serum sodium levels(p value=0.004)whereas other biochemical parameters like K, Ca, Mg, RBS did not correlate with the mortality outcome (Table 3).

The mortality outcome correlated well to individual parameters of ABG like pH (p value=0.000), paO2 (p value=0.000), paCO2(p value=0.000), SpO2(p value=0.004) (Table 4).

Table 3: Correlation of various biochemical parameters to final outcome.

Biochemical variant	Mean ±SD		p value
	Recovered	Died	
Hb	9.65±1.36	8.67±0.99	0.000
TLC	11061.94±5412.91	10689.28±6201.81	0.015
BUN	24.87±19.78	43.13±27.55	0.000
Creatinine	2.30±2.78	4.41±3.52	0.000
Na	134.94±7.95	134.25±14.56	0.004
K	4.11±0.93	4.46±0.91	0.432
Ca	9.37±0.81	9.61±2.29	0.093
Mg	1.95±0.29	1.96±0.29	0.977
RBS	100.32±6.75	110.78±6.98	0.300

(Hb= haemoglobin, TLC=total leucocyte count, BUN=blood urea nitrogen, Na= serum sodium, K= serum potassium, Ca= serum calcium, Mg= serum magnesium, RBS= random blood sugar).

Each component of GCS i.e. E (eye response), V (verbal response) and M (motor response) correlated well with mortality outcome in patients with ACS as shown by the

p value of 0.000 which was highly significant. Patients with poorer GCS had higher mortality (Table 5).

The patients with ABG abnormalities, poor GCS score, azotemia had statistically significant correlation to the hospital stay, which was prolonged in these patients (p value =0.000).

Table 4: Correlation of ABG parameters to final outcome.

ABG parameter	Mean±SD		p value
	Recovered	Died	
Ph	7.4±0.07	7.17±0.24	0.000
paO2	94.18±4.36	83.28±7.48	0.000
paCO2	32.43±10.07	24.85±22.14	0.000
SpO2	96.09±4.10	84.14±7.65	0.004
HCO3	24.81±6.75	14.89±11.93	0.001

Table 5: Correlation of components of GCS to outcome.

GCS components	Mean±SD		p value
	Recovered	Died	
E	3.52±0.62	2.14±0.80	0.000
V	3.73±0.55	2.67±0.94	0.000
M	5.52±0.82	3.32±1.46	0.000

Each component of GCS i.e. E (eye response), V (verbal response) and M (motor response) correlated well with mortality outcome in patients with ACS as shown by the p value of 0.000 which was highly significant. Patients with poorer GCS had higher mortality (Table 5).

The patients with ABG abnormalities, poor GCS score, azotemia had statistically significant correlation to the hospital stay, which was prolonged in these patients (p value =0.000)

Maximum number of deaths (25%) were observed in patients whose hospital stay was complicated by aspiration pneumonia and acute kidney injury each (p value=0.000).

Mortality was maximally observed (64.2%) in patients with hospital stay between 13-16 days (p value=0.000).

The provisional diagnosis made on the basis of history and clinical examination matched with final diagnosis significantly (p value=0.000) in all the diagnostic groups except the sepsis group was most underdiagnosed.

Hospital stay was prolonged (>13 days) in patients with sepsis, however it was shorter in patients with unprovoked seizures. Patients with metabolic encephalopathy and meningoencephalitis had hospital stay between 5-8 days. (p value=0.054).

DISCUSSION

This was a hospital based, prospective, observational study, which was conducted on 100 patients of ACS. This

study emphasizes the importance of history taking and clinical examination in the diagnosis of the ACS and the need for early diagnosis and prompt treatment, as these states may have poor outcome in terms of morbidity and mortality. These states are almost always associated with one or the other predisposing factors, which needs to be identified, to influence the overall outcome.

Most patients were in the age group of 61-80 years, mean age was 54.77±18.50 years which was consistent with the study done by Sumji S et al, where majority of the patients were in age group of 61-70 years and mean age 60±17.80 years.⁶

There was male predominance with 66% of males and 34% of the females. Similarly, in the study done by Rai D et al, 61.5% were males and 38% were females.⁷

ACS was associated with one or the other predisposing factors in 85% of the patients, only 15% of the patients had no such risk factors. Out of total 100 patients, 19% of the patients were hypertensive, 17% had uncomplicated diabetes, CKD in 13% of patients, CLD in 13% patients, complicated diabetes in 6% of the patients, multidrug abuse in 6%, malignancy 6%, alcohol usage in 4%. The study was supported by Rai D et al, where hypertension was the most common precipitating factor among the 26.9% patients of ACS.⁷

The presentation of ACS was quite varied ranging from complaints of lethargy or difficult arousal (n=79), agitation and unusual behaviour in (n=18) patients and seizures in (n= 9) patients. Kanich W et al, found that majority of patients presented with complaints of lethargy / difficult arousal / drowsiness (46%), unresponsiveness (24%), unusual behaviour (18%), agitation in (12%) of the patients.⁸

On clinical examination, patients with ACS were found to have asterixis in 46%, meningeal sign sin 24%, hemiparesis in 18%, aphasia in 15% and cerebellar signs in 2% of the patients. These findings corroborated with the findings of the study done by Islam S et al, where 32% had hemiparesis, 27% had asterixis and 6% had meningeal signs.⁹

Based on psychomotor activity, patients of ACS were identified with hypoactive type of ACS in 79% patients (a state where patients were lethargic/ withdrawn/ quiet and apathetic), 18% patients had hyperactive type of ACS (where patients were agitated / hyper arousable) and mixed in 3% of the patients. Similar findings were observed in the study done by Spiller JA et al, where hypoactive type of ACS was most common (86%).¹⁰

Majority of the patients (72%) had GCS between 12-15 . 15% of the patients had GCS <8 and 13% had GCS between 8-11. Mean GCS was 11.53±2.92. Study corroborated with the study done by Sumji S et al, where also majority of the patients (46.8%) had GCS between

12-15, 36.5% of the patients had GCS of 8-11 and 16.8% of the patients had GCS <8.⁶

Based on the history and clinical examination, patients of ACS were provisionally diagnosed to have neurological cause of ACS in 51% of the patients and non-neurological cause in 49% of the patients. Which was in contrast to the study done by Kanich W et al, where ACS was broadly caused by non-neurological causes in 78% of the patients and neurologic causes in 28% of the patients. The difference was probably attributed to trauma (14%) and psychiatric causes (14%), both of which were excluded from this study.⁸

Among the patients of ACS, majority (25%) of the patients had hyponatremia as the major electrolyte abnormality. Comparable to the study done by Rai D et al, hyponatremia was the dominant metabolic abnormality, present in 37.3% of the patients of ACS.⁷

The final diagnosis made after subjecting the patients to relevant investigations were metabolic in 37% of the patients, meningoencephalitis in 20%, CVA in 18%, sepsis in 12%, unprovoked seizures in 6%, poisoning in 6% and undetermined in 1% of the patients. This was supported by the study done by O'Keeffe, where the most common cause was metabolic in 65%, structural in psychiatric in 2%.¹¹ In another study done by Prinka AS et al, ACS was caused most commonly by metabolic causes in 42% of the patients.¹²

A positive correlation between age and cause of ACS was established(p value=0.004),with most of the patients (43.2%) of the metabolic encephalopathy, 50% of the sepsis, 50% of the unprovoked seizures and 45% of the meningoencephalitis occurred in the age group of 41-60 years. CVA was seen more commonly in elderly in 61-8 years, poisoning was common in younger patients in age group of 21-40 years. Similarly, in the study conducted by Sumji S et al, CVA was seen in older age group and highest in 6thdecade. Poisoning was exclusively seen in <50 years of age. Metabolic cause and sepsis were seen in age group 71-80 years.⁶

Sepsis was more common in females (23.5%). Unprovoked seizures (21.1%), CVA (7.6%) and poisoning (9.1%) were more common in males (p value=0.032). Similarly, Nadeem MA et al, revealed that leading causes among males were poisoning and CVA while among female's metabolic encephalopathy was more common.¹³

Hypertension was highest among the CVA group (83.3%), Diabetes was highest among meningoencephalitis (35%), CLD was highest in metabolic encephalopathy (29.7%) (p value= 0.001). These findings were supported by study done by Sumji S et al where hypertension was highest in CVA (73.3%), diabetes in 26%.⁶

Overall mortality was 28%, with full recovery in 72% of the patients. Comparable to the study done by Grover S et al where 65.9% patients had improved, 8.8% recovered, 6.6% died.¹⁴

Highest mortality (32.1%) was observed in metabolic group followed by 28.6% in sepsis, 25% in CVA, 10.7% in meningoencephalitis. Unprovoked seizures and poisoning had no mortality in the group (p value=0.004). In the study done by Sumji S et al, poisoning, intracranial infections and seizures had significantly decreased mortality whereas shock, sepsis and CVA group had increased mortality.⁶

Highest mortality(50%) was observed in age group of 61-80years, 7.14% in >80 years, lowest mortality was seen in <20 years (3.5%).Comparable to this, in the study done by Xiao HY et al, death rate was higher in elderly patients (>60years) than in younger patients (10.8%).¹⁵

GCS score and its individual components correlated well to outcome (p value=0.000). Patients with <8 GCS had 86.65 mortality, 8-11 GCS had 92.3% mortality and those with GCS 12-15 had 4.16% mortality. In the study done by Iqbal F et al, patients were divided into three groups, same as in this study, with significantly higher mortality in <8 GCS.¹⁶

Table 6: Correlation of various prognostic factors on hospital stay.

Prognostic factors	Hospital stay (in days)				p value
	0-4	5-8	9-12	13-16	
E	3.64±0.49	3.48±0.66	2.33±1.11	2.05±0.55	0.000
V	3.58±0.61	3.73±0.58	2.66±1.22	2.82±0.88	0.000
M	5.64±0.49	5.44±0.89	3.33±2.17	3.35±1.27	0.000
GCS	12.88±1.11	12.76±1.73	8.33±0.44	8.11±2.02	0.000
BUN	30.82±27.58	25.38±20.74	51.33±25.48	71.82±22.73	0.000
Ph	7.42±0.11	7.40±0.07	7.22±0.23	7.15±0.25	0.000
PaO ₂	94.76±4.54	93.64±4.75	83.88±9.37	83.41±7.41	0.000
HcO ₃	26.17±9.84	23.69±6.24	19.55±12.24	14.64±12.54	0.001
SpO ₂	96.00±4.94	95.68±4.49	84.77±9.60	84.28±7.68	0.000

Patients with poor GCS, poor ABG parameters and high BUN were significantly related with longer hospital stay. (p value <0.05) (Table 6).

Likewise, in the study done by O'Keeffe, ACS was independently associated with prolonged hospital stay, functional decline during hospitalization, increased risk of developing a hospital acquired complication.¹¹

In this study, poor GCS, biochemical derangement like low Hb, high TLC, high BUN, high creatinine, low sodium, low pH, low pao₂, high paco₂, low HCO₃ and low Spo₂ were significantly related to mortality (p value <0.05).

CONCLUSION

Study was designed to evaluate the etiology of ACS, and the precipitating causes of this state. It was found that the presentation of ACS was very variable, patients may even have a hypoactive type of ACS which may be easily missed as patients can be quiet and apathetic. Age and sex were also important predictors of ACS. As CVA, metabolic, sepsis, unprovoked seizures and meningoencephalitis are more commonly seen in elderly while poisoning was seen in younger patients. The various causes of ACS should be kept in mind while confronting such patients so as to identify and correct them early. ACS should be treated as an emergency. Hence, treatment and further workup should run parallelly to avoid the morbidity and mortality associated with these states.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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