Aetiologic Profile of Patients with Altered Mental Status in Medical Emergency in a Tertiary Care Medical Institute - A Cross Sectional Observational Study

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ABSTRACT

BACKGROUND

Altered mental status (AMS) is a symptom complex that may arise from a variety of primary neurologic disorders and systemic illnesses. The underlying diagnosis affects final outcome of patients that may be predicted by use of objective tools. This study was conducted to describe the aetiologic distribution of such patients presenting to emergency room and assess the utility of Richmond Agitation Sedation Scale (RASS) and Glasgow Coma Scale (GCS) as prognostic tools.

METHODS

In this cross-sectional observational study, we identified such 120 adult patients at a single centre tertiary care facility and documented their bio-demographic profile, RASS & GCS scores, routine metabolic profile, specific investigations (like neuro-imaging, lumbar puncture, toxicologic screen) as indicated, along with patient outcome at 2 weeks.

RESULTS

The mean age of patients was 49.76 ± 18.72 years with 79 (66 %) patients being male. The aetiologic distribution was as follows; cerebrovascular (N = 24; 20 %), infections (N = 40; 33 %), metabolic (N = 37; 30.8 %), toxicologic (11; 9.2 %) and seizure disorder (N = 8; 6.7 %). The total mortality rate was 38 % as assessed at the end of two weeks. While RASS did not fare well as a prognostic tool, GCS score less than 8 was associated with statistically significant increase in mortality rates (52 % vs. 31 %).

CONCLUSIONS

Altered mental status has varied presentation and the aetiologies for AMS are evenly distributed among primary central nervous system (CNS) causes and systemic causes leading to secondary AMS. It is helpful to use some standardised scoring systems that bring uniformity in the assessment as well as prognostic implications.

KEYWORDS

Alerted Mental Status, Aetiologic Distribution, Outcome, RASS, GCS

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BACKGROUND

Altered mental status a common presenting feature often without a definite localisation is a challenge for the emergency physician. The patients presenting with AMS constitute a significant proportion of the ones presenting to emergency rooms, require considerable resource utilisation and have high mortality rates. AMS may result from any disease process affecting central nervous system directly such as head trauma, mass lesion, meningitis or indirectly as in case of sepsis, cardiogenic shock, or intoxication. Kanich et al. observed that the most frequent causes were neurologic followed by toxicologic, trauma, psychiatric, infectious and metabolic.[1] Another study by Kekec Z et. also showed that the majority of the aetiologic diagnoses were primarily neurological followed by endocrine / metabolic.[2] Amongst the neurological causes the common ones were intracranial stroke, convulsion or status epilepticus and encephalitis. Clinicians must recognise potentially reversible cognitive aetiologies such as systemic infection and medication side effects, which can be treated easily.[3] In addition, the mortality rates rise if AMS persists for a longer duration, as observed by Aslaner M et al.[4,5]

The aetiology also varies depending on the age of the patient.[6,7] In a prospective study from Malaysia, the authors observed that in the younger age group of 16 – 64 years, the psychiatric and toxicologic aetiologies were relatively more common. In the older age group, neurological, and metabolic aetiologies were more common.[8] In another study done by Henna Naqash et al. the most common cause of admission in young and middle-aged patients was infection followed by seizures and cardio-embolic strokes.[9]

The use of qualitative terms like "confuse, drowsy or obtunded" defies accurate description. To overcome this, a variety of quantitative scales have been developed. The Richmond Agitation and Sedation Scale was developed for optimisation of sedation in intensive care units while GCS was initially developed to assess patients with traumatic brain injury.[10,11] However, there is paucity of literature regarding their utility in medical emergency room scenario and their role as prognostic indicators in these patients is far from established.

Since, the aetiologic diagnoses may vary as per the demographic profile of the patients & the regional healthcare settings and no such studies being reported from Northern India; we undertook this study to describe the profile of patients presenting to emergency room with AMS and observe their outcome at the end of two weeks. We also wanted to evaluate RASS and GCS as prognostic tool for these patients.

METHODS

This was a cross-sectional observational study approved from institutional ethics committee conducted from December 2018 to August 2019 in the medicine emergency of a tertiary care facility of Department of General Medicine in Government Medical College and Hospital, Chandigarh. All adult patients presenting to emergency room with altered mental status were enrolled and screened. AMS was defined as anyone of the following: GCS less than 15, RASS readings other than 0, inappropriate behaviour or hallucinations. The following patients were excluded from the study: a) those who were being re-admitted with the same or similar symptoms during the period of study and had already been enrolled in the study earlier. b) Known cases with dementia or irreversible brain damage.

A total of 120 patients were included in the study. The patients were assessed by standard clinical examination, evaluation scales and treated by the resident clinicians as per the existing institutional protocols. Patient's demographic and clinical data were recorded which included detailed history of current illness, past medical history, family history, personal history, socio-economic status along with findings of vitals at the time of admission, general physical examination, detailed neurological examination and other systemic examination. The level of consciousness was graded by RASS & Glasgow Coma Scale at the time of admission and the initial scores were taken into consideration for study results. RASS is a 10-point scale, cantered at 0, which indicates alert and calm. Positive RASS scores indicate restlessness (+ 1), agitation (+ 2 to + 3), or combative behaviour (+ 4). Negative RASS scores represent lethargy (- 1), poor response to verbal stimulus (- 2 to - 3), responsive only to physical stimulus (- 4), and unresponsive (- 5). The GCS monitors levels of consciousness by observing, assessing and recording eye opening and verbal responses, as well as motor responses to a range of stimuli, such as voice, touch and pain. Points are allocated for each response, and the sum of these points indicates the severity of impaired consciousness. The maximum score a patient can get in GCS is 15. Based on this scale, reduced consciousness has been classified into mild (GCS: 13 - 14), moderate (GCS: 9 - 12) and severe (GCS: 3 - 8) level.

All patients underwent initial routine blood investigations including complete haemogram, renal and liver function tests, serum electrolytes (Na^+, K^+, Mg^{2+}, Ca^{2+}, PO_4), blood glucose, arterial blood gas analysis, chest X-ray, electrocardiogram (ECG) and urine routine-microscopy while the decision for lumbar puncture and radio-imaging (CT-head) was left to the clinical judgment of the treating physician. The patients were followed up for 2 weeks from the time of admission and the outcome was assessed as recovered, improved, deteriorated or died. The required data collection comprising demographic profile, clinical details and investigations was recorded on predesigned research proforma during the hospital stay.

Statistical Analysis

Descriptive statistical analysis was done by using mean and standard deviation for quantitative data and by using proportions or percentages for qualitative data.

Clinical presentations in different subgroups were compared by using normal tests of proportions for qualitative parameters and by using Student's 't' test for comparison of means in two groups.

Analysis of variance (ANOVA) was used for testing the significance of variability in different subgroups. Outcomes

were compared by using ANOVA and tests of proportions. Chi-square test was used for testing association of different outcomes with demographic characteristics. The level of significance was $P < 0.05$. SPSS 22.0 package was used for data analysis.

RESULTS

A total of 120 patients with AMS were enrolled from December 2018 to August 2019 and prospectively evaluated for outcomes at 2 weeks from time of admission. Table 1 describes the demographic profile of the study subjects. The mean age of the patients enrolled in the study was 49.76 ± 18.72 years (range 18 - 91 years).

Seventy-five (62.5 %) patients of the study group had at least one co-morbid illness. The most common co-morbidity was hypertension followed by diabetes mellitus and chronic liver disease in patients. Patients with diabetes mellitus as a co-morbidity had a poorer prognosis as compared to others ($P < 0.037$). We also observed that forty-one patients (34.2 %) were taking alcohol, twelve patients (11.9 %) were using tobacco as in smoking or chewable forms while five (4.2 %) were taking opium derivatives. An alleged history of poisoning was present in six patients (5 %).

On clinical assessment the most frequently reported associated symptoms were fever or headache with or without vomiting (38 %). Seizures or any focal neurologic deficit was observed only in 3 % of patients while neck stiffness was present in 22 (18 %) patients. Tachypnoea was observed in majority of patients (53 %) and hypotension was present in 20 % of them; all were responsive to fluid resuscitation.

A vast majority of patients 99 (82 %) presented with negative scores as assessed with RASS implying a common presentation with drowsiness or unresponsiveness rather than positive symptoms such as agitated / inappropriate behaviour or hallucination. Also, the patients predominantly had severe impairment on GCS as 82 (68 %) and had GCS score of equal to or less than eight.

Laboratory Investigations

All the patients were subjected to routine metabolic profile and it was found that fourteen patients (12 %) had blood glucose levels above 200 mg % while five patients (4 %) had hypoglycaemia. The rest were euglycemic. Thirty-three patients (28 %) had serum sodium levels above 145 mg % while twenty-one patients (18 %) had hyponatremia with serum sodium levels below 135 mg %. Patients with altered sensorium and having hyponatremia had a poorer outcome than those who had normal or higher serum sodium levels with a significant P value ($P < 0.022$). Diagnostic lumbar puncture was performed in 28 (23.3 %) patients. Meningitis was identified in 23 (19.1 %) patients out of whom 13 (10.8 %) patients had CSF profile suggestive of tubercular meningitis.

Neuro-Radiologic Investigations

A total of 81 patients underwent non-contrast computed tomography (CT) of head and aetiologic diagnosis was found in 23 of them. The most common diagnostic finding was haemorrhagic stroke in 11 (10 %) patients, ischemic stroke and hydrocephalus with 6 (5 %) patients each.

Aetiologic Diagnosis of Patients

The distribution of aetiologic causes for AMS was expectedly quite varied. A primary central nervous system disorder was identified in 55 (47 %) patients and the rest constituted systemic causes like sepsis, metabolic causes or poisoning. A detailed description of the aetiologic spectrum is as follows:

a) Cerebrovascular causes: It included both haemorrhagic and non-haemorrhagic strokes and transient ischemic attacks and was seen in 24 (20 %) patients with equivocal distribution of patients in haemorrhagic and non-haemorrhagic group. Ten out of thirteen patients with haemorrhagic stroke showed poor outcome (died / deteriorated) as compared to five patients out of eleven for ischemic stroke.
b) Infections: CNS infections (including meningitis or meningoencephalitis) and septic encephalopathy were seen in 40 (33 %) patients. While majority of patients with meningoencephalitis (15 out of 22) had a favourable outcome (recovered / improved); for those with septic encephalopathy, outcome was almost evenly distributed (7 out of 18).
c) Metabolic / endocrine: Included the metabolic (hypoglycaemia and hyponatremia), endocrine (diabetic ketoacidosis) and hepatic (encephalopathy) causes and were seen in 37 (30.8 %) patients. A vast majority of patients (27 out of 37) had a favourable outcome.
d) Toxicological / drug overdose: Included toxic drug intake, any drug overdose and snake bite and was seen in 11 (9.2 %) patients. All but one patient recovered without any sequelae. For the single mortality in this group, the type of poison remained unknown and index presentation was in a state of haemodynamic instability (shock).
e) Seizures: Included both generalised and focal seizures which were seen in 8 (6.7 %) patients. Out of a total of 5 such patients 4 patients recovered completely while one patient presented in status epilepticus and died.

It was observed that infections were the major aetiologic diagnoses in the younger and middle age groups with 57.5 % and 22.5 % respectively whereas cerebrovascular accidents were the major ones (54.2 %) in the elderly age group. Patients with secondary involvement of CNS like those with infections, metabolic / endocrine causes and poisoning had more chances of having positive outcome; whereas patients with primary CNS causes like cerebrovascular disease were more likely to have a negative outcome (75 %). Patients with meningoencephalitis predominantly had a favourable outcome.

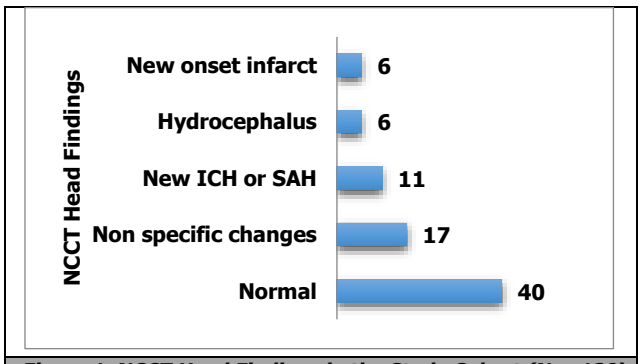

Figure 1. NCCT Head Findings in the Study Cohort (N = 120)

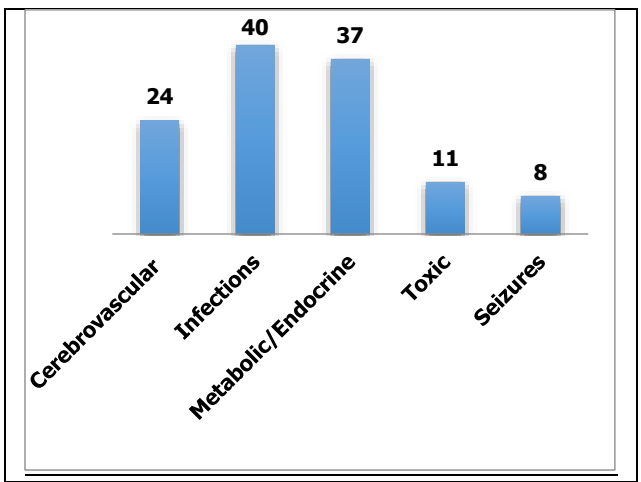

Figure 2. Distribution of Aetiological Diagnosis among the Patients (N = 120)

Variables	Number of Patients
Age (years) < 45	52 (43 %)
Gender: Male	79 (66 %)
Co-morbidities	
i) With at least one co-morbidity	75 (62 %)
ii) Hypertension	31 (32 %)
iii) Diabetes mellitus	26 (22 %)
iv) Chronic liver disease	20 (17 %)
Substance abuse	
i) Alcohol	41 (34 %)
ii) Tobacco	12 (10 %)
iii) Opium	5 (4 %)
Poisoning / drug overdose	6 (5 %)

Table 1. Demographic Profile in the Study Cohort (N = 120)

Outcome	Frequency (%)	RASS		GCS	
		Positive Score (+ 1 to + 4)	Negative Score (- 1 to - 5)	> 8	≤ 8
Recovered	36 (30 %)	7	29	25	11
Improved	36 (30 %)	9	27	30	6
Deteriorated	2 (1.7 %)	0	2	1	1
Died	46 (38.3 %)	5	41	26	20
Total		**21 (17.5 %)**	**99 (82.5 %)**	**82 (68.3 %)**	**38 (31.7 %)**

Table 2. Outcomes of Patients and Co-Relation with RASS & GCS Score (N = 120)

Outcome of Patients with Altered Sensorium

The outcomes were assessed at 2 weeks from the time of admission. Nearly 72 (60 %) patients either showed recovering pattern or were discharged from hospital. About 46 (38 %) patients died within these 2 weeks of admission while 2 patients showed a deteriorating trend and later died. It was seen that patients with age groups (18 - 45) and (46 - 60) years had better outcomes as compared to the elderly age group (> 60 years) where the patients either deteriorated or died which was statistically significant with ($P < 0.044$). It was also observed that males had a significantly better outcome than females ($P < 0.05$). Also, patients presenting with post-ictal confusion had comparatively better outcome than those presenting with other complaint ($P < 0.05$). Although patients with positive RASS score had a better outcome as compared to patients with a negative RASS score but it was not statistically significant. Patients with GCS score of greater than eight (38, 31.7 %) had a better outcome than those with GCS score less than eight which was statistically significant ($P < 0.02$).

DISCUSSION

Altered sensorium comprises a group of clinical symptoms rather than a specific diagnosis, and includes cognitive disorders, attention disorders, arousal disorders, and decreased level of consciousness.[11] Thus, aetiologic diagnosis and treatment of altered mental status are highly challenging for emergency physicians. The RASS and GCS score may be a reasonable method to screen for altered mental status in the fast-paced emergency department (ED) environment. The present study aimed at determining the aetiologic distribution and clinical outcome of AMS patients and prognostic value of RASS & GCS for such patients.

The mean age of the patients was 49.76 ± 18.72 years with majority of patients in the age group (18 - 45 years) constituting 43.3 % of the total population. Males constituted the majority (65.8 %) of patients. It was also seen that male gender had a better outcome as compared to females and this was statistically significant ($P < 0.05$); probably because of social neglect of women leading to hospital visits late in the course of disease.

In the present study 62.5 % of the patients had one or more co-morbidities. These were mostly present in the 45 - 60 years and > 60 years age groups. The most common co-morbidity was hypertension (HTN) in 25.8 % patients followed by diabetes mellitus (DM) present in 21.7 % of the patients. These patients had a poorer outcome as compared to those who did not have hypertension or diabetes which was statistically significant ($P < 0.05$). In addition, hyponatremia proved to be an independent prognostic marker for AMS patients as those having hyponatremia (17.5 %) had poorer outcomes compared to others and it was statistically significant with ($P < 0.05$). Hence, there is an urgent need to correct these electrolyte abnormalities to decrease the mortality and morbidity in such patients.

As evident, altered sensorium has a multitude of possible aetiologies involving both primary CNS events as well as secondary processes with an effect on the CNS. From this region of the subcontinent, very limited epidemiological studies have focused on altered mental status in this regard.[2] In our study the most common cause of altered sensorium was infections (33 %) which included CNS infections and sepsis, followed by metabolic and endocrine causes. This is in contrast to other studies where the most common causes for altered mental state were primarily

neurological.[1,12] In a study done by Hai-yu Xiao the most common aetiological factors were neurological (35 %), pharmacological and toxicological (23 %), systemic and organic (14.5 %) followed by infectious (9.1 %) causes.[12]

Here, the setting where the study is conducted could play an important determinant as medicine emergency room is more likely to receive patients with mixed patient population as against dedicated neurology care settings where referred patients are more likely to have primarily neurologic aetiologies. India being a developing country, where infections are a major cause of mortality and morbidity, identifying and treating these infectious causes can improve the outcomes significantly.

It was also seen that the reversible and treatable causes (infectious, metabolic, toxicological, seizures etc.) of altered sensorium were most prevalent in the younger and middle age groups as compared to the older age group (> 60 years) where the most common cause was cerebrovascular accidents like haemorrhagic and non-haemorrhagic strokes.

As expected, patients with infectious, metabolic and toxicological causes for the altered sensorium had better outcomes as compared to cerebrovascular causes in which outcome was predominantly negative and it constituted 37.5 % of the total mortality.

In a study by Lim Beng Leong, it was found that majority of younger (18 - 64 years) patients died from haemorrhagic stroke, while in older patients, mortality was distributed amongst ischaemic stroke (38 %) and haemorrhagic stroke (30 %).[8] Hence, determining the cause of altered sensorium in different age groups is important as the treatment is different for each aetiology and if not identified at the earliest, the mortality rates are high.

In our study, patients were initially assessed using GCS and RASS. It was seen that GCS as a screening tool in patients with AMS is a good predictor of outcome. A GCS score ≤ 8 was seen in 68.3 % patients. Patients with GCS score > 8 had a better outcome than the patients with GCS score ≤ 8 which was statistically significant ($P < 0.05$). In a study done by Buist M et al. a GCS score of 3 and a decrease in GCS score by more than 2 points was independently associated with mortality.[13]

We observed a RASS score of (- 1 to - 5) in 82.5 % of the patients and a RASS score of (+ 1 to + 4) in 7.5 % of the patients. It was seen that effect of RASS score on the outcome of patients was statistically insignificant which was similar to a study done by Sessler CN et al.[14] Thus, it has no prognostic implication whether the patient with AMS presents with negative RASS score like lethargy, obtunded sensorium, social withdrawal or positive RASS score like agitation, combative behaviour, hallucinations etc. Nevertheless, RASS may still be utilised for early recognition for subtle manifestation of altered mental status and to compare different studies conducted in various clinical and geographically diverse settings.

Although the outcome of patients with AMS is contingent upon multiplicity of factors like duration of AMS, presence of co-morbidities, age of the patient and aetiologic diagnosis, in our study we observed that nearly 40 % of the patients died or showed a deteriorating trend. This constitutes a subgroup of patients that is most likely to exceedingly consume healthcare resources and add to the workload and exigency to already overburdened emergency services. Also, altered sensorium is very difficult to express in a graded or stratified manner and may have many different interpretations to different observers, therefore some standard scales may be useful. In an emergency department, we should be aware of the demographic / epidemiologic profile for likely diagnosis and outcomes so as to prioritise and treat these patients more efficiently.

CONCLUSIONS

Altered mental status has varied presentation and the aetiologies for AMS are evenly distributed among primary CNS causes and systemic causes leading to secondary AMS. While meningoencephalitis appears to have better outcome as against stroke for primary AMS; those with poisoning have more favourable prognosis for secondary AMS patients. The subjective description of AMS may not be the best way for documentation. It is helpful to use some standardised scoring systems that bring uniformity in assessment as well as prognostic implications. There is a need for development of dedicated objective tools for use in emergency room scenario.

Limitations

Ours being a single centre study in a tertiary care setting, may not represent the patient population in other healthcare facility and thus, has limited external validation. Also, the observation period of two weeks for outcome assessment regarding neurologic recovery may be rather short for certain subgroups of patients likes those with stroke. Thirdly, the study suffers from limited sample size.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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