

Etiology, Clinical profile and Outcome of Acute Encephalopathy in Adult Patients: A hospital based cross sectional study from Northern India.

Rozia Bukhari¹, Irfan Ahmad Shah², Pratap Sharma¹, Hardeep Singh³, Shoaib Yousuf⁴, Adil Ahmad¹

1. Postgraduate, Department of Medicine Government Medical College Srinagar
2. Assistant professor, Department of Medicine Government Medical College Srinagar
3. Professor, Department of Medicine Government Medical College Srinagar
4. Lecturer, Department of Medicine Government Medical College Srinagar

Corresponding author:

Dr. Irfan Ahmad Shah

Assistant Professor, Department of Medicine Government Medical College Srinagar.

Address: Faculty quarter G, GMC boys hostel Bemina Srinagar J&K.

Email: irfanskims@gmail.com

Abstract

Acute encephalopathies or acute confusional states are among the commonest causes of hospital admissions especially among the elderly population. A treating physician needs to have a thorough knowledge of the various etiologies, clinical presentations and associations of acute encephalopathy in order to manage these patients in a timely and efficient manner. The present study was a prospective cross sectional study conducted over a period of one year aimed to know the dynamics of encephalopathy patients attending the medical emergency. Patients who met the inclusion and exclusion criteria were included after taking consent from the attendants. The mean age of the patients was 60 years for males and 61.8 years for females. About 19.7% patients admitted in emergency department had acute confusional state. The most common etiologies in the study were strokes (25.6%), metabolic (24.9%) and septic (18.5%) encephalopathies followed by seizures (13%) and intracranial infections (5%). About 35.5% cases had multiples factors responsible for encephalopathy. The most frequent symptoms besides encephalopathy included weakness on one side of the body (15.8 %), headache (14.1%), cough (12.6%), incontinence (10.7), breathlessness (10.1%) and fever (10.2%). The overall mortality in the study was 16.5%. Mortality was significantly higher in patients with weak or non-palpable pulses, hypotensive patients, patients with aberrant pupillary responses, patients admitted in winter period and obese patients. Also low mean arterial PH, oxygen saturation and mean diastolic BP and high total leukocyte count and potassium were significantly associated with mortality.

Keywords: acute confusional state; delirium; altered sensorium; coma; sepsis; stroke.

Introduction

Encephalopathy en-cephalo (in Greek, means "brain") and pathos (suffering) refers to a change in mental state that affects the patient's consciousness or level of enthusiasm. Encephalopathy, rather than a diagnostic, defines a disorder with multiple possible causes. While encephalopathy can refer to changes in mental status caused by either focal or widespread brain injuries, the term is most usually used to refer to the latter¹. The global syndrome of encephalopathy condition can be mimicked by focal cognitive abnormalities

such as aphasia or forgetfulness. Common neurological signs of encephalopathy include progressive loss of memory and cognitive capacity, subtle personality changes, inability to focus, tiredness, and progressive loss of consciousness. Other neurological symptoms may include myoclonus, nystagmus, tremor, muscle atrophy and weakness, dementia, seizures².

Acute confusional states (ACS) are typically brought on by a stroke, an electrolyte imbalance, or a systemic illness in older age groups. Acute poisoning, central nervous system illness, or seizures are the most frequent aetiologies of acute confusional condition in younger age groups. It is crucial to remember that many reasons of altered awareness, such as infections and metabolic disorders, are totally curable with timely diagnosis and appropriate medication. On the basis of phenomenology, encephalopathy has been divided into subtypes. The psychomotor activity has received the most attention. There have been proposed classifications for the types of hyper-activity (15-29%), hypo-activity (19-43%), mixed type (43-52%), and no psychomotor disruption (0-14%)^{3, 4, 5}. Except for the theory that encephalopathy from drug withdrawal states has a hyperactive presentation, it is unclear whether the subtype and risk factors for encephalopathy or aetiologies are related. It has been hypothesised that hypoactive encephalopathy episodes result in a longer hospital stay, which implies a potentially worse prognosis^{3, 4}. Around 15% to 20% of all general hospital admissions result due to an acute confusional state. It is the most frequent hospitalization-related complication in the senior population, with occurrence rates ranging from 11 to 42%⁶. Additionally, those who already have some form of cognitive impairment have a higher incidence. Also acquired immunodeficiency syndrome (AIDS) and cancer patients had higher prevalence rates of delirium⁷. Despite these facts, acute confusional state is still poorly understood and treated; in certain centres, up to two thirds of patients go undiagnosed. Acute confusional states can be prevented in up to one-third of instances and the lack of awareness results in significant morbidity and mortality as well as a financial load on the national health system⁶.

Amongst the etiologies of encephalopathy, neurological causes are the commonest. Encephalopathy continues to be the most prevalent mental health condition affecting senior hospital patients today, impacting 14–56% of them, and those in nursing homes, affecting about 6-24% of them⁸. The exact prevalence of encephalopathy in the general population is yet unknown; however it may be 1% of those over the age of 55. The outcome of encephalopathy in the adults is variable, ranging from complete recovery to permanent brain damage or death and depends on early diagnosis and appropriate management with the help of laboratory investigations and imaging. Medical literature has only scarce data regarding encephalopathy in adults with even fewer studies in Indian adults. Hence this study will be undertaken to evaluate the etiology, clinical profile and outcome of encephalopathy in adult patients.

Materials and Methods

The study prospectively enrolled all patients with acute confusional states admitted in the emergency department of a tertiary care hospital in Srinagar over a period of 12 months between April 1, 2021, and March 31, 2022. Adult male and female patients who satisfied the inclusion and exclusion criteria were enrolled in the study. Informed consent was taken from the attendants/companions of the patients for participation in the study.

A patient was included and deemed to have acute confusional state if the attending physician identifies any one of the following criteria for the patient at the time of initial presentation: Glasgow coma scale score(GCS) less than 15, Mini mental state examination scores less than 24, Quick confusional score less than 15⁹, was not alert and oriented to person, place and or time, diminished responsiveness to verbal or physical stimulation, difficult to arouse, unable to remain awake or conversant, hallucinations, confusion, bizarre or inappropriate behaviour. Patients were excluded if they had one of the following: Age less than 18, any obvious evidence of head trauma, current or chronic psychiatric disease, dementia, pregnancy or was a known case of hepatic Encephalopathy.

An initial history of presenting illness, relevant past and comorbid history and drug/exposure details were taken in the emergency. Complete systemic and general physical examination was done at presentation. Initial tests like haemogram, kidney function test, liver function test, blood sugar, electrocardiogram, chest X-ray, and arterial blood gas testing were performed routinely in all patients. Within six hours of being admitted to the hospital, patients got a cranial computed tomography (CT) scan. Specific tests including cerebrospinal fluid analysis were ordered wherever necessary. History and examination were reviewed wherever there was diagnostic dilemma. The parameters that were assessed in our study participants included clinical presenting symptoms and signs, severity of symptoms, GCS score and its prognostic value, past significant medical illness and risk factor assessment, etiology, mortality/ morbidity and factors affecting mortality. Also comparisons between initial and final diagnosis were made and factors affecting diagnosis were analyzed. A diagnosis was said to be partially matched if the initial and final diagnosis were different but were from the same group. Complete recovery was defined as patient returning to baseline functional status at the time of discharge. Partial recovery was defined as patients as patients who were not fully functional at discharge or bedbound due to disease or its complications. The study was approved by ethical committee of the institute vide letter no. IEC-GMC-SGR/M/36.

After data collection, the data was presented in 'data matrix' in the form of ungrouped data for further analysis. Frequency estimation, percentages and paired t-test were done. The data were analyzed using SPSS statistical software. The values were expressed as mean with standard deviation and percentages and p value of ≤ 0.05 was taken as statistically significant.

Results

Most of the patients were in the age group of 61-70 years. Mean age was 60 ± 17.80 years for males with maximum 105 years and minimum 18 years. For females mean age was 61.8 ± 15.8 with minimum of 18 years and maximum of 96 years.. The distribution among sexes was fairly equal with 53.7% comprised by males and 46.3% comprised by female patients (**Table 1**).

A total of 3202 patients were admitted overall during the study period. Of these, 631 patients had acute confusional states. Therefore, 19.7% of participants in our study had acute confusional state. The mean GCS was 10.5 (SD 2.45) with a minimum of 3 and maximum of 15 median GCS was 11. The frequency in various groups in descending order being 12-15 having 295 patients (46.8%), then 8-11 group having 230 patients (36.5%) followed by <8 group having 106 patients (16.8%) .

The various etiological groups in our patients have been listed in **table 2**. Strokes, metabolic and septic conditions constituted the three most common aetiologies in decreasing order of frequency. The conditions listed under Cerebrovascular accident (CVA) group (total 161) included ischemic stroke (98), Transient ischemic attack (2), subarachnoid haemorrhage (9), and intracranial haemorrhage (98). The putamen made up 55.1% of the bleed locations in the ICH subgroup, followed by the thalamus (21.4%), pontine (7.3%), cortical (5.1%), cerebellar (5.1%), ventricular (3%), and lobar (3%). In the seizure group of 83 patients 60 patients had new onset seizures and 23 were known seizures or with past history of seizures. Among the patients with new onset seizures, 35 case had symptomatic seizures and the most common etiology was past stroke (14), hyponatremia (06), hypoglycaemia(06) and intracranial space occupying lesion {(ICSOL)04}.

Respiratory failure (23.6%), renal failure/uremia (21%), hyponatremia (17.8%), hypoglycaemia (16.6%), hepatic encephalopathy (14%), toxic/alcoholic conditions (3.8%), hypercalcemia (1.9%), and hyperglycemia(1.3%) comprised the metabolic group in decreased order of frequency respectively. The metabolic encephalopathy group in our study consisted of 157 patients and was a sizable group in itself. In the poisoning group, organophosphorous poisoning was the most common (04 patients), followed by intravenous opioid overdose (03). Infection related diagnoses included Respiratory infections which constituted about 55.5% of cases in the sepsis / infection category, followed by urinary tract infections (30.0%), nonspecific (10.2%), and viral syndromes (4.3%). Intracranial infections accounted for about 5 % of cases in which chronic meningitis accounted for 40.6% of diagnoses, followed by encephalitis (37.5%), acute meningoencephalitis (12.5%), and brain abscess (9.4%). Subdural hematoma (SDH) accounted for 09(1.5 %) cases among which 05 had 'acute on chronic' and 04 had large chronic subdural hematomas. Patients who expired before final diagnosis or improved without any specific intervention were placed in the unknown group and accounted for 17 cases.

Besides encephalopathy, other symptoms were present in the patients in varying degrees.

Table 3 lists the common symptoms other than acute confusion. The most frequent symptoms included weakness on one side of the body (15.8 %), headache (14.1%), cough (12.6%), incontinence (10.7), breathlessness (10.1%) and fever (10.2%). In the past and personal history, 242 individuals (38%) in the sub groups had hypertension. CVA had the highest prevalence of hypertension (73.3%). 169 individuals (26%) had diabetes mellitus. Diabetes was present in 45.2% of the metabolic derangement group's subgroups, followed by 35.9% in sepsis group. 13% of CVA patients had a prior history of stroke, and 10% of patients had a prior history of an acute confusional condition of a similar nature. In patients in the metabolic and seizure groups, prior similar history was most frequent (19.1% and 15.6%, respectively). 127 patients (19%) had a history of smoking, or about one out of every five patients. Smoking was prevalent in 33.5% of CVA, 51.6% of CVS/shock, and 19.1% of the metabolic group, among other categories.

A total of 35.5% of patients did not fit into a single diagnosis and had multiple causative factors, each of which contributed to acute confusional condition (**Table 4**). Multifactorial aetiology was mostly considered in patients in the infectious and metabolic groups. 72 out of 117 cases in the sepsis group, 59 out of 157 in the metabolic group were considered to have

multifactorial etiology on detailed evaluation. Analyzing the relationship between the final diagnosis and the one made based on the initial clinical evaluation, 6.4% of patients had mismatched diagnoses, 19.4% had partial mismatches, and 74.2% had no mismatch. When we combined the entirely and partially matched groups, we discovered that a sizable portion of patients, 93.6%, had the appropriate working diagnosis following the initial evaluation (history and examination). 147 patients with CVAs (82.2%), 81 patients with seizures (90.0%), and 8 patients with poisoning (100%) had accurate diagnoses. 70.8%, 60% and 50% cases respectively in the metabolic, intracranial infection and ICSOL groups had correct diagnosis on initial clinical evaluation.

Out of the 631 individuals, 104 people died with mortality rate 16.5%. 98 individuals (15.5%) had a partial recovery, while 429 (68%) had a full recovery. Amongst the subgroups of Glassgow coma scale, the mortality rates were 63% (67 out of 106), 11% (25 out of 230), and 4% (12 out of 295) respectively for ≤ 8 , 8-11 and 12-15 subgroups. The mortality was significantly impacted by the aetiology of ACS. Seizures (3.6%), cerebral infections (6.3%), and poisoning (12.5%) had lower fatality rates. Sepsis (25.6%), CVA (24.9%), and CVS/Shock groups (45.2%) all exhibited considerably higher fatality rates.

When comparing the various laboratory factors among patients who survived and those who expired, mean Leukocyte count and mean serum potassium was higher in expired patients (15.17 vs 10.22) and (4.08 vs 3.67) respectively (**Table 5**). Also mean PH (7.32 vs 7.37), mean saturation (89.28 vs 92.44) and mean BP (87.02 vs 96.77) was lower in the patients who died compared to those who survived. All the above differences were statistically significant.

Tables

Age group (Yrs)	Male	Female	Total
18-30	32 (9.5%)	17 (5.8%)	49 (7.8%)
31-40	23 (6.8%)	22 (7.6%)	45 (7.1%)
41-50	32 (9.5%)	25 (8.6%)	57 (9.0%)
51-60	70 (20.6%)	46 (15.7%)	116 (18.4%)
61-70	102 (30.0%)	97 (33.2%)	199 (31.5%)
71-80	50 (14.7%)	58 (19.9%)	107 (17.0%)
81-90	20 (5.9%)	20 (6.8%)	41 (6.5%)
>90	10 (3.0%)	7 (2.4%)	17 (2.7%)
Total	339 (53.7 %)	292 (46.3%)	631 (100%)

Table 1: Age and sex distribution of patients

Diagnosis	Number(%age)
CVA	161 (25.6%)
Metabolic	157 (24.9%)
Sepsis	117 (18.5%)
Seizure	83 (13.0%)

Intracranial infections	32 (5.0%)
Shock	31 (4.9%)
ICSOL	16 (2.6%)
Poisoning/ drugs	8 (1.3%)
SDH	9 (1.5 %)
Unknown causes	17 (2.7 %)
Total	631 (100%)

Table 2: Etiological groups of Patients in our study.

Symptoms	Number	Percentage
Weakness of one side of body	100	15.8
Headache	89	14.1
Cough	80	12.6
Urinary Incontinence	68	10.7
Drowsiness	64	10.1
breathlessness	58	9.2
Irrelevant talking	56	8.8
Fever	52	8.2
Slurred speech	52	8.2
Seizures	51	8
Vomiting	47	7.4
Decreased urine output	43	6.8
Pedal edema	41	6.4
Constipation	39	6.1
Pain abdomen	34	5.3
Constitutional	34	5.3
Diarrhoea	30	4.7
Jaundice	27	4.2
Dysuria	23	3.6
Abnormal behaviour	22	3.4
Edema	21	3.3
Miscellaneous	21	3.3
Vertigo	20	3.1

Abdominal distention	19	3
Drug overdose	16	2.5
Osmotic symptoms	12	1.9
Irritable	10	1.5

Table 3: Various symptoms apart from Acute Confusion

Diagnosis	Multifactorial Etiology		Total
	No	Yes	
CVA	120	41	161
Metabolic	98	59	157
Sepsis/infections	45	72	117
Seizures	70	13	83
Intracranial Infections	27	5	32
Shock	10	21	31
ICSOL	14	2	16
Poisoning	7	1	8
SDH	6	3	9

Table 4: Patients having Multifactorial Causes (p value = 0.001)

Prognostic Factor	Mean Survived (n= 527)	Mean Dead (n= 140)	P Value
TLC	10.233	15.172	0.023
PH	7.3766	7.3285	0.009
SAO ₂	92.44	89.28	0.002
Potassium	3.677	4.008	0.041
Diastolic BP	78.84	70.07	0.048
Mean BP	96.77	87.02	0.042

Table 5: Effect of Laboratory Factors and blood pressure on Mortality.

Discussion

A total of 3202 patients in total sought medical attention during the course of the study period of 365 days. Among them 631 patients who presented to the emergency department (ED) had an acute confusional state. According to studies by Harrison and Holden J et al, 2008) the proportion of patients with acute encephalopathy in the overall ED census was 21% and 23%, respectively^{10, 11}. So our results are in line with their findings. The age group 61 to 70 years represented the majority of entries. Mean age of males was 60 years while for females mean age was 61.8 years. Males made up 339 (or 53.7% of the population) and females 292 (or

46.3%). In the Kanich et al investigation, there were 43% (137) females and 57% (180) males¹².

In our study, the most frequent final diagnosis was CVA (cerebrovascular accidents), which affected 25.6% cases followed by metabolic and septic causes. Intracranial infections affected 5.0% patients followed by the cardiovascular/shock group (4.9%), ICSOL (2.6%), poisoning (1.3%), SDH (1.5%), and unknown (2.7%). According to the study by Mallik and David, neurologic (28%) and toxicological (21%) diagnoses accounted for the majority of cases of altered mental status, followed by trauma (14%), psychiatric (14%), infectious (10%) and endocrine/metabolic (5%), causes¹³. About 25.8% of the subjects in the Meagher et al. study had structural causes for their comas. The majority of these individuals (24.1%) had a CVA¹⁴. Metabolic derangements were the second most common cause of encephalopathy in our study. Respiratory failure was the most frequent diagnosis among the metabolic conditions followed by renal failure. Infections group was the third most common and among infections, respiratory infections were the most common followed by urinary tract infections. In the study on delirium by George J et al. among older patients with confusion as one of their complaints, the aetiologies were infection 35% (75), metabolic 15% (34), CVA 11% (24), drug-related 11% (24), cancer 5% (10), ICSOL 0.5% (1), SDH 1% (2), fractures 5% (10), and other 6% (12)¹⁵.

A total of 220 (35%) individuals had other coexisting issues that, in addition to the major issue, may have contributed to the severity of confusional state. Some people had one coexisting condition, while some had two to three. The metabolic group and the sepsis groups had the most of them followed by the CVA group. Renal impairment was the complicating condition that was present the most frequently followed by infections, hypoglycaemia, seizures, and dehydration. About 25% in the research by Wofford et al. had two or more equally contributing factors¹⁶. In our study majority of patients had an appropriate diagnosis during the initial evaluation in the emergency department and only about 6.4% patients had a completely mismatched diagnosis finally. Besides alteration in sensorium, the major associated symptoms in our patients were weakness of one side, headache, cough, breathlessness and fever. The higher prevalence of neurological symptoms was probably because strokes were a major category in our study. Hypertension was the most common comorbid condition seen in about 38% of patients followed by diabetes in about 26% of patients. Hypertension was more common in the stroke group while diabetes was most prevalent in the metabolic and sepsis groups. About 10% had prior history of similar illness of acute confusional mostly in the seizure and metabolic groups. Smoking was mostly prevalent in stroke and shock groups.

The overall mortality in our series was 16.5%. In the study conducted by Kanich et al, 91% of the patients survived, whereas 2% died in the emergency department (ED) and 7% died after being admitted to the hospital¹². A higher mortality in our series was probably due to higher number of patients with haemorrhagic stroke and shock. On the basis of GCS, the ≤ 8 group had 63.0% mortality, 8-11 had 11.0% mortality and patients in 12-15 GCS group had 4.0% mortality. Similar to our study, Farrukh et al divided the patients into three groups according to GCS¹⁷. In the group with ≤ 8 GCS, mortality was considerably greater. The increased risk of death in the intracerebral bleed as opposed to cerebral infraction was also

worse according to GCS rating, as was the conscious level. Hence mortality and GCS are inversely associated in encephalopathy patients. The mortality was also determined by the cause of encephalopathy. The shock group had the highest mortality followed by the sepsis group and the CVA groups respectively. The study by Nadeem et al. found that hemorrhagic CVA had a mortality of 63%, ischemic CVA had a mortality of 36%, and overall structural coma had the poorest prognosis with 43% patients dying of it¹⁸.

Among the clinical and laboratory factors, mortality was higher in patients with weak or non-palpable pulses, hypotensive patients, patients with aberrant pupillary responses, obese patients, and patients admitted during the winter and all these differences were clinically significant. In their research of juvenile age group non-traumatic coma patients, Bansal et al. discovered that circulatory instability and inadequate pulse volume at admission and after 48 hours were linked to 66% death. They also noticed that hypotension was a poor prognostic indicator, with two-thirds of patients who had it at the time of admission passing away¹⁹. Pupillary and oculocephalic reflexes were shown to be statistically significant to assess prognosis in the Sharma et al. investigation, and when any two brainstem reflexes were missing, no patient had a successful recovery²⁰. Mean TLC (15.1 vs 10.2) and serum potassium (4.1 vs 3.6) were higher in patients who died than who survived. Also mean arterial PH, oxygen saturation and mean diastolic BP were lower in the patients who expired than those who survived and the differences were significant.

To conclude, the present study was an attempt to identify significant and common causes of acute confusional state and its outcome in our population. This will help in timely identification of various diseases when treating patients with acute confusional state. Although this cross-sectional randomised research with a small sample size may not accurately reflect the state of the community, its resemblance to reality may not be understated and gives a fair idea of the state of affairs of patients of acute encephalopathy visiting our emergency departments.

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