

Clinical profile and outcome of acute encephalitis syndrome (AES) patients treated in College of Medical Sciences-Teaching Hospital

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ABSTRACT

Objective

Acute encephalitis syndrome is a cause of significant morbidity and mortality in Nepal. Although Japanese encephalitis virus (JEV) was thought to be a major cause for acute encephalitis syndrome, more non-Japanese encephalitis virus cases are reported. The outcome of patients with acute encephalitis syndrome is variable. Our study was designed to study the clinical profile and outcome of patients with acute encephalitis syndrome managed in tertiary care center in central Nepal.

Methods

The record of patients admitted with diagnosis of acute encephalitis syndrome, from January 2010 to December 2010 in College of Medical Sciences-Teaching Hospital (CMS-TH) was reviewed. They were classified clinically as meningitis, encephalitis and meningoencephalitis. The clinical details and reports of the patients were recorded and analyzed.

Results

Total of 85 cases of meningitis and encephalitis were identified. Mean age was 19.18 years. Fifty-six (65.9%) patients were males and 29 (34.1%) were females. Sixty (70.58%) patients had meningitis, 8 (9.41%) had encephalitis, and 17 (20.0%) had meningoencephalitis. JE serology was positive in 4 patients (4.7%). Seventy-two (84.7%) patients made full recovery and were discharged from hospital. Thirteen (15.3%) patients left against medical advice (LAMA).

Conclusion

Acute encephalitis syndrome is still a major public health problem in Nepal. Few of these patients have Japanese Encephalitis. There is a trend towards improved outcome because of availability of improved health services. However, financial constraint remains a challenge in management of acute encephalitis syndrome.

KEY WORDS: Acute encephalitis syndrome, encephalitis, Japanese encephalitis, meningitis, meningoencephalitis.

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INTRODUCTION

Acute encephalitis syndrome (AES) is defined as acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures) in a person of any age at any time of year.¹ Japanese encephalitis (JE), a leading cause of AES in our continent,² affects about 50,000 people and causes 10,000 deaths each year.¹ However, because of incomplete surveillance in many affected areas, reported cases of JE greatly under-represent the true impact.¹ Even though to control JE, the identification of patients with AES is essential, AES case definition for children on hospital admission

had only 65% sensitivity for JEV-infected cases.³ The first outbreak of JE in Nepal was reported in 1978 from Rupandehi, a terai district.⁴ Outbreak of JE in the hilly region(Kathmandu valley) was confirmed in 1997,⁵ and in 2006 JE endemicity in Kathmandu was established.⁶ Total 24 Terai districts are known to be endemic (Figure: 1) with case fatality rate (CFR) ranging from 5-29% (average 10%). Average case fatality in all ages is about 20% in Nepal.⁴ The landscape of AES in India has changed in the previous decade, and both outbreak investigations and surveillance studies have increasingly reported non-JEV aetiologies.⁷ Our study was designed to describe the clinical profile of AES and understand their clinical outcome.

Japanese encephalitis endemic districts-Nepal

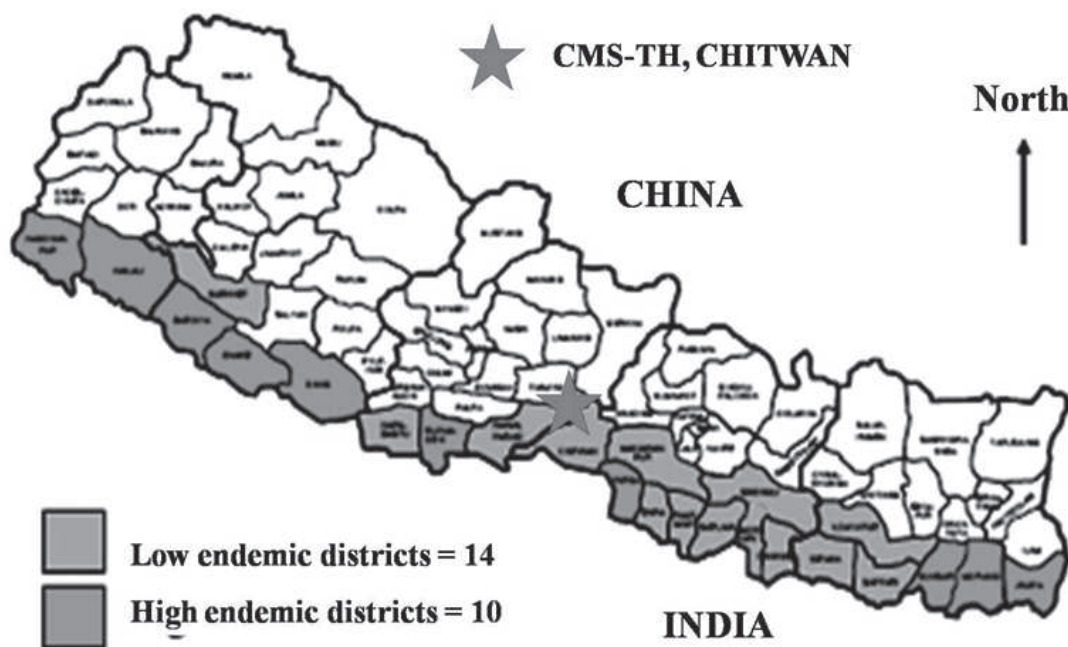


Figure 1: Terai districts of Nepal. CMS-TH location (Star) showing its broad catchment area

METHODS

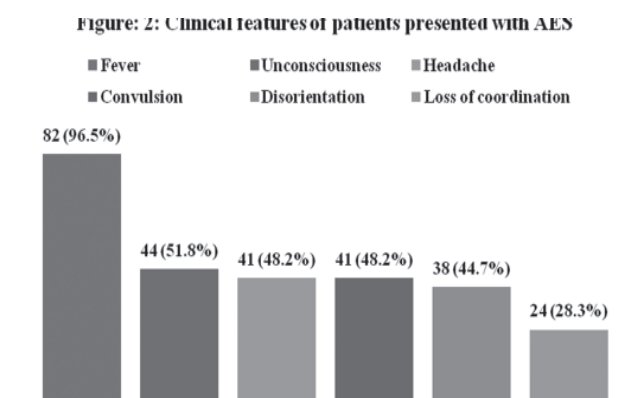
This is a descriptive, cross-sectional study of patients admitted from January 2010 to December 2010 with diagnosis of AES in CMS-TH, a tertiary care neurological center in Chitwan. Records of

all the patients having features of AES as WHO case definition criteria were included in the study. Clinically they were classified as: (a) meningitis, if they had fever with meningeal signs and absence of seizure, (b) encephalitis, if they had fever with

seizure but absence of meningeal signs, and (c) meningoencephalitis, if patients had fever, seizure and altered sensorium. Clinical details and investigations particularly JE serology (ELISA for IgM) and their clinical outcome were recorded and analyzed. The results of JE serology was obtained from Nepal Public Health Laboratory, Teku Kathmandu through the local government agency.

RESULTS

Total 85 cases of AES were admitted from the January 2010 to December 2010. Males were more than females [56 (65.9%): 29 (34.1%)]. Age ranged from 0.08 year to 86 years (Mean age: 19.18 years). Forty-nine (57.6%) patients were from Chitwan district. Others were from neighboring districts: 30 (35.3%) from Makwanpur, 5 (5.9%) from Bara and 1 (1.2%) from Parsa. Clinical features included fever in 82 (96.5%) patients, unconsciousness in 44 (51.8%), headache in 41 (48.2%), convulsion in 41 (48.2%), disorientation in 38 (44.7%), loss of coordination in 24 (28.3%) patients.(Figure: 2)



Fifty-nine (69.41%) cases had presented with clinical meningitis out of which 40 (47.05%) were males and 19 (22.35%) were females. Similarly, 17 (20.0%) cases presented with

meningoencephalitis, out of which 9 (10.58%) were males and 8 (9.41%) were females. Eight (9.41%) patients presented with encephalitis, 6 (7.05%) males and 2 (2.35%) females. 1 (1.17%) patient was diagnosed to have TB meningitis. (Table 1)

Table 1: Patterns of the distribution of cases (n=85)

Diagnosis	Male	Female	Total
Meningitis	40(47.05%)	19(22.35%)	59(69.41%)
Meningo encephalitis	9(10.58%)	8(9.41%)	17(20.0%)
Encephalitis	6(7.05%)	2(2.35%)	8(9.41%)
TB Meningitis	1(1.17%)	0(0%)	1(1.17%)

Serology for JE had been tested from CSF in 4 (4.7%) patients, serum in 45 (52.9%) patients and both serum and CSF in 36 (42.4%) patients. Out of 85 cases 4 (4.70%) were JE serology (IgM) positive: 2 patients (50%) from Chitwan and 2 (50%) neonates from Makwanpur.

Seventy-two (84.7%) patients made full recovery and were discharged from the hospital. Thirteen (15.3%) patients left against medical advice (LAMA) because of financial constraints.

Fifty-one (86.44%) out of 59 patients with meningitis made full recovery. Similarly, 13 (76.47%) out of 17 patients of meningoencephalitis recovered and all (100%) of patients with encephalitis made full recover and discharged. Nine patients (15.25%) of meningitis and 4 patients (23.52%) of meningoencephalitis patients left against medical advice due to financial reasons.(Table 2)

Table 2: Outcomes of the cases (n=85)

Diagnosis	Discharged	LAMA	Total
Meningitis	50(84.74%)	9 (15.25%)	59(100%)
Meningoencephalitis	13(76.47%)	4(23.52%)	17(100%)
Encephalitis	8(100%)	0(0%)	8(100%)
TB Meningitis	1(100%)	0(0%)	1(100%)
Total	72(84.7%)	13(15.29%)	85(100%)

DISCUSSION

Our study showed that AES affected entire age group from children to elderly patients. Although children are more vulnerable, a person of any age, at any time of a year is known to be affected by AES although there is tendency for high incidence specifically during monsoon and post monsoon period.^{8,9,10,11}

JE is one of the important causes of AES. Although reports emphasize JE in pediatric populations, JE also produce morbidity and mortality in adults in Nepal.¹²

Vaccination has brought a marked difference in incidence of JE. Hoke et al have demonstrated this difference; 51 per 100,000 in vaccinated when compared to 5 per 100,000 in non-vaccinated.¹³ Vaccination campaigns with SA-14-14-2 vaccine are although protecting the children less than 15 years, older people are more affected.¹⁴ To note, none of our patients were vaccinated against JE.

Males were more affected in our cohort. Similar pattern was observed in surveillance in Bangladesh where amongst 218 patients, 66% of the affected were males.¹¹

Kakkar et al and Thomas et al also demonstrated males to be affected more than females.^{8,12}

Interestingly, Roy et al have postulated that the male dominance may be due to the reason of males sleeping outside the houses with bare body and hence more prone for mosquito bite.¹⁵ However, exact reason for male dominance in AES still remains elusive.

Majority (57.6%) of our patients were from Chitwan, a terai district. Terai districts in Nepal are known to be “hot spot” for JE. In 1978, the first outbreak of JE in Nepal was documented from Rupandehi, a terai district.⁴ JE recently is observed to affect hilly region as documented by identification of JE in Kathmandu valley in 1997¹⁶ and 2006.¹⁷

By now we know that JE is not uniformly distributed in our country, but is found to be primarily confined to 24 districts of Terai that border India.¹² Although AES is not synonymous with JE, the spatial, temporal, and landcover configuration distributions of JE and AES has been observed to have a high similarity in pattern between JE and AES across all three dimensions

of comparison.¹⁸ However, we did not have any patients from hilly regions.

The major clinical presentations of AES in our study were fever, unconsciousness, headache, convulsion, disorientation and lack of coordination in decreasing frequency. All of these features plus ocular palsies, hemiplegia, extrapyramidal dysfunctions have been documented in various studies.^{15,16,17,19} Early clinical findings suggested in AES are an increase in irritability, somnolence or abnormal behavior greater than that seen with usual febrile illness.⁹

Amongst the clinical subtypes, clinical meningitis was the major presentation followed by meningoencephalitis and encephalitis. Intriguingly, males predominated throughout entire clinical subtypes. One patient was diagnosed as TB meningitis. Serology for JE (IgM) was tested in all 85 cases and four patients (4.07%) were found to be positive. This low positivity for JE is not unusual in AES because JE once thought to be the major identified cause of AES is however, not synonymous to AES. AES is associated with a variety of other pathogens including other viruses, bacteria and parasites. It has been estimated that a quarter to one-third of AES cases in Nepal are due to JE.^{12,20} At this point it has to be however understood that an Indonesian study with special attention to testing protocol detected 30% more JE infections²¹ but a study from Nepal, after increasing the case load by 30% from originally detected JE cases, still found a significant number of JE negative cases presenting as AES.¹² In a study from Japan, among 105 aetiologically diagnosed cases of AES, the most common causative agents were measles virus (23%), rubella virus (23%) and HSV

(20%).²² After carefully observing the clinical pattern and reviewing literatures, we are convinced that we also have causes other than JEV that cause AES in our set-up but because of limited resources, we are not able to test for different etiologies.

Outcome in AES is variable in different studies especially in JE positive and JE negative cases. Some study demonstrated similar deaths¹² while other emphasizes AES due to JE to have better outcome.²⁰ To note, Thomas et al have demonstrated higher mortality in adults over 35 years.¹² Majority (84.7%; n=72) of our patients made full recovery and were discharged. All our patients with JE made full recovery, although the number of patients was less. However, similar results are less likely to be obtained in a large scale study. But better services and management protocols followed in our institution definitely have an influence on better outcome of our patients. We did not find the record of neurologic sequelae of our patients at discharge.

Leaving against medical advice (LAMA) is usual in developing countries like ours where we do not have proper health policy and where patients have to pay for the treatment. Thirteen (15.3%) patients left against medical advice (LAMA) because of financial constraints. Similar trend is also reported from our neighboring country.²³

LIMITATIONS

Our study has an inherent limitation of a retrospective study. In addition we were unable to retrieve lab data and describe CSF profiles of all patients. Because of lack of lab support we were not able to get other virological profile, which may have identified other causes of AES.

CONCLUSION

AES is a major burden in our clinical practice. Non-JE causes for AES should be strongly considered as there is documentation of other etiologic agents. Better treatment facility and protocols may have better outcome in these patients. Financial constraint remains a major challenge in management.

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