A Clinico-Demographic Profile of Acute Encephalitis Syndrome and its Outcome Among Children

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ABSTRACT

Introduction: Acute Encephalitis Syndrome (AES) is defined as acute onset of fever and a change in mental status and/or new onset of seizures in a person of any age, in any geographical region, at any time of year. It may be due to viral or bacterial aetiology. Dysfunction of motor system and mental retardation are common complications.

Methods: A prospective cross-sectional hospital based study was done among children from one month to 15 years of age admitted with diagnosis of AES from October 2014 to October 2015. The clinical details and reports of CSF analysis were recorded and analysed.

Results: Out of 70 patients of AES admitted, 40 (57.10%) were male and 30 (42.90%) were female. The highest number of cases were in age group of six to 10 years i.e. 26 (37.2%); whereas 20 (28.5%) were 11 to 15 years, 17 (24.30%) were among two to five years and seven (10%) were below two years. The patients were predominantly from Far-Western and Mid-Western region of Nepal. The maximum AES cases were of farmers of lower education level from rural area with low socio economic group and were reported during monsoon. The clinical profiles of AES were fever, altered sensorium and convulsion followed by irritability, headache, vomiting, lethargy, photophobia and ear discharge. 50 patients had AES with viral origin where nine were Japanese Encephalitis, 41 were viral with unknown aetiology and 20 were of bacterial origin of which 15 were bacterial (septic) meningitis and five of Tubercular meningitis. Three children (4.3%) died with diagnosis of viral encephalitis, 29 (41.4%) had complete recovery and 15 (21.4%) had partial recovery, nine (12.9%) went LAMA (Left Against Medical Advice) and 14 (20%) were DOPR (Discharge On Patient Request). The partially recovered patients had sequelae of motor system dysfunction and mental retardation.

Conclusions: Acute encephalitis syndrome is a medical emergency in which early detection and treatment is very essential and remains a serious threat to global health, especially in the developing countries.

Keywords: Acute encephalitis syndrome (AES); Bacterial meningitis

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INTRODUCTION

Acute Encephalitis Syndrome (AES) is defined as acute onset of fever, change in mental status and/or new onset of seizures in a person of any age, in any geographical region, at any time of the year. Based on results of microbiological and serological tests, it is classified as AES of suspected viral etiology and AES of non-viral etiology.[1] AES may present as encephalitis, meningoencephalitis or meningitis.[2] The incidence of AES ranges from 3.5 to 7.4 cases per 100,000 patient per year.[3] It is associated with complications including impaired consciousness, seizure, limb paresis or death.[4]

The AES cases, based on the results of their microbiological and serological tests, is classified as AES of suspected viral etiology (Confirmed JE, Non-JE and JE Status unknown) and AES of non-viral etiology (AES - bacterial or parasitic etiology).[1] Viruses are regarded as the most important cause of the acute encephalitis syndrome worldwide.[2] Enteroviruses are the most common cause of viral meningoencephalitis. Other viruses are arboviruses, coxsackie viruses and herpes viruses (Simplex, Zoster and HHV-6). Mumps and measles viruses are the common pathogens in regions where the mumps and measles vaccine are not widely used.[5]

Bacterial meningitis occurs in infants and older children.[5] Streptococcus pneumonia, Neisseria meningitides and Haemophilus influenza type B account for 80% of cases in developing countries. Tubercular meningitis (TBM) occurs within 12 months of primary infection mostly in children under five years of age.[6]

AES is common in male below 10 years of age. The case fatality rate of AES in Nepal was in range from 9.8% to 46.3% from year 1978 to 2003. The mortality rate was of 2% to 3% and 16% to 17% had complications during discharge.[7,8,9,10]

As there have been little publications on clinical, demographic parameters, and outcome among AES patients in children in Nepal,[4,10,11,13] a hospital based study was done.

METHODS

A prospective observational cross-sectional study was done in Paediatric Intensive Care Unit (PICU) of tertiary care hospital in Mid-western region of Nepal from October 2014 to October 2015 after an ethical approval from Institutional Review Board. After obtaining written informed consent from parents of children willing to participate in the study, 50 children from one month to 15 years of age admitted in PICU with clinical diagnosis of AES as per WHO criteria[1] were included in the study. According to the WHO criteria, Acute Encephalitis Syndrome (AES) is defined as acute onset of fever and a change in mental status and/or new onset of seizures in a person of any age, in any geographical region, at any time of year. Neurological sequelae is defined by the presence of one or more of the following signs at discharge; impaired consciousness, weakness (monoparesis, hemiparesis, and quadriparesis), focal or generalised abnormal limb tone and focal or generalised abnormal limb reflexes.[6]

Detailed history including demographic details, fever, abnormal body movement, headache, vomiting, photophobia, ear discharge, cough, running nose, loose motion etc were asked. Detailed clinical examination including consciousness level and central nervous system examination was done. Investigations done to rule out cause of fever were complete blood count, urine routine, stool routine, peripheral blood smear including Optimal test to rule out malaria, dengue serology to rule out dengue, blood culture and Widal test to rule out enteric fever and Japanese Encephalitis (JE) serology test (Immunoglobulin

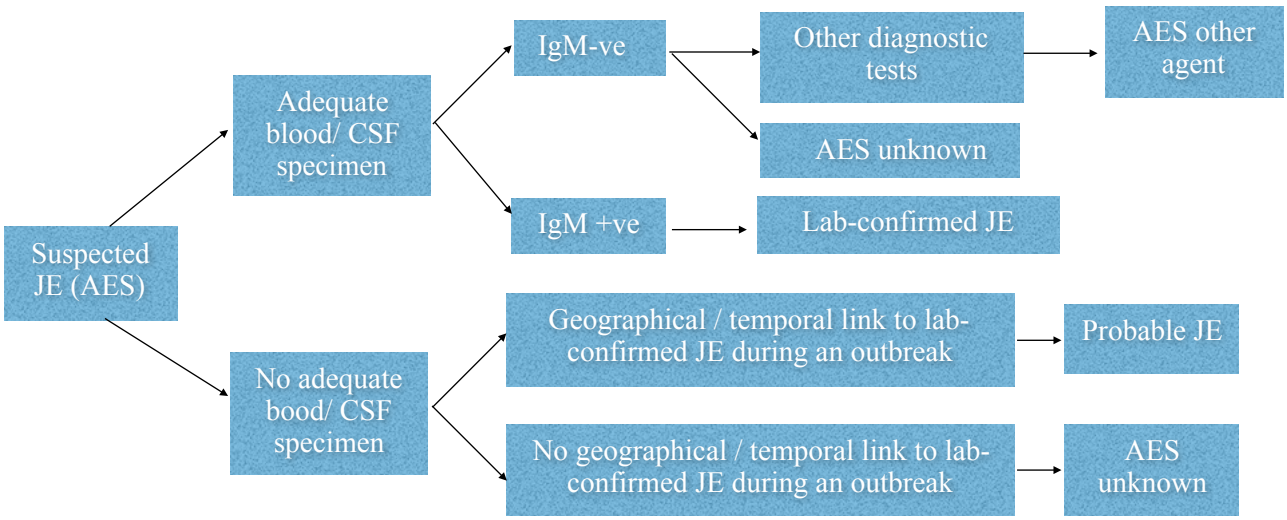

Fig 1. Final classification scheme for AES cases

M) were done. After ruling out raised intracranial pressure by Computed Tomogram of head, lumbar puncture was done for cerebrospinal fluid (CSF) analysis. AES was classified according to CSF analysis and JE serology.

Confirmation of diagnosis of JE is usually done by JE specific titer of IgM antibodies in a single sample of serum and or in CSF as detected by an IgM capture ELISA specifically for JE virus during acute illness of suspected AES cases.[1]

AES with acute bacterial meningitis: Case of AES with a CSF cell count (100 to 10,000) or more cells/mm^3, a pleocytosis with a polymorph predominance (75 to 95%) and raised CSF protein usually (100 to 500 mg/dl) and CSF/plasma glucose <50% and/or positive Gram stain from CSF and /or bacterial culture from CSF.

Partially treated bacterial meningitis: Cases of AES with CSF cell count 5 to 10,000 cells/mm^3, PMNs usual but mononuclear cells may predominate if pretreated for extended period, protein usually 100-500 mg/dl glucose normal or decreased.

AES of suspected viral aetiology: Cases of AES having a CSF cell count <1000 cells/mm^3 with a lymphocyte predominance, protein usually 50 to 100 mg/dl, CSF/plasma glucose generally normal or decrease to <40%, with no positive identification of non-viral pathogens (e.g. bacteria or parasites) in the CSF or blood.

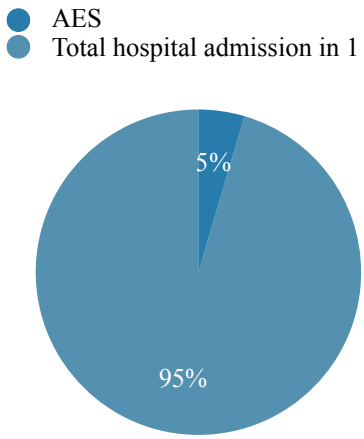

Fig 2. Hospital based incidence of AES cases

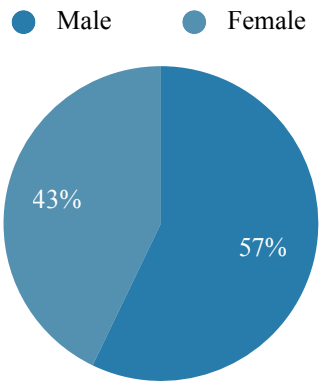

Fig 3. Sex wise distribution of AES cases

Table 1. Age wise distribution of AES cases

Age in years	Frequency	Percentage (%)
<2	7	10.0
2-5	17	24.3
6-10	26	37.2
11-15	20	28.5
Total	70	100

AES of TB meningitis: Cases of AES having a CSF cell count of 10-500 cells/mm^3 with a lymphocyte predominance, CSF/plasma glucose <50 mg/dl, with protein 100-3000 mg/dl.

Classification of AES was done according to the scheme given in Fig 1. Outcome of the study was done in terms of duration of hospital stay and discharge with or without sequelae. The data were entered in database and statistical analysis was done by using SPSS version 20.0 software.

RESULTS

Out of 1535 children admitted during the study period, 70 patients (4.88%) were diagnosed as AES. Out of 70 patients of AES admitted, 40 (57.10%) were males and 30 (42.90%) were females. The highest number of cases were in age group of six to 10 years i.e. 26 (37.2%); whereas 20 (28.5%) were 11 to 15 years, 17 (24.30%) were among two to five years and seven (10%) were below two years. The patients were predominantly from Far-Western and Mid-Western region of Nepal. This is correlated with the location of the study centre in Mid Western region of the country

Table 2. Education status of parents of AES cases

Education level	Frequency	Percentage (%)
Illiterate	41	58.6
Primary	25	35.7
Secondary	4	5.7
Total	70	100.0

The maximum AES cases were of farmers of lower education level from rural area with low socio economic group and were reported during monsoon as shown in following tables and graphs. The clinical profiles of AES showed that fever, altered sensorium and convulsion were the commonest symptoms followed by irritability, headache, vomiting, lethargy, photophobia and ear discharge.

Similarly, low Glasgow coma scale, exaggerated jerks and plantar extensor response were the

Fig 4. Geographical distribution of AES cases

Table 3. Economic status of parents of AES

Economic status	Frequency	Percentage (%)
Lower	62	88.60
Lower middle	1	1.40
Lower upper	6	8.60
Upper	1	1.40
Upper middle	0	0
Total	70	100

commonest signs followed by neck rigidity, hepatosplenomegaly, Kernig's sign and Brudzinski's sign.

34.30% patients (24 out of 70) had status epilepticus and 25.70% patients (18 out of 70) had generalised tonic clonic seizures. 50 patients had AES with viral origin including nine Japanese Encephalitis, 41 viral with unknown etiology whereas 20 were of bacterial origin which included 15 bacterial (septic) meningitis and five of Tubercular meningitis.

Table 5. Clinical profile (Signs) of AES

Symptoms	Frequency	Percentage (%)
GCS <8	30	42.8
Bulging fontanel	4	5.7
Neck rigidity	13	18.6
Kernig's sign	4	5.7
Brudzinski's sign	1	1.4
Extensor plantar response	30	42.8
Exaggerated deep tendon reflexes	40	57.1
Hepatomegaly	12	17.1
Splenomegaly	5	7.1

Table 4. Clinical profile (Symptoms) of AES

Symptoms	Frequency	Percentage (%)
Fever	70	100
Headache	41	51.6
Vomiting	30	42.85
Altered sensorium	70	100
Seizure	70	100
Irritability	50	71.4
Lethargy	20	28.6
Photophobia	5	7.14
Ear discharge	5	7.14

Table 6. Diagnosis in AES cases

Diagnosis	Frequency	Percentage (%)
Viral etiology	50	71.40
Unknown viruses	41	58.60
Japanese encephalitis	9	12.80
Bacterial origin	20	28.60
Bacterial meningitis (septic)	15	21.40
Tubercular meningitis	5	7.10
Total	70	100

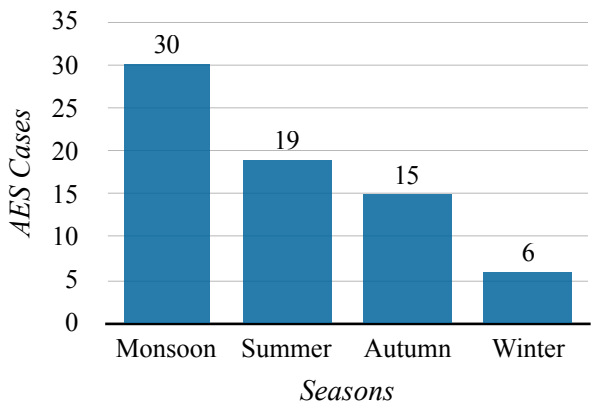

Fig 5. Seasonal variations of AES cases

Table 7. Duration of hospital stay of AES cases

Duration of hospital stay (days)	Frequency	Percentage (%)
1-3	16	22.9
4-6	17	24.28
7-9	16	22.85
10-12	12	17.14
13-15	5	7.14
16-18	1	1.42
19-21	0	0
22-24	2	2.85
35	1	1.42
Total	70	100

Maximum duration of hospital stay was 35 days and minimum duration was one to three days as shown in Table 7. Three children (4.3%) died with diagnosis of viral encephalitis, 29 (41.4%) had complete recovery and 15 (21.4%) had partial recovery, nine (12.9%) went LAMA (left against medical advice) and 14 (20%) were DOPR (Discharge On Patient Request). The partially recovered patients had sequelae of motor system dysfunction and mental retardation. Longer duration of fever had more neurological sequelae with five patients having neurological sequelae in 11-15 days of fever as shown in Table 9.

Table 8. Outcome of AES cases

Total number of discharges	Frequency	Percentage (%)
Discharged with sequelae	15	21.4
Discharged without sequelae	29	41.4
Total	44	62.8
LAMA	9	12.9
DOPR	14	20
Expired	3	4.3
Total	70	100

Table 9. Correlation of duration of fever with neurological sequelae

Duration of fever (days)	Neurological sequelae		Total (%)	p value
	Present (%)	Absent/ DOPR/ LAMA/ Death (%)		
1-5	4 (7.84)	47 (92.15)	52 (74.2)	0.001
6-10	6 (50.0)	6 (50.0)	12 (17.1)	
11-15	5 (71.40)	2 (28.57)	7 (10.0)	
Total	15 (21.42)	55 (78.5)	70 (100)	

DISCUSSION

Acute Encephalitis Syndrome is one of the most common causes of hospital admission in Western and Far Western region of Nepal. AES is a medical emergency in which early detection and treatment is very essential and remains a serious threat to global health, especially in the developing countries.[1] Therefore, we have designed this study to achieve modest goals regarding the clinico-demographic profile of AES and its outcome among children.

Our study shows higher incidence of AES (4.88%) as compared to that done by Trevejo RT in California, USA which may be due to being a hospital based report from an area which is endemic for AES with poor environmental sanitation and high incidence of malnutrition. The male to female ratio in our study was 1.35:1 may be because males are slightly more than females in population under 15 years of age which was similar to study done by Rayamajhi et al.[4] (2:1) and Dangol et al.[10] (2.6:1). Highest number of cases

were in age group of six to 10 years with 37.20% (26 out of 70) which may be due to more ambulation (playing outdoors, going to school, agriculture rice fields) predisposing to mosquito bites which was similar to study done by Shrestha SR et al.[11] (71.20% in below 10 years) and Dangol et al.[10] (59.57%).

In our study AES was seen more common in Far Western and Mid-Western region due to poor socioeconomic condition, poor hygiene and lack of well trained doctors, nurses and medical facilities correlating with the location of our centre. In our study, AES was seen in farmers (52.90%) with low socioeconomic status (88.60%) as agriculture being the main occupation in the areas. These findings were similar to that done by Kolakati et al.[12] where AES was seen in 90% rural and 63% of low socioeconomic group. Monsoon season was the common season of occurrence of AES in our study (42.90%) which was similar to that done by Bista MB and Shrestha JM.[13]

Clinical profile of AES in our study was similar to that done by Rayamajhi et al.[4], Khinchi et al.[14] and Kolkati et al.[12] The incidence of JE (12.80%) was higher than that of Dangol et al.[10] (2.10%) as our study area is endemic for JE. However, it is lower than Kolkati et al.[12] (30%) done in India due to current AES/JE surveillance system and free vaccination program in India.

CONCLUSIONS

In a hospital based study done in 70 patients, higher incidence of AES was seen in rural area of Far-western and Mid-western region in monsoon season among children of age one month to 15 years belonging to illiterate parents with low socioeconomic status. Fever, altered sensorium and seizures were common presentations where as lumbar puncture was gold standard diagnostic tool to differentiate different causes of AES.

Recommendations:

To minimise the incidence of AES with improvement in its outcome, we propose following recommendations:

1. Gender bias for early seeking medical care should be eliminated.

2. Education level and socioeconomic status should be improved.

3. Public health departments will have to concentrate more on health education, environmental sanitation, improve lab facilities, improve vaccination coverage against JE and protected water supplies for reducing fecal-oral infections.

4. A good quality surveillance system with lab support should be established for early diagnosis.

5. Doctors and nurses should be motivated with training and resources for early diagnosis and effective management.

The study may not be entirely representative for the whole paediatric population of the country. Tendency of all treating paediatrician to give antibiotic to children of AES irrespective to the diagnosis may have cause sterile CSF culture. Failure to give LP consent by all 70 cases of AES may also have cause missing of AES cases.

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Conflict of Interest: None declared

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