IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 12 Ver. VII (Dec. 2017), PP 22-26
www.iosrjournals.org

A Hospital Based Observational Study To Find The Correlation of The Demographic Profile And Clinical Features With The Outcome In Patients With Acute Encephalitis Syndrome And To Study The Disease Pattern In The Population

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Abstract
Introduction:*Acute Encephalitic syndrome(AES) is a major public health problem worldwide.Japanese encephalitis(JE) is one of the leading causes of acute encephalopathy affecting children.*
Aims&Objectives*:1/To find out the correlation of demographic profile and clinical features with the outcome of AES patients(recovery with or without sequelae or death)*
2/To study the outcome and common etiological agents of AES
Materials&Methods*:Patients admitted in the Paediatrics Department of AMCH with diagnosis of AES in 1 year were enrolled at admission. Informed consent was taken from the guardians.Ethical committee clearance was taken. Demographic profile, clinical features& outcome was observed in these patients.Analysis was done by SPSS.16*
Result:*Total 201 cases were admitted during the study period(Male:124,female:77, children less than 1 year:21, 1 to <5 years:68 ,5- 7 years:112).No significant correlation of age(p0.23), sex(p0.71),time interval between disease onset to hospital admission(p0.398),distance of home to nearby health facility(0.917) with outcome was found while there was significant correlation of ethnic group(p0.002),nutritional status(p0.000),socioeconomic status(p0.001),temperature(p0.000),GCS(p0.000)&episodes of seizure(p0.000)with outcome in AES patients. AES cases occurred more in Tea tribe community& adverse outcome(fatality and death) is also more in the population(n=54,57%).Significant correlation of JE with JE vaccination(p0.000) and outcome(p0.000) was found.Common neurological sequelae were aphasia(97%), behavioural disorders(57%),motor deficit (49%),cranial nerve palsy(22%), abnormal movements like facial tics(11%).Most common etiological agent was Japanese encephalitis(57%,n=114).*
Conclusion*:This is the first study done in this population trying to look at the demographic& clinical parameters which can be used to predict the outcome in AES patients without using any laboratory parameter.Most of the factors found associated with adverse outcome are preventable to a greater excent.*

Date of Submission: 06-12-2017 Date of acceptance: 14-12-2017

I. Introduction

Acute Encephalitis Syndrome (AES) is a group of clinical neurologic manifestations caused by a wide range of viruses, bacteria, fungi, parasites, spirochetes, chemicals and toxins.Japanese encephalitis (JE) is one of the leading causes of acute encephalopathy affecting children andadolescents in the tropical countries[1]. It is numerically one of the most important causes of viral encephalitis worldwide, with an estimated 50,000 cases and 15,000 deaths annually[2,3].The various studies showed different results with only a few consistent findings. Most of the studies involved serological assays which are quite expensive. So, in our study we have tried to find out if there are any clinical parameters which can help in predicting the outcome in these patients. Besides, this type of study has not previously been performed in our population. Therefore, we have also tried to find out if the demographic profile of the patients has any effect on the outcome.

II. Aims & Objectives

1/ Tofind out the correlation of demographic profile and clinical features with the outcome of patients with Acute Encephalitis Syndrome(AES) at the time of discharge (recovery with or without sequelae) or death.
2/ To study the outcome and common etiological agents of AES.

III. Materials And Methods

3.1 Place of Study: The study was conducted in the Department of Paediatrics, Assam Medical College& hospital.

3.2 Duration Of Study:12 months, i.e., June, 2015 to May, 2016

3.3 Study Design:Hospital-based observational study

3.4 Case Definition: Clinically, a case of AES is defined as "**a person of any age, at any time of year with** the 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)".

IV. Method of Study

Patients admitted in the Paediatrics Department of AMCH with diagnosis of AES were enrolled at admission. Informed consent was taken from the guardians. Ethical committee clearance was obtained. Patients with pre-existing neurological deficit prior to the onset of the disease(AES) and who left hospital against medical advice were excluded from the study.

4.1 The demographic profile was studied as a)Age, b)Sex, c)Ethnicity, d)Nutritional status, e)Time interval between disease onset and hospital admission, f)Malnutrition, g)Distance of home to nearby health facility, h)Socioeconomic status.

4.2 The clinical features studied at the time of hospital admission were i/ Neurological status (in terms of Glasgow Coma Scale score), ii/ Number of episodes of seizures, iii/ Grade of fever

4.3Outcome was studied under 3 headings –a)Death, b)Recovery with neurological sequelae, c)Recovery without any neurological sequelae.

The diagnosis was confirmed by and the aetiological agent was identified by the Microbiology department , Assam Medical college and hospital.

V. Statistical Methods

The data obtained was tabulated and analysed statistically using social science system version SPSS.16. Chi square test or fisher's exact test was used whichever applicable.

VI. Results And Observations

6.1 Analysis of the data showed the following-

Total 201 cases of AES were admitted during the study period. Out of this 124(62%) were males and 77(38%) females. Children less than 1 year constituted 10%(n-21), 1 to <5 years constituted 34%(n-68),5-12 years56%(n-112).Ahoms(n=27,13%), Mishings(n=23,12%), Moran-Muttucks(n=8,4%),tea tribes(n=95, 47%) and other groups(n=48,24%) constituted the study population.In our study, there was no significant correlation ofage(p-0.23), sex(p-0.71), time interval between disease onset to hospital admission(p0.398), distance of home to nearby health facility(0.917) with outcome in AES patients as the p value is more than 0.05. There was significant correlation of ethnicity(p0.002), nutritional status(p0.000) and socio-economic status(p0.001) with outcome in AES patients as the p-value is less than 0.05.Maximum number of patients who expired(n=32, 56%), recovered with neurological sequelae (n=22, 59%) and also who recovered without neurological sequelae (n=58, 54%) were in the age group of 5 -12 years.Maximum number of patients who expired(n=35, 61%) and recovered without neurological sequelae(n=72, 67%) were males. Maximum number of patients who recovered with neurological sequelae(n=20, 54%) were females.

Maximum number of patients who expired(n=37, 65%) belongedto the tea-garden community, next higher(n=10, 18%) were in others group. Maximum number of patients who recovered with neurological sequelae(n=17, 46%) were in tea-tribe community. Next higher number of patients in the group(n=9, 24%) were in the Mishing community. Maximum number of patients who recovered without neurological sequelae(n=41, 38%) were in the tea-tribe community. Next higher number(n=32, 30%) were in the others group. In tea-tribe community total 95 patients were admitted, death occurred in 39%(n=37), recovery without neurological sequelae occurred in 43%(n=41) and recovery with neurological sequelae occurred in 18%(n=17).

Maximum number of patients who expired(n=30, 53%) had Grade III & IV malnutrition. Maximum number of patients who recovered with neurological sequelae(n=26, 70%) had Grade II & III malnutrition. Maximum number of patients who recovered without neurological sequelae(n=82, 77%) had less than Grade II malnutrition. Thus, increased severity of malnutrition is associated with more adverse outcome(death or neurological sequelae)

Maximum number of patients who expired(n=36, 63%), recovered with neurological sequelae (n=23, 62%) and recovered without neurological sequelae(n=68, 64%) reported within 3 days from the onset of symptoms.Maximum number of patients who expired(n=30, 53%),recovered with neurological sequelae (n=23, 62%) and recovered without neurological sequelae(n=63, 59%) lived within 1-5 km distance from nearby health facility.Maximum number of patients who expired (n=42, 74%) belonged to upper lower and lower socio-

economic class. Maximum number of patients who recovered with neurological sequelae (n=35, 95%) were lower middle and upper lower class. Maximum number of patients who recovered without neurological sequelae (n=59, 55%) were upper middle and lower middle class. Thus, poor socio-economic status is associated with more adverse outcome (death or neurological sequelae).

There is a significant correlation of temperature (p0.000), GCS (p0.000) and episodes of seizure(p0.000) at the time of hospital admission with outcome in AES patients as the p-value is less than 0.05. Maximum number of patients who expired(n=40, 70%) had temperatures more than102^{o}F, next higher number of patients who expired(n=15, 26%) had temperatures between 100-102^{o}F. Maximum number of patients who recovered with neurological sequelae(n=24, 65%)had temperatures between 100-102^{o}F. Next higher group who recovered with neurological sequelae(n=12, 32%) had temperatures>102^{o}F. Maximum number of patients who recovered without neurological sequelae(n=56, 52%) had temperatures between 100-102^{o}F. Next higher group who recovered without neurological sequelae(n=46, 43%) had temperatures between 97- <100^{o}F. No AES patient came with temperature less than 97^{o}F. Thus, higher temperature is associated with more adverse outcome (death or sequelae).Maximum number of patients who expired(n=45, 79%) had GCS less than 9. Maximum number of patients who recovered with neurological sequelae(n=33, 89%) had GCS between 6-12. Maximum number of patients who recovered without neurological sequelae(n=82, 77%) had GCS more than 9. Thus, lower GCS score is associated with adverse outcome (death or sequelae).

Maximum number of patients who expired(n=23, 40%) had more than 9 episodes of seizure. Maximum number of patients who recovered with neurological sequelae(n=15, 41%) had 3-6 episodes of seizure. Maximum number of patients who recovered without neurological sequelae(n=64, 60%) had 2 or less episodes of seizure. Thus,more episodes of seizure is associated with adverse outcome (death or neurological sequelae).

Fever was present in 100%(n=201),Altered sensorium in 96%(n=193) cases, seizures in 95%(n=191), headache in 55% cases(n=110), vomiting in 51% cases(n=103), diarrhoea in 20% cases(n=41), neck rigidity in 28% cases(n=57%), pallor in 24% cases(n=49%) and shock in 20% cases(n=41).There is a significant correlation between JE vaccination and JE positivity as the p-value (0.000) is less than 0.05. Maximum number of JE(IgM) positive patients(n=87, 76%) were JE non-vaccinated. But 24%(n=27) of JE vaccinated patients were also JE (IgM) positive. There is a significant correlation between Japanese encephalitis and outcome in AES patients as the p-value(0.000) is less than 0.05. Maximum number of patients who expired(n=36, 63%) had Japanese encephalitis. Maximum number of patients who recovered with neurological sequelae(n=31, 84%) had Japanese encephalitis. Maximum number of patients who recovered without neurological sequelae(n=60, 56%) were JE IgM negative. Thus, Japanese encephalitis is associated with adverse outcome (death or neurological sequelae).

Most common neurological sequelae was aphasia(n=36, 97%), followed by behavioural disorders(n=21, 57%) like emotional lability. Other neurological deficits in descending order were motor deficit(49%), cranial nerve palsy of which most common was facial nerve palsy(22%), abnormal movements like facial tics(11%).

Most common etiological agent was Japanese encephalitis, detected in 57% cases(n=114).

Amongst those who survived, average duration of hospital stay was 12 days(± 4 days). Minimum duration of hospital stay was 5 days and maximum was 22 days.Amongst those who expired, average duration of hospital stay after which death occurred was 3 days(± 2 days). Minimum duration of hospital stay after which death occurred was 1 day and maximum was 13 days.

VII. Discussion

In our study, we found no significant correlation of age, sex, time interval between disease onset to hospital admission, distance of home to nearby health facility with outcome, whereas, there was significant correlation of ethnicity, nutritional status and socio-economic status with outcome in AES patients. Maximum AES patients were in the age group 5-12 years.Solomon T, Dung NM, Kneen R, et al[4] found 5-10 years as the commonest affected age-group. Luo D, Song J, Ying H et al[5] found that acute JE at younger age was a marker for unfavourable outcome (sequelae or fatal). But in our study no age-group was found to be associated with poor prognostic outcome. In all age-groups there was male preponderance, male to female ratio in AES cases was 62 : 38. Khinchi YR, Kumar A, Yadav S et al[6] also found male : female ratio 66: 34. Burke DS, Lorsomrudee W, Leake CJ et al [7] did not find any association between sex and outcome in AES patients.

AES cases occurred more in tea-tribe community and adverse outcome(sequelae and death) is also more in this population(n=54,57%). No previous study was done to compare ethnicity with outcome in AES patients. The reason for tea-tribe community being affected more can be malnutrition. Whether there is any genetic predisposition for the group to be affected more is still unknown.In our study we have found increased severity of malnutrition to be associated with more adverse outcome.Baruah HC, Biswas D, Patgiri D et al[8] in their study did not find any significant correlation of malnutrition with outcome.We did not find any significant correlation of duration of symptoms and distance of home to nearby hospital with outcome in AES patients. Burke DSet al [7]also found days ill before admission, distance of home to nearby hospital are not significant risk factors for fatal outcome.

Maximum number of patients who expired belonged to upper lower and lower class and those who recovered with neurological sequelae were of lower middle and upper lower class. Thus, poor socio-economic status is associated with adverse outcome (death or neurological sequelae). Baruah HC et al[8] also found similar results.

Among the clinical factors we found significant correlation of temperature,GCS and episodes of seizure at the time of hospital admission with outcome in AES patients.Maximum number of patients who expired(70%) had temperatures>102 ^{o} F and those who recovered with neurological sequelae(65%)had temperatures between 100-102^{o}F. Thus, higher temperature is associated with adverse outcome. Chaudhari N et al [9] and Luo D et al[5] also found higher body temperature to be a poor prognostic factor.Maximum number of patients who expired(79%) had GCS less than 9. Maximum number of patients who recovered with neurological sequelae(89%) had GCS between 6-12. Maximum number of patients who recovered without neurological sequelae(77%) had GCS more than 9. Thus, lower GCS score is associated with adverse outcome. Luo D et al[5]andKumar R et al [10] found mortality as significantly related to deep coma. Chaudhari N et al [9]also found deep coma present at hospital admission to be marker for unfavourable outcome(sequelae or fatal).Maximum number of patients who expired had more than 9 episodes of seizure and those who recovered with neurological sequelae had 3-6 episodes of seizure. Thus, greater number of episodes of seizure is associated with more adverse outcome. As reported by Kumar Ret al[10]in their study mortality was significantly related to abnormalities in tone and decerebrate posturing.

Fever was present in 100% cases, altered sensorium in 96% cases, seizures in 95%, headache in 55% cases, vomiting in 55% cases, diarrhoea in 20% cases, neck rigidity in 28%,pallor in 24% and shock in 20%.Khan SA, Dutta P, Borah J et al[11] found altered sensorium in 62.5%, headache in 50.0%, nausea 50%, vomiting in 37.5%, diarrhoea in 37.5%, neck rigidity 25.0% and seizures in 25.0% of AES cases.

Maximum number of JE patients(76%) were JE non-vaccinated. But 24% of JE vaccinated patients also developed JE. Khinchi YR et al[6] in their study found JE in 5 per 100,000 vaccinated while 51 per 100,000 in non-vaccinated patients. Japanese Encephalitis disease in JE vaccinated casesmay be because when the disease developed protective antibody was not yet produced in their body.

Maximum number of patients who expired(63%) and recovered with neurological sequelae(84%) had Japanese encephalitis. Thus, Japanese encephalitis was associated with more adverse outcome(death or neurological sequelae. Kumar Ret al[10] found Japanese encephalitis to be associated with increased mortality and disabling sequelae.Most common neurological sequelae was aphasia followed by behavioural disorders like emotional lability. Other neurological deficits in descending order were motor deficit, cranial nerve palsy (most commonly facial nerve palsy), abnormal movements like facial tics and lip smacking. Tsai TF, Saluzzo JF, Dodet B et al[12] in their study have mentioned that the classic description of Japanese encephalitis includes a dull flat mask-like facies, tremor, generalised hypertonia, and cogwheel rigidity,head nodding,choreoathetosis, bizarre facial grimacing and lip smacking.Upper motor neuron facial nerve palsies occur in around 10% of children.Most common etiological agent of AES was Japanese encephalitis (57% cases).

VIII. Conclusion

This is the first study done in this population trying to look at the demographic and clinical parameters which can be used to predict the outcome in AES patients without using any laboratory parameter. We have found ethnicity to have significant correlation with outcome. Tea-tribe community was affected more with more adverse outcome. No other study has seen this fact before. Most of the factors associated with adverse outcome in our study are preventable to a great extent. Awareness about the disease was low in the people. With proper awareness, improvement in nutritional and socio-economic status, compulsory JE vaccination, prompt management of high temperature and seizure, both the disease and adverse outcome associated with it can be prevented.

1. Studies have been done in the past comparing age, sex, time interval between hospital admission , nutritional status and socio economic factors with outcome but no study has been done comparing ethnicity with outcome. In our study we have found ethnicity to have a significant correlation with outcome. In future, studies can be done using this as reference to see if there is some genetic predisposition which increases the chances of AES and that is why AES and JE are typically clustered around particular geographical area.
2. Studies done in the past have used laboratory parameters to asses the outcome in AES patients but we have only used demographic and clinical features to asses the outcome. This can be useful tool in peripheral areas where they have remote asses to laboratory parameters.

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*Dr. Murchana Khound. "A Hospital Based Observational Study To Find The Correlation of The Demographic Profile And Clinical Features With The Outcome In Patients With Acute Encephalitis Syndrome And To Study The Disease Pattern In The Population." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 16.12 (2017): 22-26