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Original Research Article

A clinico-epidemiological profile of acute encephalitis syndrome in children of Bellary, Karnataka, India

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ABSTRACT

Background: Acute encephalitis syndrome (AES) is defined as the acute-onset of fever and a change in mental status (including signs and symptoms such as confusion, disorientation, delirium or coma) and/or new-onset of seizures (excluding simple febrile seizures) in a person of any age at any time of the year. The clinical definition of AES was introduced to facilitate surveillance for Japanese encephalitis (JE), mosquito-borne viral encephalitis. Most AES is considered to be due to a viral-encephalitis, virus like West Nile, Herpes simplex virus, Flaviviruse like JE and dengue are more prevalent in South East Asia. Various subsequent studies confirmed that most AES in India are due to JE, which has been considered as the only major cause of AES in India.
Methods: A case series study was undertaken at the department of pediatrics, VIMS, Bellary. Children aged 0- 15 years with fever or h/o fever (>380c), altered level of consciousness persisting for >24hrs, convulsions, change in behavior were included as study subjects. Non probability purposive sampling was adopted to select study subjects. Data collection was done by using predesigned, pretested structured proforma & analyzed by using software SPSS version 22.
Results: A total of 136 cases formed as study subjects. With higher proportion of subjects were toddlers (30.1%), followed by pre-school children (26.5%). Majority of them being males 88 (64.7%) and 44 (32.3%) were females. More than half of study subjects were residing in rural area 80 (58.8%). The predominant presenting feature was fever, followed by convulsions 102 (75%) and vomiting 85 (62.5%). A higher proportion of cases were reported during post-monsoon period 62 (45.1%) followed by monsoon 41(30.1%). Among the 136 study AES cases, 115 (84.5%) were suspected for viral etiology (JE and dengue).
Conclusions: Majority of cases were in the age-group of 1-5 years, with male predominance. The peak in occurrence of cases was during post-monsoon period (October-February).

Keywords: AES, CSF, Dengue, JE

INTRODUCTION

Acute encephalitis syndrome (AES) is defined as the acute-onset of fever and a change in mental status (including signs and symptoms such as confusion, disorientation, delirium or coma) and/or new-onset of seizures (excluding simple febrile seizures) in a person of any age at any time of the year.[1] The clinical definition of AES was introduced to facilitate surveillance for Japanese encephalitis (JE), a mosquito-borne viral encephalitis.[2] Japanese encephalitis is one of the most important forms of epidemic and sporadic encephalitis in the tropical regions of Asia, including Japan, China, Taiwan, Korea, Philippines, all of Southeastern Asia, and India.[3] JE affects over 50,000 people annually, leading to 8-30% mortality and 50-60% disability, with children bearing the brunt of the disease burden.[4] The history of

AES in India has paralleled that of JE, with the virus first being reported from southern India, Vellore, Tamil Nadu in 1955.[5] In India, JE as a disease was first reported in 1955 when clinical cases were detected in Vellore and Pondicherry in southern India.[6] In India approximately 597,542,000 people live in JE-endemic regions, and 1,500 to 4,000 cases are reported every year. 375million Populations are at risk of developing AES in India alone. 70-75% of disease burden was in UP.[7] The earliest evidence of JE virus activity in Bellary district came in 1981. The first and major outbreak of JE reported from Bellary and adjoining areas in 1986-1987 and affected more than 219 people, of which 61 died.[8] These figures are based on total reported cases; it is possible that many cases are unreported and hence the actual magnitude of the threat of JE may be considerably higher, both in the Indian and in the global context. In endemic areas, the highest age-specific attack rates occur in children of 3 to 6 years (<15years) of age.[9,10] As part of the effort to control Japanese encephalitis (JE), the World Health Organization (WHO) is producing a set of standards for JE surveillance. The surveillance consists of identifying patients with acute encephalitis syndrome (AES), and then classifying the patients according to the results of laboratory diagnostic tests.[11] Transmission is seasonal and mainly related to rainy season in south-east Asia region.[12]

Our aim is to study the clinical features of AES in relation with the epidemiological aspects in our study area so that by understanding the main epidemiological features of these infections would assist clinicians in formulating etiological hypothesis, in the event of laboratory findings being inconclusive. Also the study will form the basis for ongoing sentinel virological surveillance, which would be adaptable to any infection/syndrome including emerging diseases.

Objectives

- To know the clinico - epidemiological profile of acute encephalitis syndrome (AES).
- To find out the proportion of JE and dengue among AES cases.

METHODS

A descriptive case-series study was conducted at the department of pediatrics, VIMS, Bellary among children aged 0 – 15 years.

Sampling technique

Non probability purposive sampling.

Source of data

The primary data was obtained by interviewing the parents of children 0-15 years admitted in wards of pediatric department. The secondary data was collected from the clinical records & reports of the relevant clinical investigations done on respective patients.

Methodology

A pre-designed semi-structured questionnaire was used to obtain data after explaining the purpose of the study and obtaining written informed consent. A relevant primary data on socio-demographic profile, clinical profile was collected by interviewing the parents/accompanying person of the patient and the secondary data regarding the investigations performed on children suspected of AES was collected from the reports

Study design

Hospital based case series study

Study period

1st June 2013 to 31st may 2014.

Statistical analysis

Proportions & Chi-Square

Inclusion criteria

All the children 0-15 years admitted to department of pediatrics VIMS, Bellary with fever or h/o fever (>38^0c), Altered level of consciousness persisting for >24hrs, Convulsions, lethargy/irritability, change in personality & behavior.

Exclusion criteria

- Patients with viral aseptic meningitis without encephalopathy.
- Patients with non-infectious CNS disorders due to hypoxic, ischaemic, vascular, toxic and metabolic causes.
- Patients with history of CNS disorder.

RESULTS

Among 136 study subjects, 41 (30%) were toddlers followed by 36 (26.3%) pre-school and 34 (25%)school going children. Majority of subjects were Hindu by religion 115 (84.5%) followed by Muslims 17(12.4%), more than half were residing in rural area 80(58.8%) and 56 (41.2%) of them were from urban areas. Majority of them belong to nuclear family 83 (61%) More than one third of cases were from upper lower class 52(38.2%) followed by 37 (27.2%) from upper middle class, 33 (24.2%) were from lower middle class and only 2 (1.4%) from lower class A higher proportion of parents were engaged in agricultural activity 118(86.8%), followed by business 15 (11%), Most of study subjects dwelling consists of both indoor 83 (61%) and outdoor 99 (72.8%)

vector breeding sites along with pigs /cattle sheds 74 (54.4%) around the houses (Table 1).

Table 1: Sociodemographic profile of study subjects.

Variables	Frequency (n=136)	Percentage
Age group		
Infancy	25	18.4
Toddler	41	30.1
Pre-school	36	26.5
School going	34	25
Religion		
Hindu	115	84.5
Muslims	17	12.4
Others	4	3.1
Type of family		
Nuclear	83	61
Joint	53	39
Parents occupation		
Agriculturists	118	86.8
Business	15	11.1
Unemployed	3	2.2
Socioeconomic class		
Upper	12	8.8
Upper middle	37	27.2
Lower middle	33	24.3
Upper lower	52	38.2
Lower	2	1.4
Potential vector breeding sites		
Indoor		
Present	83	61
Absent	53	39
Outdoor		
Present	99	72.8
Absent	37	27.2
Pigs/cattle sheds		
Present	74	54.4
Absent	62	45.6

A higher proportion of AES cases were reported during post-monsoon period (45.1%), followed by monsoon (30.1%) and pre-monsoon seasons (14.7%). Out of four JE positives cases, two cases where positive during the month of September 2013, one in October and two in November 2013 (Table 2).

Table 2: Distribution of study subjects according to seasonal occurrence.

Season	Frequency	Percentage
Pre- monsoon	20	14.7
Monsoon	41	30.1
Post-monsoon	62	45.4
Total	**136**	**100**

Figure 1 Shows distribution of cases according to their month of occurrence.

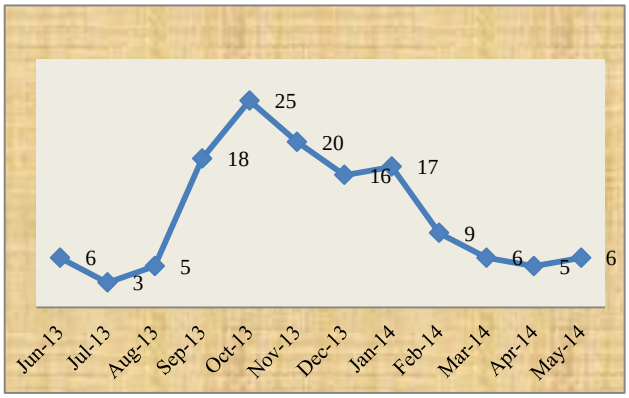

Figure 1: Distribution of cases according to season of occurrence.

The proportion with h/o complete immunization was high among females 26 (54.2%) than that of males 40 (45.5%), and this relation between gender and immunization status was found to be statistically significant Table 3.

Table 3: Relation between gender and immunization status of study subjects.

Immunization history	Female	Male	Total
Immunized	26(54.2%)	40(45.5%)	66(48.5%)
Partial	8(16.7%)	32(36.4%)	40(29.4%)
Unimmunized	14(29.2%)	16(18.2%)	30(22.1%)
Total	48(100%)	88(100%)	136(100%)

Chi square: 6.28; p-value: 0.043.

Out of 117 study subjects, most CSF analysis was suggestive of viral agents, with higher proportion in females than males, followed by similar findings with pyogenic meningitis and Japanese encephalitis but the proportion of Tubercular meningitis was high among males than females and this differences in relation was statistically not significant Table 4.

Table 4: Relation between gender and CSF analysis reporting.

CSF suggestive of	Females	Males	Total
Viral	36(75%)	58(65.9%)	94(69%)
Pyogenic	3(6.3%)	4(4.5%)	7(75.1%)
TBM	0	5(5.7%)	5(3.7%)
JE	3(6.3%)	2(2.3%)	5(3.7%)
Normal	1(2.1%)	5(5.7%)	6(4.4%)
Not done	5(10.4%)	14(15.9%)	19(14%)
Total	48(100%)	88(100%)	136(100%)

Chi square: 6.19; P-value: 0.2.

Out of 136 AES suspects, 115 (84.5%) have been suspected for viral etiology including J.E and Dengue, 11 (9.5%) of them were suspected of AES-other agents like non-viral (bacteria) and 8 (5.8%) cases were suspected for AES of unknown etiology (Table 5).

Table 5: Distribution of suspected- AES cases according to guidelines for surveillance of AES by Government of Karnataka 13.[13]

Suspected case *	Frequency	Percentage
AES-viral etiology (JE & Dengue)	115	84.5
AES- Other agents (pyogenic, TB, varicella)	13	9.5
AES- unknown etiology	8	5.8
Total	136	100

DISCUSSION

In our study a total of 136 AES cases formed as study subjects during the study period (1st June 2013 to 31st may 2014) where in most of subjects were between 1-5yrs with mean age of 4.1years and SD:39.2. The proportion of AES was high in males (64.7%) than females (35.9%). Similar results were observed in some of the studies done in our country by Thapa LJ et al, Khinchi YR et al.[14,15] Whereas there was equal distribution of cases among both the sexes and higher proportion of cases were in the age-group of 5-12 years in studies conducted by Kabilan L et al and Sharma J et al.[16,17] In our study the seasonal occurrence of AES cases was peak during post-monsoon(October –February) and out of five JE positive cases two occurred in September, one in October and two in November each respectively. which was similar with findings in study by Khinchi YR et al, Anuradha et al however a difference in pattern of seasonal distribution of AES-JE cases was seen in studies by Kabilan L et al, JE occurrence was perennial, with a peak in the month of December and in a study by Sarkar et al found that cases were more in the monsoon and post-monsoon period.[15,16,18,19] This difference in observations may be due to ecological variations of distribution of Culex mosquitoes. However, this was enumerated with the results obtained in an ecological study by Kanojia PC on mosquito vectors of Japanese encephalitis virus in Bellary district, Karnataka at National Institute of Virology(ICMR), Pune, where the general mosquito population showed bimodal pattern of peak occurrence.[20] An early summer peak was observed in February [259.0 per man hour density (PMHD)] wherein, *Cx. tritateniorhynchus* contributed maximum in the entire population (214.7 PMHD). Later a tall peak was noticed in October (428.4 PMHD) and once again *Cx.tritateniorhynchus* played major role in elevating combined population density. During JE transmission period, *Cx. tritateniorhynchus*, the major vector of JE in India was the predominant species constituted 74.9 per cent of the total catch. Generally cases started occurring in September and continuing until January with the highest occurrence in November coinciding with the elevation in mosquito density, particularly *Cx. tritaeniorhynchus* and paddy. And also similar bi-model peak was observed in the study done on culex mosquitoes with special ref to JE vectors in Kottayam district, Kerala by Jomon KV et al.[21]

Potential vector breeding sites

Most of our study subjects coming from rural background, gave history of contact with potential vector breeding sites both indoor and outdoor (Indoor 83 (61%) and outdoor 99 (72.8%) along with pigs /cattle sheds, 74 (54.4%) around the houses). Similar results were found in studies conducted by Anuradha et al.[18] In this study, out of 82 patients studied all had history of (H/O) having contact with domestic animals (pigs, cattle or birds chicken) which are reservoir hosts for JE 48 (58.6%) had H/O contact with pigs, 23 (28%) had H/O contact with cattle and 11(13.4%) had H/O contact with chicken) & Sarkar et al observed in most of the cases (74.3%), persons were living in close proximity to rice fields/lakes/ponds.[19]

Diagnosis

In our study majority of study subjects were suspected to be AES cases (77.2%) followed by pyogenic meningitis (5.1%), atypical seizures, tubercular meningitis, (4.1%) Japanese encephalitis, dengue encephalitis, febrile seizures and HIE & Varicella. In contrast to the study findings by Beig FK et al in children of western Uttar Pradesh, India.[22] This difference in etiological findings of suspected AES cases is due to the geographic features of this region which favour in spread of JEV- an abundance of rice fields and high temperature and relative humidity, provides a suitable environment for JEV transmission.[23] UP alone contributes to 70-75% of total disease burden in India.[7]

However, Bhatt GC et al conducted a cross-sectional study on clinic-laboratory profile of acute encephalitis syndrome on 100 patients in the eastern Uttar Pradesh region of India.[24] Cerebrospinal fluid and serum samples were tested for: Japanese encephalitis (JE) virus; Chandipura virus; Coxsackie virus; Dengue virus; enterovirus 76; and West Nile virus. Twenty-two (22.0%) patients were confirmed JE cases and 17% had parasitic or bacteriological aetiology. The remaining 61 cases (61.0%) in which no viral aetiological agent was found were grouped as non-JE cases. A high mortality of 26.5% was seen in patients with confirmed or presumptive viral encephalitis (22/83). Early recognition of these signs may help clinicians to manage these cases.

Rao BL et al conducted a study during the large outbreak of AES in children in AP during 2003, which was found to be associated with chandipur virus clinical samples tested negative for IgM antibodies to Japanese

encephalitis, West Nile, dengue, and measles viruses, and for RNA of coronavirus, paramyxovirus, enterovirus, and influenza viruses.[25] Virus was isolated from six patients with encephalitis and was identified as Chandipura virus by electron microscopy, complement fixation, and neutralisation tests, adding to the evidence suggesting that this virus should be considered as an important emerging pathogen. These variations are due to the difference in the ecological and entomological distribution patterns.

CONCLUSION

A total of 136 AES cases were formed as study subjects, occurrence of cases was peak during the months of Oct-February (post monsoon). Most of cases were in the age group of 1-5years, with predominant cases being males, more than half of them were partially or unimmunized, residing in kuccha house with majority of them dwelling around potential outdoor vector breeding sites. They belong to upper lower group and most of their parents were agriculturists by occupation, predominantly cultivating paddy (twice a year). Higher proportion of them had viral etiology on CSF analysis, among which five of them where positive for J.E & four of them had Dengue encephalitis, which was confirmed by laboratory profile.

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