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Original Research Article

A six years prospective epidemiological study of acute encephalitis syndrome among children admitted in a rural tertiary care center

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ABSTRACT

Background: Acute Encephalitis Syndrome (AES) is a major public health issue in India. The common etiologies of AES in India are various infectious agents. There are seasonal and regional variations in etiologies making diagnosis and effective intervention often difficult. Our study represents the epidemiological data that will help in planning management in larger perspective.
Methods: This is a six years prospective observational study conducted in the Department of Pediatrics, North Bengal Medical College Hospital, Darjeeling from January 1st, 2013 to December 31st, 2018. In this study all clinically diagnosed AES cases were included fulfilling inclusion and exclusion criterion.
Results: 585 out of 39420 patients (1.48%) were diagnosed clinically as AES over six years. Male patients (372) contributing to 63.6% and female patients (213) 36.4% of the study. Majority cases (271) were seen in the age group of 1-5 years amounting to 46.3% with mean age 5.1±3.6 years. In July 2014 number of cases were maximum 59 (10%) followed by May 2013 20 (3.4%). Among the 585 AES cases, 263 (45%) were suspected for viral etiology (JE= 84, 14.3%). Total 457 cases (78.1%) were alive with insignificant to age and gender variance. Vaccination status revealed 11 among 15 JE deaths were unimmunized which is statistically significant ($p < 0.05$) by Chi-square test.
Conclusions: The magnitude and etiologies of AES need to be explored and understood in various geographic regions and in different seasons to have a better insight for development of future policies to reduce the burden.

Keywords: Acute encephalitis syndrome, Epidemiological study, Japanese B encephalitis

INTRODUCTION

Acute Encephalitis Syndrome (AES) is a major public health in India. It is defined as acute-onset of fever with clinical neurological manifestations (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 the year. The common etiology of AES in India is infectious agents (virus, bacteria, fungus, parasites, spirochetes, leptospira, toxoplasma, rickettsia etc.) viruses being the most common.[1] Japanese Encephalitis, a vector (mosquito) born viral encephalitis is one of the types of AES.

There are seasonal and regional variations in etiology, making the critical window for diagnosis and effective intervention often short. In this context, our study presents the epidemiological data that will help in planning management in larger perspective.

METHODS

This is a six years prospective observational study conducted in the Department of Pediatrics, North Bengal Medical College Hospital, Darjeeling from January 1st, 2013 to December 31st, 2018 among all clinically diagnosed AES cases. Relevant investigations were done accordingly and for JE surveillance samples (serum/CSF)

were sent for detection of JE Ig-M antibodies in acute stage of AES.

Inclusion criteria

All the children 0-12 years admitted to department of pediatrics, NBMCH, Darjeeling with fever or history recent onset fever (>38ºc), altered level of consciousness, convulsions, lethargy/irritability, change in personality or behaviour.

Exclusion criteria

- Patients with congenital central nervous system (CNS) disorder
- Patients with noninfectious etiologies (toxin induced, seizure disorder, metabolic encephalopathies and inborn error of metabolism).

Data collection

Clinically diagnosed AES cases admitted in pediatric ward within the study period were enlisted. Proper history was obtained by interviewing parents, patients were clinically examined and relevant investigations including CSF and serum for IgM antibody were performed.

Statistical method

Collected data were checked for consistency and completeness and were entered in Microsoft Excel data sheet. Data were organized and presented using the principles of descriptive and inferential statistics. Data were presented in tables and diagrams. Diagrams were done by Microsoft Excel software. Categorical data was expressed in proportions. Chi-square is applied to test the significance. P value less than 0.05 was considered as statistically significant. Analysis of the data was done by IBM SPSS version 20.

RESULTS

There was 39420 patients admitted during the study period, out of these 585 (1.48%) were diagnosed clinically as AES. Male patients (372) contributing to 63.6% and female patients (213) 36.4%. Majority cases (271) were seen in the age group of 1-5 years amounting to 46.3% followed by 30.4% in 6-10 years age group (178) with mean age 5.1±3.6 years.

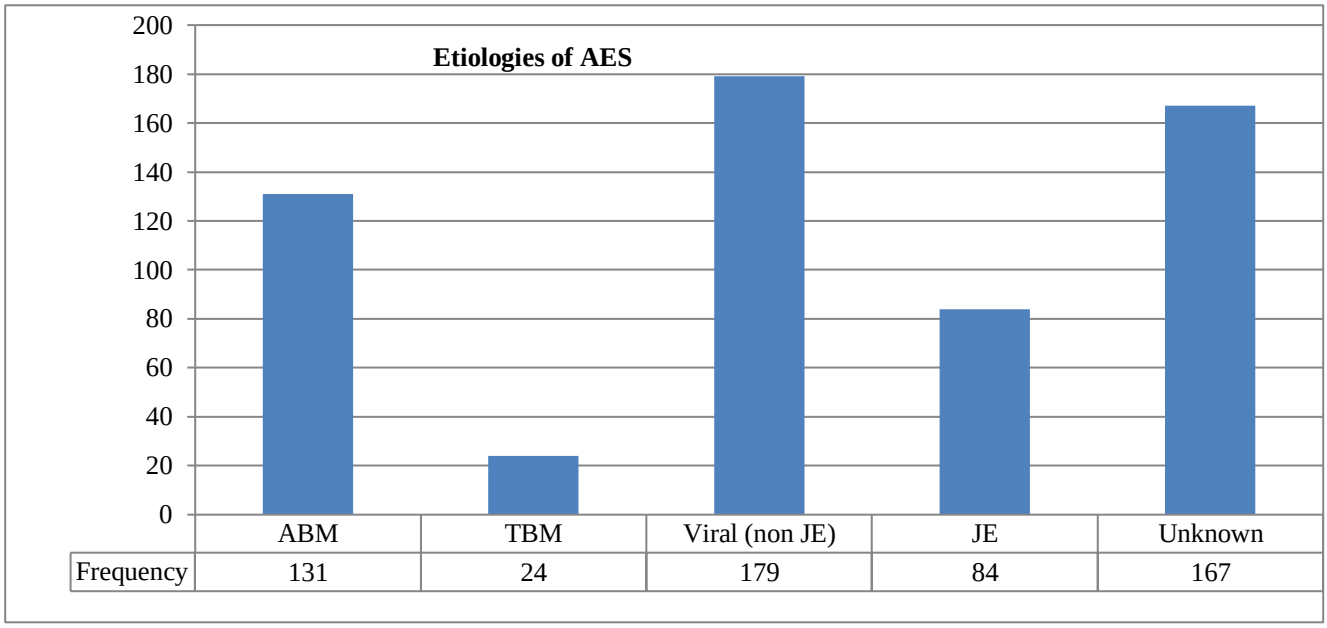


Figure 1: The etiologies of AES.

In July 2014 number of cases were maximum 59 (10%) followed by May 2013 20 (3.4%), number of cases of AES were least (0) in February 2018. Maximum numbers of cases were from Jalpaiguri district (222) 37.9% followed by Darjeeling district (150) 25.6% in West Bengal (94.2%). 23 (3.9%) cases were from Bihar, 7 (1.2%) from Nepal and 4 (0.7%) from Assam.

Among the 585 AES cases, 263 (45%) were suspected for viral etiology [JE= 84 (male - 54, female -30) 14.3%] followed by bacterial meningitis 131 (22.3%), tubercular meningitis 24 (4.2%). 167 (28.5%) cases constitute other group including dengue, scrub typhus, Neurocysticercosis, etc. (Table 1 and 2 and Figure 1 and 2).

Table 1: Description of various parameters regarding AES.

Parameter/variables	Description n= 585 (AES cases)				
Association between age group & sex with outcome of the study subjects					
Gender	Outcome		Total		Male mortality higher than female. Pearson Chi-Square 0.084, df=1,p=.772
	Died	Discharged			
Female	48(22.5%)	165(77.5%)	213(100.0)		
Male	80(21.5%)	292(78.5%)	372(100.0)		
Total	128(21.9%)	457(78.1%)	585(100.0)		
Gender	Frequency	Percent	Valid Percent	Cumulative Percent	Male contributing more than female in AES cases
Female	213	36.4	36.4	36.4	
Male	372	63.6	63.6	100.0	
Total	585	100.0	100.0		
Age group	Frequency	Percent	Valid Percent	Cumulative Percent	Mean age 5.1±3.6 years
< 1 year	67	11.5	11.5	11.5	
>10 year	69	11.8	11.8	23.2	
1-5 year	271	46.3	46.3	69.6	
6-10 year	178	30.4	30.4	100.0	
Total	585	100.0	100.0		
Outcome	Frequency	Percent	Valid Percent	Cumulative Percent	Died: JE 15 + Non JE 113 ; Discharged: JE 69 + Non JE 388
Died	128	21.9	21.9	21.9	
Discharged	457	78.1	78.1	100.0	
Total	585	100.0	100.0		
Laboratory profile of the study subjects in relation with cerebrospinal fluid (CSF) for JE					
CSF for JE	Frequency		Percentage		CSF is investigated for IgM antibody after 72 hours
Positive	34		5.8		
Negative	187		32.0		
Equivocal	3		0.5		
Not sent	361		61.7		
Total	585		100.0		
Laboratory profile of the study subjects in relation with serum for JE					
Serum for JE	Frequency		Percentage		Serum is investigated for IgM antibody after 72 hours
Positive	53		9.1		
Negative	177		30.3		
Equivocal	48		8.2		
Report pending	15		2.5		
Not sent	292		49.9		
Total	585		100.0		

Among 585 AES cases 34 (5.8%) were positive for JE in cerebrospinal fluid (CSF and serum positivity for JE were 53 (9.1%) and 3 were both CSF and serum positive. 27 (32.14%) JE cases were < 5 years of age and 57 (67.86%) were > 5 years age group, p value <0.05 by Chi-square test. Total 457 cases (78.1%) were alive (male 292, 78.5% and female 165, 77.5%). Among 128 dead (21.9%), 80 were male (64%) and 48 were female (36%). There is a slight predominance seen in below 5 years mortality, 70 cases (54.68%) against 58 cases (45.32%) in those were above 5 years. JE death was 15 (male 8, female 7; 11.7% of total death) 17.9% of all JE cases. 11 among 15 JE deaths were unimmunized which is statistically significant (p <0.05) by Chi-square test. (Table 1 and 2).

DISCUSSION

Acute Encephalitis Syndrome (AES) is an important cause of mortality and morbidity in children. The etiological agents are varied. Viruses are one of the main causes of AES in India. The causative agent of AES

varies with season and geographical location. There are numerous gaps in our knowledge, paucity of data about the regional epidemiology and etiologies, lack of diagnostic facilities; making it difficult to manage patients and inappropriate responses during outbreak. Few studies have been conducted in southern part of India and in Uttar Pradesh, unable to depict the true extent and nature of the problem in the country as a whole including West Bengal.

Table 2: Descriptive parameters of Japanese B Encephalitis (JE).

Composite table for Japanese B Encephalitis (JE) , outcome and immunisation status n=84			
Gender	JE (+) Frequency	Percent	
Male	54	64.3%	Male predominance
Female	30	35.7%	
Total	84	100%	
Age wise distribution of Japanese B Encephalitis (JE)			
Age group	JE Positive Frequency	Percent	
< 5 year	27	32.1%	JE Positivity is more above 5years of age
>5 year	57	67.9%	
Total	84	100%	
Outcome of Japanese B Encephalitis (JE) in relation of gender			
Gender	JE Positive death	JE Positive alive	Chi-square- 0.954074, degrees of freedom- 1, p = 0.3287
Male	8	46	
Female	7	23	
Total	15	69	
Outcome of Japanese B Encephalitis (JE) in relation age			
Age group	JE Positive death	JE Positive alive	Chi-square- 0.0118654, degrees of freedom- 1, p = 0.9133
< 5 year	5	22	
>5 year	10	47	
Total	15	69	
Immunisation status among Japanese B Encephalitis (JE) positive cases			
Immunization among JE Positive	Male	Female	Total
Yes	46	23	69
No	7	4	11
Unknown	1	3	4
Total	54	30	84
Immunisation status and outcome among Japanese B Encephalitis (JE) positive cases			
Immunization status	JE Positive death	JE Positive alive	Chi-square- 59.324, degrees of freedom- 2, p < 0.05, significant
Vaccinated	3	66	
Non vaccinated	11	0	
Unknown	1	3	
Total	15	69	
Comparison between JE and Non-JE contributing AES cases			
Distribution	Frequency	Percentage	Non JE contribute more than JE for AES
JE	84	14.3	
Non-JE	501	85.7	
Total	585	100	
Gender distribution between JE and Non-JE contributing AES cases			
Gender	JE	Non-JE	Chi-square- 0.0205196, degrees of freedom- 1, p = 0.8861
Male	54	318	
Female	30	183	
Total	84	501	

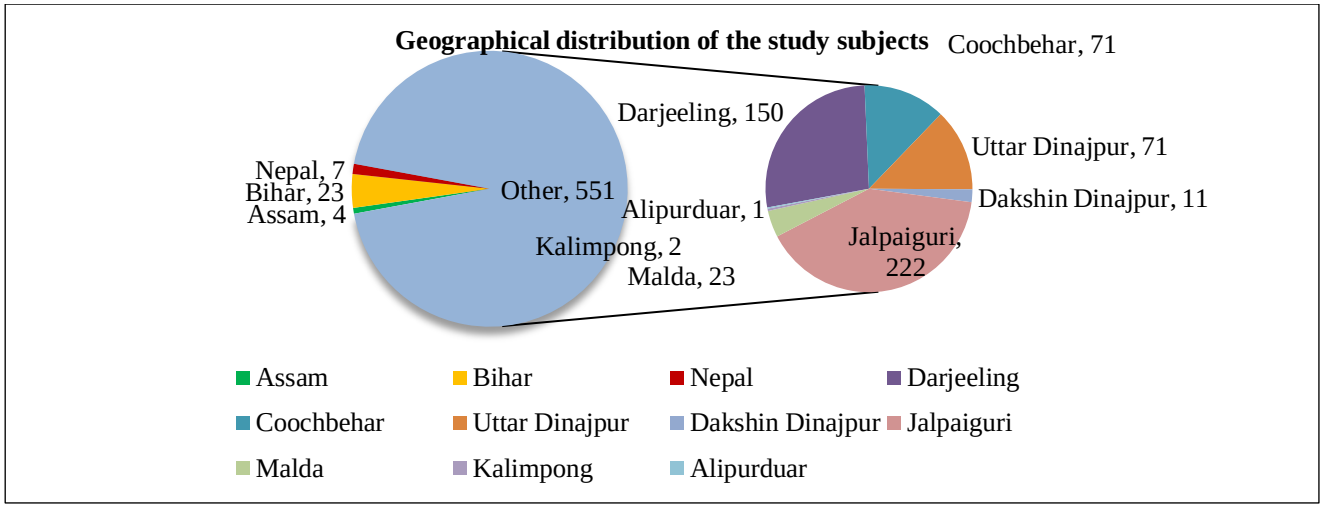
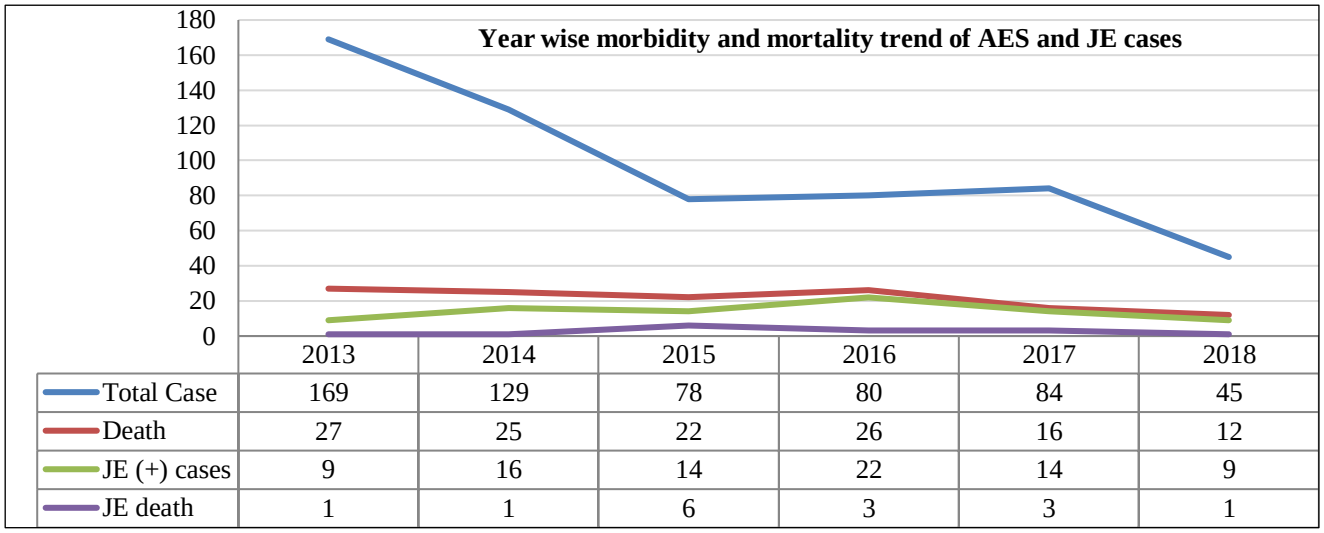


Figure 2: The geographical distribution of AES.



	2013	2014	2015	2016	2017	2018
Total Case	169	129	78	80	84	45
Death	27	25	22	26	16	12
JE (+) cases	9	16	14	22	14	9
JE death	1	1	6	3	3	1

Figure 3: Year wise morbidity and mortality trend of AES and JE cases.

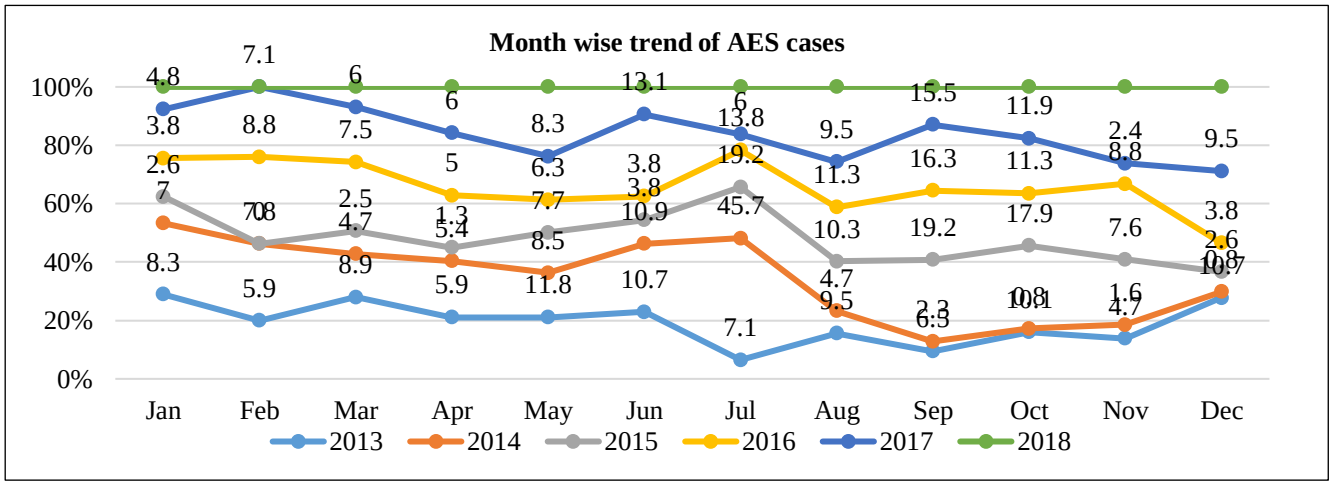


Figure 4: Month wise trend of the AES cases.

In our study 585 out of 39420 cases (1.48%) were diagnosed as AES, whereas population based other studies show the incidence ranges between 3.5 and 7.4 cases per 100000 patient years.[2] Bihar showed that AES

comprise of 2% and 1.77% of total pediatric hospital admission respectively.[3,4] This can be explained by sharing of similar geographical and socio-economical factors as neighbor states.

Male patients (372) contributing to 63.6% and female patients (213) 36.4%. Similar results were observed, AES was high in males (64.7%) than females (35.3%) in Karnataka, India and in Nepal 34 (72.34%) male in comparison to 13 (27.65%) female.[5,6]

Common age group is 1-5 years similar to study done followed by 6-10 years age group but majority belongs to age group >5-10 years.[3,4] Similar result as higher proportion of subjects were toddlers (30.1%) followed by pre-school children (26.5%).[5]

Month wise distribution of cases were maximum in July contributes to 110 (18.8%) followed by September 59 (10%), October 56 (9.5%), May 55 (9.4%). Least number of cases were admitted in November 29 (4.9%) followed by January and February 33 cases each (5.6%). In our study the seasonal occurrence of AES cases was peak during July to October but Rayamajhi A et al[7] showed clear peak in JE case admissions in August and September following rainy seasons. And in case of non-JE patients they didn't demonstrate any clear seasonal variation. Whereas in our study we found JE cases were more in numbers in July (27 cases) and August (20 cases) same as other AES cases. Sarkar et al[8] found that cases were more in the monsoon and post-monsoon period which supports our study. The difference between seasonal trends may be due ecological variations.[5,7] (Figure 3 and 4).

Maximum number of cases were from West Bengal (94.2%) followed by Bihar (3.9%), Nepal (1.2%) and Assam (0.4%) as our institution is in the vicinity of Bihar, Nepal and Assam. Large proportion of cases were from Jalpaiguri district (222) 37.9% followed by Darjeeling district (150) 25.6%, Coochbehar (71) 12.1% and least from Alipurduar (1) 0.2% and Kalimpong (2) 0.3%. District having more population and easily accessible from our institution have larger contribution. (Figure 2).

Among the 585 AES cases, 263 (45%) were suspected for viral etiology [JE= 84 (male – 54, female -30) 14.3%] followed by bacterial meningitis 131 (22.3%), tubercular meningitis 24 (4.2%). 167 (28.5%) cases constitute other group including dengue, scrub typhus, neurocysticercosis and of unknown etiology. Similar results are shown where viral etiology is most common.[5-7]

JE cases contribute to 14.35% of total cases. Similar result was found where 12.21% cases were found to be positive for JE.[9] But 22.04% of JE cases in their study.[4] Documented only 3.7% of JE cases among suspected AES cases.[5] This difference is due to the geographic features of various regions which indulge the spread of JE virus; abundance of paddy fields, hot and humid temperature, provides a suitable environment for JEV transmission.

Among 84 JE cases (male - 54, female - 30), there is male predominance. The result coincides with the result.[10,11] Males are more involved with outdoor activities than females; males are more exposed to mosquito bites that may explain male predominance. On the contrary found female predominance in JE cases. This difference may be due to sexual disparity.[12]

Analysis by JE positive in different age group, 27 (32.1%) JE cases were <5 years of age and 57 (67.9%) were >5 years age group ($p < 0.05$). Similar result was found on study.[13] Children more than 5 years are relatively active and play outdoor games, whereas below 5 years children mostly remain home under strict supervision of their parents. This explains the JE cases in different age groups.[14]

Among 63.1% were serum positive for JE IgM and 40.5% were CSF positive for JE IgM and 3.6% were positive for both. Majority of cases were diagnosed by serum study (82%) and a minor group by CSF study (18%).[14] This finding may be due to the fact that lumbar punctures being undertaken less frequently on children who were critically ill.

Favourable outcome was seen in case diagnosed with JE as 69 (82.1%) cases were discharged compared to overall AES discharge 457 (78.1%), where non-JE (585-84=501) discharge (457-69=388) is 77.5% (388/501). This result is supported by the study conducted, where 66% of JE cases were discharged successfully against 51% of overall AES discharge.[4] Cross-protection by other flaviviral diseases, such as, dengue and mass vaccination programme against JE under supervision of The State Health Department of Government of West Bengal using live attenuated JE vaccine SA-14-14-2 could be main reasons for declining incidence and good outcome for JE.[9]

Among 128 dead (21.9%), 80 were male (64%) and 48 were female (36%). There is a slight predominance seen in below 5 years mortality, 70 cases (54.68%) against 58 cases (45.32%) in those were above 5 years. JE death was 15 (male 8, female 7; 11.7% of total death) 17.9% of all JE cases. 10 JE deaths (66.66%) were above 5 years of age and remaining 33.34% are below 5 years. 6 JE deaths were occurred in 2015, 3 each in 2016, 2017 and only 1 death in 2018. This decreasing trend may be due to active surveillance of JE cases.

In India study regarding burden of AES/JE with special reference to immunization status are limited so we are not able to compare our result. In our study 11 (7 males, 4 female) among 15 JE death were unimmunized which is statistically significant ($p < 0.05$) by Chi-square test.

Our study has a number of drawbacks firstly sample size is small which may affect results' external validity in few instances; second, if we used community based data in place of hospital based data it would have been revealed the actual scenario better.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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