

Original Research Article

Seroprevalence of Japanese encephalitis amongst cases of acute encephalitis syndrome in a tertiary care centre of north east India: a four year retrospective study

Daiji G. Mohan¹, Mayuri Gogoi^{2*}, Ajanta Sharma²

¹Department of Microbiology, Tezpur Medical College and Hospital, Tezpur, Assam, India

²Department of Microbiology, Gauhati Medical College and Hospital, Guwahati, Assam, India

Received: 17 June 2019

Accepted: 03 August 2019

*Correspondence:

Dr. Mayuri Gogoi,

E-mail: mayurigogoi84@rediffmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: The present study was undertaken to investigate the trend of JE and the different parameters associated with it.

Methods: It was a hospital-based retrospective study conducted from January 2014 to December 2017. A total of 3531 consecutive non-repetitive patients, satisfying the clinical case definition of AES as per the WHO guidelines, were included in the study. Cerebrospinal fluid (CSF) and serum samples were tested for JEV-specific IgM antibodies by the NIV JE IgM Capture ELISA Kit.

Results: Of the 3531 patients admitted, 838(23.7%) cases were positive for JE IgM antibodies. There was a significant reduction in the JE positivity rate from 32.9% in 2014 to 13.3% in 2017. The male-to-female ratio was 1.6:1. JE positivity rate was significantly higher in adults as compared to children. The majority of cases occurred during the monsoon and post-monsoon season. Fever (100%), change in mental status (87.8%), headache (70.5%), neck rigidity (32.4%), unconsciousness (35.4%), seizure (43.9%) and paralysis (5%) were the major clinical symptoms. JE positivity was seen to be higher in the rural areas of Assam.

Conclusions: A declining trend of JE was seen in this study, however further research work needs to be done to look for non-JE causes of AES.

Keywords: Acute Encephalitis syndrome, Cerebrospinal fluid, Japanese encephalitis, JE trend, Immuno globulin Enzyme-Linked Immunosorbent Assay.

INTRODUCTION

Japanese encephalitis (JE) is a leading form of viral encephalitis worldwide, mostly prevalent in eastern and southern Asia, covering a population of over three billion.¹ The disease has public health importance because of its epidemic potential and high fatality rate. Approximately one third of patients die, and half of the survivors suffer severe neuropsychiatric sequelae from

the disease.² Japanese encephalitis virus (JEV) belongs to the family *flaviviridae* and genus *Flavivirus*.³

It is a single stranded, positive-sense polarity RNA genome of approximately 11 kb in length. The virion of JEV contains three structural proteins – nucleocapsid or core protein (C), non-glycosylated membrane protein (M), and glycosylated envelope protein (E), as well as seven non-structural (NS) proteins-NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS.⁴

The natural cycle of JE virus in Asia involves water birds and *Culex* mosquitoes. However, an amplifying host is also important in the epidemiology of human JE. In Asia, pigs are considered to be the most important amplifying host, providing a link to humans through their proximity to housing.⁵ For Southeast Asia, the main vector of JE is *C. tritaeniorhynchus*.⁶ In northern temperate areas including Northern parts of India, large epidemics occur during the summer months, roughly from May to October.⁷

In India, epidemics of JE are reported from many parts of the country. It is possible that many cases are unreported and hence the actual magnitude of the disease may be considerably higher.⁷ The disease has appeared in sporadic outbreaks or epidemic forms in Assam, since 1976. Approximately 597,542,000 people in India live in JE-endemic regions, and 1,500 to 4,000 cases are reported every year.⁸ The mortality rate of JE is approximately 25% to 30%.^{1,9} 50% of those who recover suffer from neurological deficit.¹⁰ Some effects, such as learning difficulties and behavioural problems, can be subtle and may remain undetected for several years.^{11,12}

JE is mostly a disease of children and young adults. Infection due to JEV is most often asymptomatic.¹ The first signs of infection appear after an incubation period between 6-14 days. It usually starts with a fever above 38°C, chills, muscle pain, and meningitis-type headaches accompanied by vomiting. The initial presentation in children usually begins with gastrointestinal symptoms: nausea, vomiting, and abdominal pains.¹³ The present study was therefore undertaken to do a retrospective analysis of trend of JE in North-east India.

METHODS

The study was conducted retrospectively in the Department of Microbiology, GMCH. A total of 3531 AES cases received over a period of four years from January 2014 to December 2017 were included in the study. These 3531 AES samples included samples from patients admitted in GMCH as well as samples received from private hospitals.

The inclusion criteria included the clinical case definition of AES as per WHO guidelines according to which AES is defined as patients who present with fever, altered sensorium (including symptoms such as confusion, disorientation, coma or inability to talk), and/or new onset of seizures.¹⁴

The exclusion criteria included patients with simple febrile seizures and patients with encephalitis due to other causes like mumps, measles or varicella zoster. The medical history and clinical findings of each patient were recorded in the Laboratory request form as per guidelines of National Vector Borne Disease Control Program

(NVBDCP), Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India.¹⁵

CSF and Serum samples were collected from all the 3531 AES cases. In 308 numbers of cases only serum sample was received. CSF samples were collected in sterile vials and immediately transported to the laboratory of the Department of Microbiology, GMCH, Guwahati. All the samples were tested for IgM antibodies by the National Institute of Virology (NIV) JE IgM Capture ELISA Kit supplied by NVBDCP. If optical density (OD) value of sample tested exceeded the OD of negative control by a factor of 5, the sample was considered as positive.

All collected data were statistically analyzed using statistical software INSTAT. The results are presented as number and percentage and chi-square test was done wherever necessary to calculate the p-value. The p-value of less than 0.05 was considered to be statistically significant.

RESULTS

A total of 3531 cases of AES were included in the study. Out of the 3531 cases, 2172 (61.5%) were males and 1359 (38.4%) were females. 838 (23.7%) cases were positive for JE IgM ELISA. during this period. From Table 1 we can observe that there is a significant reduction in the JE positivity rate from 32.9% in 2014 to 13.3% in 2017. However, the increasing percentage of JE negative AES cases is an area where further studies can be done to look for other causes of AES (Table 1).

JE positivity rate is higher in adults as compared to children. The p-value is <.0001, considered extremely significant. Positivity rate in adults ranged from 66% to 82% whereas in children the positivity range was 18% to 33% (Table 2).

It was observed in the study that there was no significant difference in the positivity rate of JE among males and females. The p-value was found to be 0.8555 and hence considered insignificant. The male to female ratio was 1.6:1 (Table 3).

In this region, the virus activity starts from June onwards reaches a peak in July and lasts up to October. Sporadic cases are seen however throughout the year (Figure 1).

Considering the geographical locations from where the patients have come, the proportion of JE positive cases was found to be higher in rural areas as compared to urban areas. The Kamrup Rural, Nagaon, Barpeta, Darrang and Nalbari districts were found to have the highest incidence of JE cases (Figure 2).

Table 1: Positivity rate of JE from 2014-2017.

	2014	2015	2016	2017
Total AES cases	1145	899	774	713
JE Positive cases	377(32.9%)	222(24.6%)	144(18.6%)	95(13.3%)
JE Negative cases	678(59.2%)	594(66%)	563(72.7%)	568(79.6%)
JE Equivocal cases	90	83	67	50

Table 2: Age wise distribution of AES cases from 2014-2017.

Age	2014		2015		2016		2017	
	Total AES cases	JE positives	Total AES cases	JE positives	Total AES cases	JE positives	Total AES cases	JE positives
≤12 years	302	68(18%)	351	42(18.9%)	403	45(31.2%)	369	32(33.6%)
>12 years	843	309(81.9%)	548	180(81%)	371	99(68.7%)	344	63(66.3%)
Total	1145	377	899	222	774	144	713	95

Table 3: Sex wise distribution of AES cases for 2014-2017.

Sex	2014		2015		2016		2017	
	Total AES cases	JE positives	Total AES cases	JE positives	Total AES cases	JE positives	Total AES cases	JE positives
Male	755	240(63.6%)	527	136(61.2%)	475	90(62.5%)	415	46(48.4%)
Female	390	137(36.3%)	372	86(38.7%)	299	54(37.5%)	298	49(51.5%)
Total	1145	377	899	222	774	144	713	95

Table 4: Showing the various clinical manifestations seen among the JE positive AES cases.

Clinical feature	Number of JE positive cases showing the below symptoms (n=838)	Percentage
Fever	838	100%
Headache	591	70.5%
Altered sensorium	736	87.8%
Neck rigidity	272	32.4%
Seizure	368	43.9%
Paralysis/Hemeparesis	42	5%
Unconsciousness	297	35.4%

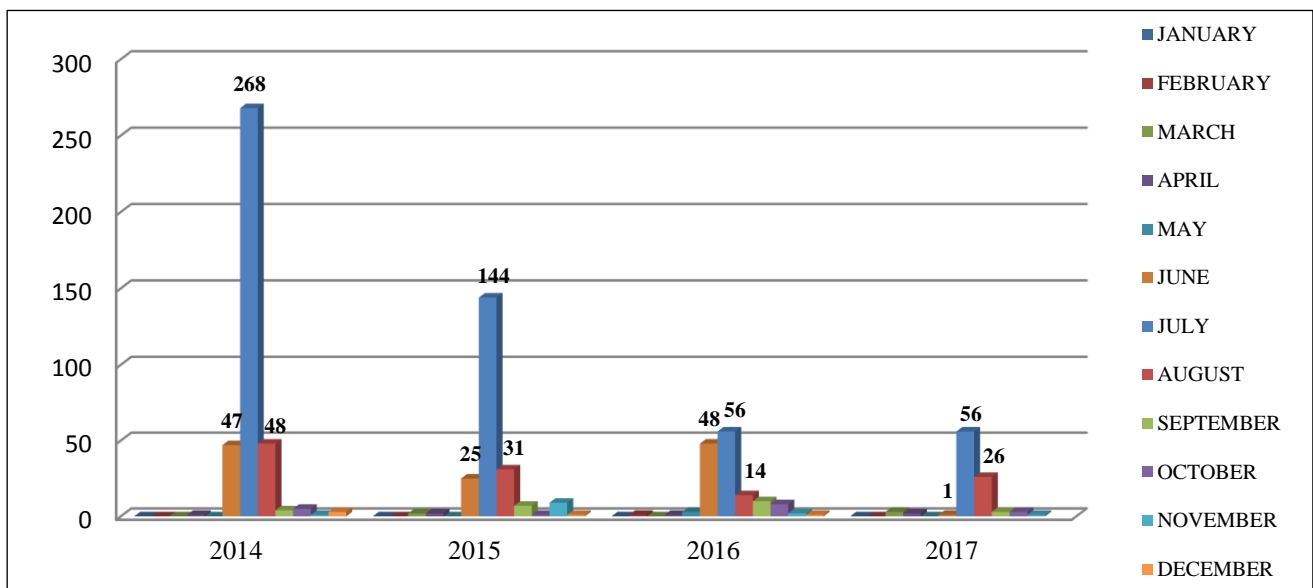


Figure 1: Month wise distribution of JE positives cases from 2014-2017.

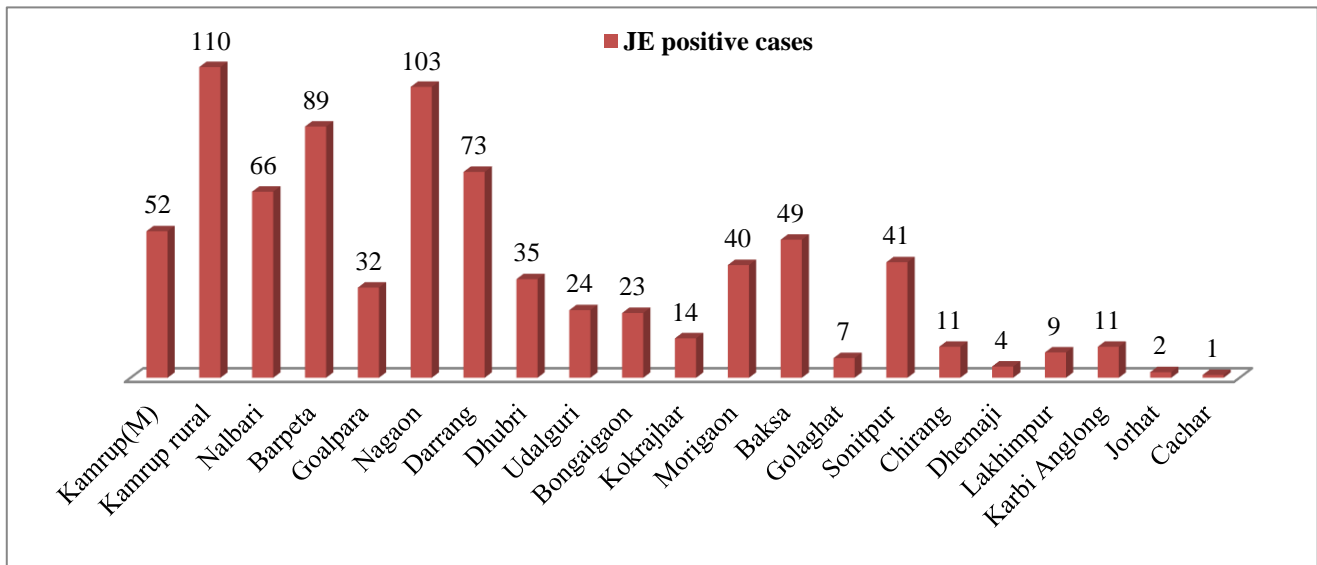


Figure 2: District-wise distribution of JE positive cases from 2014-2017.

DISCUSSION

From this study, authors have observed that over the period of four years, the JE positivity rate has significantly reduced from 32.9% in 2014 to 13.3% in 2017. Similar findings have also been reported.^{16,17} Reason for this may be better awareness programs, strengthening of laboratory services, mass vaccination or simply due to herd immunity. According to some authors, there has been a changing epidemiological trend of flavivirus mediated diseases from JE to dengue in recent years possibly due to increased urbanisation of the remote villages.^{16,18,19} Cross-protection by other flaviviral diseases, namely, dengue, could be a reason for decline of the JE cases to some extent. Although there has been a decline in the number of AES cases due to JE, there are still a large proportion of non-JE AES cases. There has been a shift in understanding of the spectrum of aetiology of AES in India and is now thought to be contributed largely by non- JE aetiology. Hence, it is important that further studies should be done to look for other etiological causes of AES.

Although studies have indicated that JE is more common in children as compared to adults, the scenario in Assam is different. Our study shows a higher prevalence of JE in adult. The findings are similar to other studies done from our region.^{17,20-23} It can be presumably due to the influence of vaccination programme targeting children between 1-15 years and also due to increased exposure of adults to mosquitoes in areas of rice cultivation as explained by some authors.¹³

No significant difference was seen among the positivity rate of JE among males and females.^{17,24-26}

The present study revealed significant number of JE cases in the monsoon season from June to September which is similar to the findings of higher incidence of JE during similar months.^{17,20-23,27,29} This can be explained by the fact that the *Culex* mosquitoes breed abundantly in the paddy fields covered with stagnant water during the rainy season.

Fever (100%) was the most predominant symptom followed by altered sensorium (87.8%) and headache (70.5%) similar to the observation of other authors.^{17,21-23}

Our study also indicates that most of the JE cases occurred in the rural districts of Assam, where the main occupation is agriculture. The JE virus is particularly common in rural areas where irrigated rice fields attract the natural avian hosts and provide abundant breeding site for the vector.^{23,24,27,29}

CONCLUSION

AES is a public health problem, aetiology and epidemiology of which still are largely unknown, which critically challenges the scientific community. The changing epidemiology particularly in the context of its varied aetiology needs further research work. Prevention and control of JE-AES may be possible only after developing a strong surveillance system together with a high-quality immunization program. Other measures include modified agricultural practices, pig vaccination, vector control, and improved living standards.

ACKNOWLEDGEMENTS

The authors are grateful to National Vector Borne Disease Control Program (NVBDCP), National Institute

of Virology (NIV), Pune, India for supply of ELISA kits. The authors sincerely thank the laboratory technicians Labanya Boro and Bharati for their dedicated work. The authors would also like to thank Nimi Baruah Das, Data Entry Operator for her support.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

- Ghosh D, Basu A. Japanese encephalitis-a pathological and clinical perspective. *PLoS Negl Trop Dis.* 2009;3(9):e437.
- Solomon T, Dung NM, Kneen R, Gainsborough M, Vaughn DW, Khanh VT. Japanese encephalitis. *J Neurol, Neurosurg Psychiatr.* 2000 Apr 1;68(4):405-15.
- Karabatsos N. International catalogue of arboviruses including certain other viruses of vertebrates, 3rd ed. San Antonio: American Society of Tropical Medicine and Hygiene; 1985.
- Chambers TJ, Hahn CS, Galler R, Rice CM. Flavivirus genome organization, expression, and replication. *Annu Rev Microbiol.* 1990;44:649-88.
- Kabilan L, Rajendran R, Arunachalam N, Ramesh S, Srinivasan S, Samuel PP, et al. Japanese encephalitis in India: an overview. *Indian J Pediatr.* 2004;71(7):609-15.
- Kanojia PC, Shetty PS, Geevarghese G. A long-term study on vector abundance & seasonal prevalence in relation to the occurrence of Japanese encephalitis in Gorakhpur district, Uttar Pradesh. *Indian J Med Res.* 2003;117:104-10.
- Tsai TF, Chang GJ, Yu YX. Japanese encephalitis vaccines. In: Plotkin SA, Orenstein WA, eds. *Vaccines.* 3rd ed. Philadelphia: WB Saunders, 1999:684-710.
- Kabilan L. Control of Japanese encephalitis in India: a reality. *Indian J Pediatr.* 2004; 71(8):707-12.
- Mackenzie JS, Gubler DJ, Petersen LR. Emerging flaviviruses: the spread and resurgence of Japanese encephalitis, West Nile and dengue viruses. *Nat Med.* 2004;10(12):S98-109.
- Kaur R, Vratil S. Development of a recombinant vaccine against Japanese encephalitis. *J Neurovirol.* 2003;9:421-31.
- Schneider RJ, Firestone MH, Edelman R, Chiewanich P, Pornpibul R. Clinical sequelae after Japanese encephalitis: a one year follow-up study in Thailand. *Southeast Asian J Trop Med Public Health.* 1974;5(4):560-8.
- Lam K, Tsang OT, Yung RW, Lau KK. Japanese encephalitis in Hong Kong. *Hong Kong Med J.* 2005;11(3):182-8.
- Burke DS, Monath TP. Flaviviruses. In: Knipe DM, Howley PM, editors. *Fields Virology.* 4th edition. Philadelphia, PA: Lippincott- Raven Publishers; 2001;1043-1125.
- World Health Organisation. WHO - Recommended Standards for surveillance of Selected Vaccine - Preventable Diseases. Geneva: WHO;2003. Available at: <http://apps.who.int/iris/bitstream/10665/68334/1/WHO-V-B-03.01-neg.pdf>, Accessed on 12 June 2018.
- Directorate of National Vector Borne Diseases Control Programme. Guidelines for Surveillance of Acute Encephalitis Syndrome (with Special Reference to Japanese Encephalitis):2006. Available at:<http://www.nvbdc.gov.in/doc/AES%20guideline.s.pdf>. Accessed on 20 January 2014.
- Bandyopadhyay B, Bhattacharyya I, Adhikary S, Konar J, Dawar N, Sarkar J, et al. A comprehensive study on the 2012 dengue fever outbreak in Kolkata, India. *ISRN Virol.* 2013 Aug 7;2013.
- Medhi M, Saikia L, Patgiri SJ, Lahkar V, Hussain ME, K Kakati S. Incidence of Japanese Encephalitis amongst Acute Encephalitis Syndrome cases in upper Assam districts from 2012 to 2014: A report from a tertiary care hospital. *Indian J Med Res.* 146, August 2017;267-71.
- Taraphdar D, Sarkar A, Bhattacharya MK, Chatterjee S. Sero diagnosis of dengue activity in an unknown febrile outbreak at the Siliguri Town, District Darjeeling, West Bengal. *Asian Pacific J Tropical Medicine.* 2010 May 1;3(5):364-6.
- A. Sarkar, D. Taraphdar, S. Chatterjee, Investigations of recurrent out breaks of unknown fever, establish rural dengue activity in west Midnapore, a costal district in west Bengal, India, *Archives of Clinical Microbiol,* 1(4);2010.
- Mohan DG, Hazarika NK. A Clinico-Pathological Study and Demographic Profile of Japanese Encephalitis from a Tertiary Care Hospital in Assam, India. *Int J Curr Microbiol App Sci.* 2015; 4(6):522-9.
- Patgiri SJ, Borthakur AK, Borkakoty B, Saikia L, Dutta R, Phukan SK. An appraisal of clinicopathological parameters in Japanese encephalitis and changing epidemiological trends in upper Assam, India. *Indian J Pathol Microbiol.* 2014;57(3):400-6.
- Borthakur A, Das N, Bora B. Data from the World Health Organization (WHO) National Network Laboratory for Japanese Encephalitis. *J Glob Infect Dis.* 2013 April;5(2):96-9.
- Phukan AC, Borah PK, Mahanta J. Japanese encephalitis in Assam, Northeast India. *Southeast Asian J Trop Med Public Health.* 2004;35:618-22.
- Dutta BS, Bezborah K, Begum S, Pathak M, Biswas S. A retrospective study of acute encephalitis syndrome with special reference to Japanese encephalitis in tertiary care centre, Tezpur, Assam. *J Entomol Zool Studies.* 2017;5(6):1231-5.
- Kumari R, Joshi PL. A review of Japanese encephalitis in Uttar Pradesh, India. *WHO South-East Asia J Public Heal.* 2012;1:374-95.
- Roy A, Mandal K, Sen S. Study of acute viral meningoencephalitis in children in sub-Himalayan

- Tarairegion: clinico-epidemiological, aetiological, and imaging profile. *Indian J Child Health.* 2015; 2(4):177-81
27. Anuradha SK, Surekha YA, Sathyanarayan MS, Suresh S, Satish P, Mariraj J, et al. Epidemiological aspects of Japanese encephalitis in Bellary, Karnataka, India. *Int J Biol Med Res.* 2011;2(3):691-5.
28. Sarkar A, Taraphdar D, Mukhopadhyay SK, Chakrabarti S, Chatterjee S. Molecular evidence for the occurrence of Japanese encephalitis virus genotype I and III infection associated with acute encephalitis in patients of West Bengal, India, 2010. *Viol J.* 2012 Dec;9(1):271.
29. Benakappa DG, Anvekar GA, Viswanath D, George S. Japanese encephalitis, *Indian Pediatr.* 1984;21,(10)811-5.

Cite this article as: Mohan DG, Gogoi M, Sharma A. Seroprevalence of Japanese encephalitis amongst cases of acute encephalitis syndrome in a tertiary care centre of north east India: a four year retrospective study. *Int J Res Med Sci* 2019;7: 3490-5.