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

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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. For Southeast Asia, the main vector of JE is C. tritaeniorhynchus. In northern temperate areas including Northern parts of India, large epidemics occur during the summer months, roughly from May to October.

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. 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. The mortality rate of JE is approximately 25% to 30%. 50% of those who recover suffer from neurological deficit. Some effects, such as learning difficulties and behavioural problems, can be subtle and may remain undetected for several years.

JE is mostly a disease of children and young adults. Infection due to JEV is most often asymptomatic. 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. 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.

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.

CSF and Serum samples were collected from all the 3531AES 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 3531cases, 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.

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

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

<table>
<thead>
<tr>
<th>Age</th>
<th>Total AES cases</th>
<th>JE positives</th>
<th>Total AES cases</th>
<th>JE positives</th>
<th>Total AES cases</th>
<th>JE positives</th>
<th>Total AES cases</th>
<th>JE positives</th>
<th>Total AES cases</th>
<th>JE positives</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤12 years</td>
<td>302</td>
<td>68(18%)</td>
<td>351</td>
<td>42(18.9%)</td>
<td>403</td>
<td>45(11.2%)</td>
<td>369</td>
<td>32(33.6%)</td>
<td>32(33.6%)</td>
<td></td>
</tr>
<tr>
<td>&gt;12 years</td>
<td>843</td>
<td>309(81.9%)</td>
<td>548</td>
<td>180(81%)</td>
<td>371</td>
<td>99(68.7%)</td>
<td>344</td>
<td>63(66.3%)</td>
<td>63(66.3%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1145</td>
<td>377</td>
<td>899</td>
<td>222</td>
<td>774</td>
<td>144</td>
<td>713</td>
<td>95</td>
<td>95</td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Sex</th>
<th>Total AES cases</th>
<th>JE positives</th>
<th>Total AES cases</th>
<th>JE positives</th>
<th>Total AES cases</th>
<th>JE positives</th>
<th>Total AES cases</th>
<th>JE positives</th>
<th>Total AES cases</th>
<th>JE positives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>755</td>
<td>240(63.6%)</td>
<td>527</td>
<td>136(61.2%)</td>
<td>475</td>
<td>90(62.5%)</td>
<td>415</td>
<td>46(48.4%)</td>
<td>46(48.4%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>390</td>
<td>137(36.3%)</td>
<td>372</td>
<td>86(38.7%)</td>
<td>299</td>
<td>54(37.5%)</td>
<td>298</td>
<td>49(51.5%)</td>
<td>49(51.5%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1145</td>
<td>377</td>
<td>899</td>
<td>222</td>
<td>774</td>
<td>144</td>
<td>713</td>
<td>95</td>
<td>95</td>
<td></td>
</tr>
</tbody>
</table>

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

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

Figure 1: Month wise distribution of JE positives 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{13}

No significant difference was seen among the positivity rate of JE among males and females.\textsuperscript{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.\textsuperscript{17,20-23,27,29} This can be explained by the fact that the \textit{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.\textsuperscript{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.\textsuperscript{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.

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