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Original Research Article

Japanese Encephalitis in Hospitalized Children with AES after Introduction of Live Attenuated SA 14-14-2 Vaccine in Endemic Districts of Assam, India

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ABSTRACT

Background: Japanese encephalitis (JE) is the leading cause of viral encephalitis across Asia. No effective antiviral drugs are currently available for treatment. Getting vaccinated is the best way to prevent JEV infection. In Assam, JE vaccinations have been conducted for children in endemic districts since 2006. We conducted a prospective study to determine the incidence of JE in hospitalized AES children after introduction of live attenuated SA 14-14-2 vaccine in EPI.
Methods: From Jan2011-Dec2013, all eligible pediatric AES patients admitted to Assam Medical College & Hospital were enrolled. JE was confirmed with Mac ELISA on detection of IgM against JEV in CSF or serum.
Results: Over all JE incidence in children was 35.3% among the AES cases. Of which 36.8% in 2011, 31.3% in 2012 and 40.9% were detected in 2013. The crude hospital based JE incidence was estimated to be 2.9/100000 children per year. Among the JE positive cases 98 (59.8%) were male and rural children were more prone (95%) to JE infection. Monthly incidence of JE cases showed a seasonal trend starting from May-September with a peak in July (59.8%).Vaccination history of JE cases revealed that only 10.5% had received SA 14-14-2 either from mass campaign or RI. JE infection was more (78.5%) in children with no vaccination history than those with unknown history of vaccination (11%).
Conclusion: JE virus infection among the hospitalized AES children is still high (35.3%) in post vaccination period. This emphasizes the need of strengthening of JE surveillance with improved quality vaccine coverage.

Key words: Japanese Encephalitis, Acute Encephalitis Syndrome, Assam, incidence, SA14-14-2

INTRODUCTION

Japanese encephalitis (JE) is a vector borne viral encephalitis primarily affects the children. It has been estimated that JE has infected ~10 million children globally, killing 3 million and causing long-term disability in 4 million.[(1)] Presently there are JE outbreaks and epidemics in large parts of Southeast Asia.[(2)] Almost in every two years, epidemics of JE occur in Indian subcontinent with a high mortality.[(3)] Outbreaks have been reported from states like Uttar Pradesh, West Bengal, Assam, Andhra Pradesh, Karnataka, Bihar, Tamil

Nadu, Haryana and other states through the years . [1]

No effective antiviral drugs are currently available for therapy of JE except supportive treatment.[4] Vaccination is the most cost effective and best means of preventing and controlling JE. The JE immunization programs conducted for children in Asian countries, such as Japan, Korea, Taiwan, China, Thailand, Sri Lanka and Nepal have obviously decreased the number of JE cases in their countries. [5,6] In India, JE mass vaccination campaigns were carried out in high risk districts in endemic states including Assam since 2006 to 2010. Children between the age group of 1 to 15 years were vaccinated with a single dose of SA 14-14-2 live attenuated JE vaccine. Following the mass campaigns the vaccine was integrated into the Universal Immunization Programme (UIP) of the same districts to cover the new cohort of children between 1-2 years of age. The status of JE incidence in children in post vaccination period in endemic districts of Assam has not been well documented. We conducted a hospital based study during January 2011 to December 2013 in Assam Medical College & Hospital to see the incidence of JE amongst the AES cases in pediatric age group.

MATERIALS AND METHODS

Over the 3-years study period from January 2011 to December 2013, all eligible pediatric AES patients belonged to the catchment districts Tinsukia, Dibrugarh, Sivasagar, Jorhat, Golaghat and Dhemaji admitted to children ward of Assam Medical College and Hospital were considered for the present study. Children up to 12 years of age meeting the clinical diagnosis of AES and willing to give consent for lumbar puncture or for collection of blood samples were included. Routinely, Lumber puncture was performed and blood samples were taken by the attending pediatricians as a part of clinical care. A part of CSF (1ml) and serum (2ml) samples were collected and stored separately at -80°C until further testing, which was all conducted at Regional Medical Research Center, (Indian Council of Medical Research), Lahowal, Assam. All CSF and serum samples were tested for antibodies against JEV. [7] A case of JE was confirmed with Mac ELISA on detection of IgM against JEV in CSF and or serum by IgM antibody capture-Enzyme – Linked Immunosorbent Assay kits obtained from National Institute of Virology (NIV), Pune, India. Clinically a case of AES is defined as fever or recent history of fever with change in mental status (including confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures). Other early clinical findings could include an increase in irritability, somnolence or abnormal behavior greater than that seen with usual febrile illness. [8,9] Clinical and demographic information were recorded in a predesigned format from all the enrollees. The Assam Medical College hospital is an apex level institute providing health care services mostly to the districts of upper Assam. Approximately 1895417 children of 0 to 12 years age (census 2011) residing in the catchment areas of this hospital susceptible to JE infection. We calculated the hospital based JE incidence by dividing the number of confirmed JE cases admitted to study hospital in one year from the catchment districts divided by the total catchment population.

Written informed consent was obtained from either parents or legal guardian before sample and data collection. The study was approved by the Institutional Ethics Committee (Human) of Regional Medical Research Centre (ICMR), Dibrugarh, Assam, India.

RESULTS

During the study period 513 children up to 12 years of age meeting the clinical case definition of AES were identified. The AES cases which were from other than the catchment districts of study center and the patient from whom we could not collect any sample were excluded. For the present analysis we enrolled only 465 AES cases which were from the different catchment districts of the study hospital. Of these 260(55.9%) were male and 447(96.1%) were from rural area.

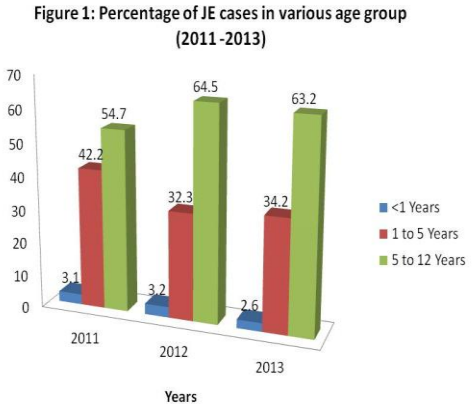


Figure 1. Percentage of JE cases in various age group (2011 -2013)

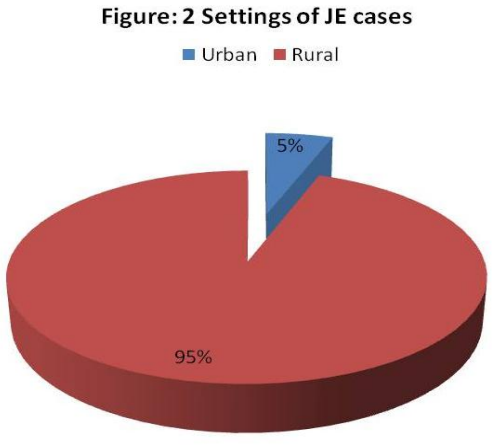


Figure 2. Settings of JE cases

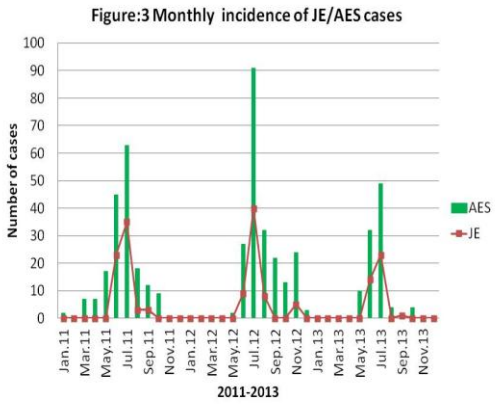


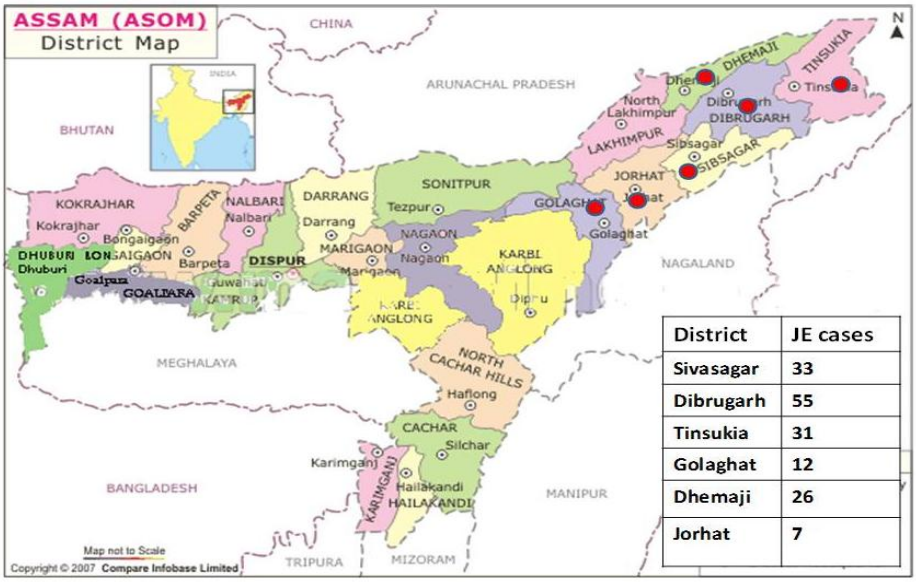
Figure 3. Monthly incidence of JE/AES cases

Among the 465 AES patients, we could collect at least one CSF or Serum sample at the time of admission for JEV specific IgM antibody detection. Among them, 164(35.3%) were found to be laboratory confirmed JE. The JE cases were confirmed following detection of JEV specific IgM antibody either in CSF or serum. All the samples were found to be negative for the presence of IgM antibody for Dengue and West Nile flavi viruses prevalent in this region. Among the JE positive patients 36 were confirmed only in Serum while 34 were only in CSF following detection of anti-JEV IgM antibodies. Another 94 JE cases were confirmed both in serum and CSF for JEV specific IgM antibody. Out of these JE positive cases, 64(36.8%) were admitted in 2011 and 62(31.3%) in 2012 while 38(40.9%) cases were found in the year 2013.It has been observed that of 164 JE positive children, 98 (59.8%) were male and maximum age group affected were 5 to 12 years (Fig-1). Children from rural area were found to be more prone (95%) to JE infection (Fig-2). Monthly incidence of JE cases during the study period as depicted by Fig-3 showed a seasonal trend starting from May-September with a peak in July (59.8%) except a few

5(3%) JE cases were detected in November 2012. Geographical distribution of JE cases among the different catchment districts showed 31 in Tinsukia, 33 in Sivasagar, 7 in Jorhat, 12 in Golaghat, 26 in Dhemaji and maximum 55 JE cases in Dibrugarh district (Fig-4). The overall hospital based JE incidence was estimated to be 2.9/100000 children up to 12 years of age in these hospital catchment districts.

Vaccination history of JE cases revealed that only 10.5% had received SA 14-14-2 either from mass campaign or RI. JE infection was more pronounced in children (78.5%) with no vaccination history than those with unknown history of vaccination (11%).

Figure: 4 Distribution of JE Cases by district, January 2011- December 2013



District	JE cases
Sivasagar	33
Dibrugarh	55
Tinsukia	31
Golaghat	12
Dhemaji	26
Jorhat	7

Figure 4. Distribution of JE Cases by district, January 2011- December 2013

DISCUSSION

The present study which was conducted over a period of three years revealed that 35.3% of hospitalized pediatric AES cases were confirmed as having JE. These confirmed JE cases belonged to six endemic catchment districts of the study center. Among these catchment districts (Tinsukia, Dibrugarh, Sivasagar, Jorhat, Golaghat, Dhemaji), maximum JE cases 33.5% were recorded from Dibrugarh district.

The overall crude hospital based incidence was 2.9/100000 children up to 12 years age. This may be the underestimate of true burden of disease as some of the ailing children may not seek treatment in this sentinel site or may die before reaching the hospital.

Our finding is similar with the estimated incidence of 5.4 cases per 100000 populations among children ≤14 years of age in JE-endemic countries. [(10)] In other JE endemic countries like Bangladesh 2.7, Taiwan 2.1 and in Thailand the JE incidence was 3-5/100000 population before the introduction of JE vaccine in NIS. [(11,12)]

In the catchment area, the most of the JE cases (96.1%) occurred in rural area and the incidence in 5-12 years age group children were more pronounced. Similar findings were also observed in other studies. [(13-15)] This is due to availability of conducive ecological conditions in rural areas that

favors in JE virus transmission in the catchment districts, including mosquito breeding grounds in paddy field, piggeries in close proximity to human dwellings and water bird to act as a virus amplifier. [16] This finding is consistent with the observation of earlier studies that JE is more prevalent in rural rice-cultivating areas in Asian countries. [17,18] Young children are more vulnerable to JE infection because of their ambulatory nature. They play game in outdoor and many of the poor children accompany with their farmer parents during the rainy season to work in paddy field and get directly exposed to the incriminated mosquito bite during dusk hours. [15,7]

In our study all JE infection were recorded during May to September except 5 cases in November 2012. Monthly incidence as depicted in Fig-4 showed a peak in July (59.8%) in all the study years. Seasonal incidence is consistent with findings of other studies conducted in Asia. [8,19,20] This may be elucidated due to high density of mosquito vector during the rainy season. As their number grow, spread of JE virus and the infection rate of pigs and wading birds also grow simultaneously and resulting in more human infection. Mass JE vaccination campaign with live attenuated SA 14-14-2 has been launched since 2006 in these catchment districts followed by integration of JE vaccine in routine immunization. However, present study revealed incidence of JE in hospitalized AES children is noticeably high and only 10.5% JE cases had received SA 14-14-2 either from mass campaign or RI. JE infection was more in children (78.5%) with no vaccination history than those with unknown history of vaccination (11%). As per the UNICEF survey data, 36 per cent of the eligible children (ages 1–15 years) received JE vaccine during the mass campaign 2006 in Dibrugarh district of Assam, [21] while the officially reported coverage was 90 per cent. [1] Conversely, the incidence of JE has been reduced dramatically in Japan, Korea, Taiwan, China and Thailand since the introduction of a JE vaccine in to the National Immunization Programme of theses country. [22-24] Widely used live attenuated SA 14-14-2 JE vaccine is cost-effective and with a single dose provides 80-96% protection. [25,26] Additionally, in recent years it has been observed that JE is no longer confined only in children population in many states of India including Assam. Increased frequency of JE infection in adult has been well noticed. Commensurate with this observation adult JE vaccination campaign was initiated in endemic districts of upper Assam. [27]

Observing the high frequency of JE cases in the present study, there is need of further investigations in better understanding of disease burden and impact of potential vaccine control programme in these JE endemic districts.

CONCLUSION

Incidence of JE infection amongst the Hospitalized AES cases in children is still high (35.3%) in post vaccination period. Although in recent years vaccination program has been introduced in JE endemic districts of Assam, our observation of still high incidence of JE in children warrants further Strengthening of AES surveillance along with a long-standing, high-quality childhood vaccination coverage in these JE endemic districts of Assam.

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Conflict of Interests: The authors declare that they have no conflict of interests.

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