Brief Research Article

Outbreaks and Sporadic Cases of Japanese Encephalitis in the State of Odisha, India: Outcome of 7 Years of Laboratory Surveillance

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Summary

Acute encephalitis syndrome (AES) is a major public health challenge in India. We report here the epidemiology of sporadics and outbreaks of Japanese Encephalitis (JE) in Odisha state during 2012–2018. A total of 4235 AES cases (sporadics – 3394, outbreak cases – 841) recorded including 42 outbreaks; majority (n = 18) of which were during 2016. Overall JE virus (JEV) positivity was 11.78% (outbreak cases – 24.5%, sporadic cases – 8.6%). Age ≤15 years were largely affected during outbreaks, while 16–60 years population was dominant among sporadics. The major outbreak (2016) involved 336 patients from a tribal dominated district, spread over 173 villages. JEV seropositivity was high (43.45%) with 28.57% mortality. Epidemiological linkage with pig rearing was documented through JEV neutralizing antibodies in 50% of pig serum samples. Although the postvaccination period (2017–18) showed increase in AES case reporting but low JE proportion. Ongoing surveillance and preparedness of the health system would be of importance, especially in tribal-dominated districts.

Key words: Acute encephalitis syndrome, Japanese encephalitis, Odisha, tribal

Acute encephalitis syndrome (AES) emerged as one of the major public health emergencies in India, characterized by a high case-fatality rate (CFR), among children. Between 2008 and 2014, around 44,000 cases and 6000 deaths were reported from encephalitis. While the Japanese encephalitis virus (JEV) is the leading diagnosis, many cases are left without an identified etiology.[1]

In Odisha, an Eastern Indian state, cases of Japanese Encephalitis (JE) reappeared in 2012, following the first report during 1989.[2] The largest of these outbreaks was reported during 2016 in a tribal area with high under-five mortality. Our laboratory evidence helped initiate JEV vaccination in endemic districts of the state (India news, Press Trust of India, December 6th, 2016). Here, we discussed the epidemiology of JE sporadic and outbreaks in Odisha during 2012–18, that covers both pre-and post-vaccination periods.

We conducted hospital-based and field investigations of sporadic and outbreaks of AES from different parts of Odisha.

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For case recruitment, we used our network with tertiary level hospitals and Integrated Disease Surveillance Programme (IDSP) of the state. We investigated the outbreaks by field survey along with peripheral health staff. Following the standard definition of AES, the cases were recruited by the treating physician or the outbreak investigating team with consent from the parents/guardians. Detailed clinical and epidemiological information was recorded, and blood samples (3 ml) and/or cerebrospinal fluid (CSF) (2–3 ml) collected under supervision following appropriate precautions. Samples were transported maintaining cold chain to the Virus

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Research and Diagnostic Laboratory at Regional Medical Research Centre, Bhubaneswar. A total of 4235 AES cases were enrolled that covered all 30 districts of Odisha state. 2333 serum and 2342 CSF samples were investigated. During the major outbreak in Malkangiri district (2016), blood samples from pigs (n = 10) were evaluated. JEV-specific immunoglobulin M (IgM) capture ELISA (MAC-ELISA kit, National Institute of Virology, Pune) and CSF polymerase chain reaction tested for JEV. Pig blood tested at National Institute of Virology (NIV), Pune, for JEV neutralizing antibody. The clinico-epidemiological data were analysed for descriptive statistics using SPSS version 20 (IBM, Armonk, New York, United States). The study was conducted following good clinical and laboratory practice guidelines under approval of institute's ethics committee.

Eight hundred and forty-one AES cases from 42 outbreaks and 3394 sporadic patients were investigated [Table 1]. The outbreaks were mostly reported from tribal majority districts such as Malkangiri, Mayurbhanj, Keonjhar, Nabarangpur, Rayagada, Koraput, Nuapada, and Sundergarh. Sporadic cases of JE were laboratory confirmed every year; while 2012, 2013, 2015, and 2016 faced small to large JE outbreaks. Case Fatality Rate (CFR) among the outbreak cases during these years varied from 4.85% to 55.34%.

The major outbreak of them affected the Southern most and tribal-dominated district of Malkanagiri that borders the states of Andhra Pradesh and Chhattisgarh. In September 2016, cases of AES were noted, which spread to over 173 villages between September 8 and November 29, 2016. Epidemic curve indicated peak of cases between September 29 and October 12. The distribution of cases and deaths during this outbreak is summarized in Table 2. Despite sufficient care, detailed clinical history could be recorded from 199 cases during this outbreak, because of remoteness and low educational status of the tribal population. Symptomatology of these cases revealed history of fever for 1–5 days' duration (90%), vomiting (56.2%), altered sensorium (65%), convulsion (19.6%), and pain abdomen (1.5%). The clinical presentation was similar among cases showing JE antibody and non-JE AES cases. The mean duration of survival of the children who succumbed to death was 3.02 days (±0.9 days; range <1–10 days) from onset of symptoms. JE seropositivity was 43.45% of the suspected patients and one of nine CSF samples showed JEV RNA. Five of ten pig blood samples revealed JEV neutralising antibodies indicating JE circulation.

Hospital-based recruitment of sporadic cases (n = 3394) and JE confirmation (n = 293) is detailed in Table 1. In-between 2012-2018, over all JE IgM positivity was 8.6% among sporadic cases where as during 2018 relatively higher number of AES cases (n=1304) were reported with 11.2% of JE IgM positivity.

Overall JEV sero confirmation from both sporadic cases and outbreaks of AES (n = 4235) was 11.59%; n = 498 (<6 years of age - 8%, 6–15 years - 14.8%, 16–30 years - 12.7%, 31–45 years - 13%, 46–60 years - 14.8%, and >60 years - 12.8%). Outbreak cases have high JEV seropositivity among children <15 years (<6 years - 24.1%, 6–15 years - 33.2%, 16–30 years - 7.4%, 31–45 years - 15.8%, 46–60 years - 10.7%, >60 years - 17.6%) while sporadic cases showed more adult contribution (<6 years - 4.2%, 6–15 years - 8.8%, 16–30 years - 14.1%, 31–45 years - 12.2%, 46–60 years - 15.2%, >60 years - 12.4%).

Moreover, the years 2017 and 2018 did not reveal any outbreak due to JEV, sporadic case distribution indicated a trend towards age shift from children to adult with a JE seropositivity of 3.4% and 6.6% in ages below 6 years, 12.2% and 17.8% among 16–30 years, 10.9% and 18% among 31–45 years, 14% and 17.6% among 46–60 years, and 11.9% and 12.3% in >60 years of age.

A series of JE outbreaks were reported from different parts of India. In 1978, cases were recorded across 21 states/UTs, and in the recent past largely affecting Assam, Andhra Pradesh, Bihar, Goa, Haryana, Kerala, Karnataka, Maharashtra, Manipur, Tamil Nadu, Uttar Pradesh, West Bengal, and Nagaland. 103,389 AES/JE cases and 33,729 deaths (CFR 32.62%)

Table 1: Distribution of outbreaks and sporadic cases of acute encephalitis syndrome with Japanese encephalitis virus confirmation (2012–2018)

Period	Outbreaks					Sporadics		
Year	Number of outbreaks	Number of districts affected	Name of districts	AES cases	JE positives (%)	Number of districts affected	AES cases	JE positives (%)
2012	3	2	Malkangiri, Nabarangpur	123	10 (8.1)	5	63	5 (7.9)
2013	3	2	Keonjhar, Malkangiri	151	28 (18.5)	6	86	7 (8.1)
2014	4	2	Keonjhar, Malkangiri	82	0	14	56	4 (7.1)
2015	13	2	Mayurbhanj, Jajpur	79	27 (34.2)	24	231	12 (5.2)
2016	18	9	Mayurbhanj, Jajpur, Malkangiri, Keonjhar, Koraput, Nuapada, Puri, Raygada, Sundergarh	399	141 (35.3)	25	601	34 (5.7)
2017	1	1	Khurda	7	0	30	1053	85 (8.1)
2018	0	0	Nil	0	0	30	1304	146 (11.2)
Total	42	11	-	841	206 (24.5)	30	3394	293 (8.6)

AES: Acute encephalitis syndrome, JE: Japanese encephalitis

Table 2: Case distribution and deaths among acute encephalitis syndrome cases and Japanese encephalitis positives in the major outbreak from Malkanagiri district (2016)

Age group	Number of AES cases (%)	Number of deaths from AES (%)	Number of JE positives (%)	Number of deaths among JE positives (%)
0–6 months	4 (1.19)	0	0	0
7 months–1 year	17 (5.06)	5 (4.85)	4 (1.19)	1 (0.68)
1–3 years	158 (47.02)	57 (55.34)	62 (18.45)	22 (15.07)
3–5 years	101 (30.06)	36 (34.95)	45 (13.39)	10 (0.68)
5–13 years	56 (16.67)	5 (4.85)	35 (10.42)	1 (0.68)
total	336	103 (30.6)	146 (43.45)	34 (23.28)

AES: Acute encephalitis syndrome, JE: Japanese encephalitis

were noted between 1978 and 2007.[3] Uttar Pradesh reported 47,509 cases between 2005 and 2018; where JE positivity was 9.98% and average CFR was 17.49%.[4]

Hence, JEV emerged as a major public health problem in the country in terms of a large number of deaths, severe neurological sequelae that needs support for daily living, and contribution toward a considerable socioeconomic burden.[5]

Our report from Odisha showed a high AES case fatality (30.6%) during 2016 from Malkangiri district. The first record (2012) of JE outbreak from the same district had shown 272 AES cases with 24 deaths (8.8%).[2] However, we are limited with the completeness of mortality data throughout the study, because laboratory surveillance was not supported with a strong case follow-up plan.

In most outbreaks, children were seen to be largely affected. An outbreak in India (2005) reported 1700 deaths mostly involving children and other reports too indicated a larger burden of JE among children in developing countries.[6] In our study, children below 15 years were largely affected in the outbreaks that put a concern for vaccination. As a response to the laboratory confirmation of JE as the etiology of AES outbreaks and public concerns over the fatal illness, JEV vaccination was implemented from 2017 in endemic districts of Odisha (business standard, November 18, 2017). In the postvaccination period (2017–2018), there was no record of JE outbreak. Improved hospital-based surveillance detected many sporadic AES cases (n = 2364) but with low JEV contribution (n = 231, 9.77%).

However, we need to have ongoing surveillance with widespread awareness among treatment providers raising clinical suspicion for seeking laboratory evaluation. This will help identify new endemic areas or epidemic foci of JE, thus planning for vaccination of the whole at-risk population in the country. Besides, the possible age shift we observed toward adults/elderly following childhood vaccination might need future attention.

It was observed that there are two epidemic seasons/periods for JE outbreaks coinciding with monsoon and postmonsoon months. The state of Odisha also experienced a marked increase in vector density during the above seasons.[7] Karnataka and Andhra Pradesh experience two episodes of epidemics every year; April–July is quite severe while September–December is milder similar to rest of India.[8] We recorded severe outbreaks from September to November in our state. However, in endemic areas, sporadic cases might occur throughout the year.[8] This can possibly be explained from our observation of circulation of JEV infection among the amplifying host, i.e. pig.

Although JEV was shown to be the major contributor towards AES cases/outbreaks, we could confirm JEV in 5.9%–37.5% of all AES cases, leaving other possibilities to be explored.

With similar clinical presentation and seasonality, dengue as the etiology could be considered and was also reported as co-infection/co-circulation in endemic areas.[1,9]

Public and expert concerns and confusions regarding the involvement of any other environmental risk factors like *Cassia occidentalis* toxicity were also observed as a challenge in framing public health intervention in the state (The Times of India dated November 19th, 2016). This is a wild shrub available in the forest localities whose tender beans were reported to have toxic effect on liver and attributed towards acute central nervous system disorders in Saharanpur, UttarPradesh.[10] It remained unsolved whether the above phytotoxin is a confounder or a co-contributor towards the illness in a situation where the seasonality was favouring both mosquito replication and fruiting of the *C. occidentalis*.

This report confirmed JEV as a major contributor toward acute encephalitis outbreaks and sporadic hospital admissions in Odisha, India. The challenges in public health diagnosis and management were evident in form of larger affection of the tribal population residing in outreach pockets and gives a message for continuing preparedness to deal with such emerging situations. Re-orientation of the health system in line of emerging viral disease investigation may be useful in keeping watch over the need of specific vaccination program.

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Conflicts of interest
There are no conflicts of interest.

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