

Epidemiological study of Acute Encephalitis Syndrome and Japanese Encephalitis burden in Sivasagar district of Assam, India

Rahim Ali Ahmed (✉ rahim.ahmed48@gmail.com)

National Vector Borne Disease Control Programme <https://orcid.org/0000-0002-3689-7206>

Daisy Konwar

National Vector Borne Disease Control Programme

Ananta Swargiary

Bodoland University

Hari Shankar

ICMR - National Institute of Malaria Research

Kuldeep Singh

ICMR - National Institute of Malaria Research

Rimen Bordoloi

D R College, Golaghat

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Abstract

Japanese Encephalitis (JE) is among the most common cause of viral encephalitis in human beings caused by the Japanese Encephalitis virus (JEV). It is found worldwide, especially in Southeast Asia and less commonly in the western pacific regions and Australia. North East India is identified as hotspot for Japanese encephalitis and is considered a major health problem in Assam. The present study assesses the epidemiology of Acute Encephalitis Syndrome (AES) and JE cases of the Sivasagar district of Assam for 2011-20. Epidemiological data of AES and JE such as disease burden, case fatality rate (CFR), etc. were collected from NVBDCP Unit of Sivasagar district. Data were obtained as a part of routine AES/JE control programme for the period 2011-20. The overall AES and JE cases during 2011-20 were 1081 and 588, and death cases 333 and 180, respectively. The CFR of the district was found to be 30.61%. AES and JE cases were highest in Galekey and Patsaku block. The AES/JE cases were significantly higher in elderly (>30 years) and male population of the district. The peak AES/JE active and death cases were reported in June and July in the study period. Routine JE vaccination was found to be carried out since 2011-20 in the age group 9-18 months, covering more than 50% of the target population size. Similarly, during the 2011-12 and 2014-15, JE vaccination campaign was carried out in 1-15- and 16-60-years age group. The prevalence of AES/JE cases in the Sivasagar district of Assam is declining. Nevertheless, there is an urgent need to intensify the AES/JE surveillance programme to detect the cases and develop strategy for better JE management. The immunization coverage for 9-18 months should be increased.

Introduction

Japanese Encephalitis is among the most common cause of viral encephalitis in human beings caused by the Japanese Encephalitis virus (JEV). It is found worldwide, especially in Southeast Asia and less commonly in the western pacific regions and Australia.¹ Over 3 billion individuals live in JE endemic countries. It is estimated that approximately 67,900 JE cases have occurred annually in 24 countries, with only 10426 cases reported in 2011.² The annual incidence of clinical disease varies both across and within endemic countries, ranging from <1 to >10 per 100 000 population or higher during outbreaks. It is estimated that nearly 68 000 clinical cases of JE globally each year, with approximately 13 600 to 20 400 deaths.³ The fatality rate in JE ranges from 20%-30%, with neurologic or psychiatric sequelae observed in 30%-50% of survivors.⁴ In India, the first human case was reported from North Acrot district of Tamil Nadu in 1955⁵ and subsequently, after the first major JE outbreak in 1973 from Burdwan district of West Bengal, the disease spread to other states. It caused a series of outbreaks in different parts of the country. In India, 171 districts from 18 states/Union Territories covering a population of 375 million are identified as JE endemic areas.⁶ In Assam, first outbreak of JE was reported in the Lakhimpur district in 1978.⁷ In 1989, a major outbreak occurred in the Lakhimpur district of Assam between July-August, affecting 90 villages, covering approximately 36000 populations with a 50% case fatality rate.⁸ Acute encephalitis syndrome (AES) is a major cause of concern and characterized by inflammation of the brain.⁹ Till 2005, all AES cases were being labeled as Japanese Encephalitis (JE). However, after 2005, the etiological diagnosis for AES is being established, and it was believed that all AES cases might not be JE positive. It

is transmitted by infective bites of female mosquitoes mainly belonging to *Culex tritaeniorhynchus*, *Culex vishnui* and *Culex pseudovishnui*. However, some other mosquito species also play a role in transmission under specific conditions.¹⁰ Hospital-based acute encephalitis syndrome (AES) surveillance in North and North East India showed that 25% of cases were positive for JE, which were prevalent mainly in children.^{11,12} Outbreak of JE was confined mainly to the Upper Assam districts till 2015. But now, the situation has changed, and there have been outbreaks of the disease in lower Assam and even the Barak valley districts. Total 134 people died of JE in 2013, 165 died in 2014, 135 in 2015, 92 in 2016, 87 in 2017 and 94 in 2018 in Assam. Ten high endemic districts in Assam – Sivasagar Barpeta, Nagaon, Sonitpur, Darrang, Udalguri, Bongaigaon, Cachar, Morigaon, and Nalbari have been included under the multi-pronged strategy adopted for prevention and control of JE.¹³ To triumph over the burden, JE vaccination campaign was launched in 2006 in Sivasagar for the first time across Assam, wherein 11 of the most sensitive districts were covered by vaccination in Assam till now. Again, in 2011, adult vaccination was introduced by the health department in mostly affected Sivasagar district of Assam to perceive the impact and efficacy of the vaccine.¹⁴ The present study was conducted to perceive the incidence of AES/JE cases in the Sivasagar district of Assam from 2011 to 2020 to know the epidemiological trends of AES/JE cases.

Materials & Methods

Study Area

The Sivasagar district earlier known as “Rangpur”, the historical city of Assam, is situated at the eastern part of Assam, India. It occupies a geographical area of 2668 sq. km between longitude 94°25'E to 95°25'E and latitude 21°45'N to 27°15'N. The district is surrounded in the north by the Brahmaputra River, in the east Dibrugarh District, in the west by Jorhat district, and in the south Nagaland state. The district shares state borders with Nagaland and Arunachal Pradesh. The major physiographic variation of the district is generally considered to be the plain except high land areas, flood prone areas and swampy areas.¹⁵ The climate of the district is congenial. The annual average temperature is 23.8° C. Average annual rainfall is about 2952 mm, and the relative humidity is about 78.8% on average. Males constitute 51.2% of the population and females 48.8% of 11.5 lakh population of the district. The district has an average literacy rate of 80.41%, higher than the national average of 59.5%: male literacy is 85.84%, and female literacy is 74.71%. In the Sivasagar district, 90.44% of the population is under rural setup, and the district shares 3.68% population to total population of the state.¹⁶

Data Collection

Epidemiological data regarding AES and JE such as disease burden, morbidity, case fatality rate, annual incidence rate, seasonal variation, age- and gender-wise distribution, and JE vaccination were collected from the Integrated Disease Surveillance Project unit and National Vector Borne Disease Control Programme Unit of Sivasagar district of Assam, India. Data were obtained as a part of routine Acute

Encephalitis Syndrome and Japanese Encephalitis surveillance for the period of 2011 to 2020. The National Vector Borne Disease Control programme modified the case definition in 2006. Since then, epidemiological surveillance for acute encephalitis syndrome (AES) was initiated, and suspected JE cases are now reported as AES, "*Clinically, a case of AES is defined as a person of any age, at any time of year with the acute onset of fever and a change in mental status (including confusion, disorientation, coma or inability to talk) or onset of seizures*" (NVBDCP, India). Clinical diagnosis was made by serum, and cerebrospinal fluid samples of suspected cases and confirmation of JE cases were done by IgM Enzyme-Linked Immunosorbent Assay (ELISA) Kit following the standard protocol of NVBDCP.¹⁷

Statistical Analysis

All the statistical calculations such as proportions, percentage, mean, etc. were carried out in Microsoft Excel. The burden of JE morbidity, annual incidence rate and case fatality rate were analyzed using Microsoft Excel ($P \leq 0.05$). Test of significance and correlation studies were carried out in OriginPro and SPSS statistical software.

Results

Demographic profile of the Sivasagar district

Table 1 showed the demography and health care facility of the Sivasagar district of Assam. With 1024 villages, the district has a population of 11.51 lakh as per the population census 2011, Government of Assam. The rural population of the district constitutes 93.90% of the total population and shares 90.44% of the total population of Assam. The population density of the district currently stands at 431 per sq km. The district also has a high sex ratio (...). The majority community in the district is Hindu (87.51%), followed by Muslim (8.30%), Christian (2.88%) and others like Sikh, Buddhist, Jain (1.3%). The district has an average literacy rate of 80.41%, which is below the literacy rate of Assam (88.88%). The district has a central District Civil Hospital (DCH) located at the Sivasagar town, the headquarters of the district and two subdistrict hospitals. In addition, the healthcare system of the district comprises eight Block Level Primary Health Centers (BPHC), namely Sapekhati, Patsaku, Galekey, Khelua, Demow, Gaurisagar, Kalogaon and Morabazar BPHCs. A total of 36 PHCs, 1 community health centers (CHC), 1 dispensary, 4 model hospitals and 220- PHC sub-centers work in collaboration with BPHC. The CHCs constitute the secondary level of healthcare designed to provide referrals as well as specialist healthcare in rural areas. CHCs have been envisaged as only one type and will act both as Block level health administrative units and gatekeepers for referrals to a higher level of facilities. All essential services such as routine and emergency care, medicine, Gynecology, Pediatrics, AYUSH, etc., are made available by CHCs. All the epidemiological disease surveillance work is carried out by PHC sub-centers distributed all across the district, and each sub-center covers about 4 to 5 villages. In addition to seven reserved beds for clinical management of JE cases, there is also a dedicated public health laboratory for JE test and serum sample analysis through IgM ELISA in DCH of Sivasagar district. In District Civil Hospital (DCH), six bedded Pediatric Intensive Care Unit (PICU) is also functioning. However, critical patients are referred to Assam

Medical College & Hospital, Dibrugarh, located at Dibrugarh town for intensive care about 80 km away from district Hospital.

Table 1 Demographic profile of Sivasagar District

Parameters	Number
Population	1151050
Rural Population	1040954
Population Density (per sq km)	431
Villages	1024
Tea Estates	98
Sex Ration (Male/Female)	1000/954
Literacy Rate (%)	84.41
District Hospital	1
Sub District Hospital	2
Block PHC	8
CHC	1
PHC	36
Dispensary	1
Model Hospital	4
Sub-centers	220

Trend of AES and JE cases in Sivasagar district

Figure 1 showed the trend of AES, JE, and fatality rates from 2011 to 2020 in the Sivasagar district of Assam. The overall AES and JE cases during the study period was found to be 1081 and 588, respectively. Similarly, the death cases were found to be 333 and 180 for AES and JE, respectively. Out of the total AES cases, 54.39% were found to be JE cases, and 54.05% deaths were reported due to JE out of 333 AES death cases. During the period of study, there was a significant decline in encephalitis cases from 2011 to 2020. The positive cases, number of deaths, and CFR were found to be the highest in the year 2011 (21.76% of total cases) followed by 2015 (11.39%), 2013, 2014 and 2017 (10.88% each)), and lowest in 2020 (3.06%). Similarly, the highest death cases were reported in 2011, followed by 2013 and 2012. However, the cases were increased in 2017 and 2019. In 2017, the cases were increased dramatically from 51 to 100 cases, an increase by double. Figure 1 also showed the Case Fatality Rate

(CFR) due to Japanese Encephalitis that ranges between 13-45% during 2011 to 2020. The overall CFR of the district during the period 2011 to 2020 was found to be 28.16%. There was a fluctuation of CFR from 2011 to 2013, reaching the highest to 45.31% and lowest to 36.72%. However, from 2014 onwards, there was a significant decline ($P \leq 0.05$ level) in JE cases in the Sivasagar district.

Age-wise distribution of AES and JE cases in Sivasagar district

The prevalence of AES cases in different age-groups of Sivasagar district of Assam during the period from 2011 to 2020 is presented in Figure 3. It is found that the AES cases were significantly higher in the age-group >30 years of the district compared to a younger age. The total number of AES cases during the period was found to be 94, 185, 208, 377, and 217 cases for the age-groups 0-5, 6-15, 16-30, 31-60, and above 60 years, respectively. Age group 31 to 60 years showed the highest susceptibility to AES (34.87%), followed by age group >60 years (20.07%). Similarly, the numbers of AES death cases were found to be much higher in age-group >31-60 years, constituting about 38.44% of the total death cases of the district, followed by age-group >60 years, which is about 30.03% of total AES death in the district for the period. The lowest cases reported from children belonging to age-group 0-5 years with 8.6% of total cases. Similarly, the lowest death reported among the children belonging to age group 0-5 years with 7.2% of total death. On the other hand, there was a steep increase of AES cases in the age-group 6-15 years during 2016-17 compared to other age groups.

Figure 3b showed the prevalence of JE cases in all the five different age-groups of Sivasagar district of Assam from 2011 to 2020. JE cases were found to be significantly different in different age-groups. Like AES, higher JE cases were observed in older people (>30 years) compared to younger age-groups (<30 years). The transmission rate among children (0-5 years) was significantly less and reported at only 6.8%. 14.45% and 16.83% of JE cases were reported in the age-group 6-15 and 15-30 years, respectively. Almost 61.9% of JE cases were reported from age group above 30 years. Total 30.61% of JE death cases were reported out of the total JE cases in the district. JE death is significantly higher in the age-group >30 years (77.22%). 40.55% death cases were reported from age group 30-60 years and 36.66% from age group >60 years.

Sex-wise distribution of AES and JE cases in Darrang district

The gender-wise distribution of AES and JE cases from 2011 to 2020 is presented in Figure 4. It is observed from the study that both the AES and JE cases were significantly higher in male population compared to female (Figure 4). Out of 1081 cases, in our study, 669 and 412 cases were reported in male and female. Both the AES and JE positive and death cases showed almost similar trends in both male and female populations. JE cases were observed in a similar pattern of occurrence in the district during the study period. Total 370 JE cases were reported in male population, while 218 cases in female population from the study area. Male and female showed significant differences ($P \leq 0.05$ level) in terms of JE susceptibility throughout study. Similarly, out of 180 JE death cases, 115 (63.89%) and 65 (36.11%) deaths were reported in males and females. It has also been observed that the JE cases were much higher in the male population in almost all the age-groups. The percent of JE cases and mortality

reported in male and female population of the district during the study period is shown in Figure 4d. Correlation study revealed that an increase in male or female cases has significant relation ($P \leq 0.01$ level) to AES or JE cases.

Seasonal prevalence of AES and JE cases in Sivasagar district

The month-wise prevalence and seasonal trend of JE cases analyzed from 2011 to 2020 are presented in Figure 5. It was observed that the spikes of JE outbreak starts from May every year and continues till August. Highest JE cases were reported in July followed by June almost every year from 2011 to 2020. Out of 588 JE cases during the study period, 561 cases (about 95.41%) occurred during the month from May to August. The number of cases reported in June and July was 133 (22.62%) and 372 (63.26%), respectively. The outbreak of JE was found to be almost dormant from September to April, although few cases were reported throughout the year. Figure 5 showed the seasonal variation of JE cases during the period 2011-20. In the year 2017 and 2019 the cases were reported from January and reached peak in June and July. However, the maximum deaths were reported only in June and July. The transmission of Japanese Encephalitis cases has increased during the rainy seasons and declined post rainy seasons.

Block-wise distribution of AES and JE cases in Darrang district

The distribution and prevalence of AES and JE cases in different blocks of Sivasagar district from 2011 to 2020 are presented in Figure 6(a-h). The study reveals differences in the prevalence of AES and JE cases in all eight blocks of Sivasagar district. During the study period (2011-20), the total numbers of AES cases were 141, 221, 60, 66, 174, 57, 216, and 146 in Demow, Galekey, Gaurisagar, Kalogaon, Khelua, Morabazar, Patsaku, and Sapekhati block. On the other hand, JE cases were found to be highest in Galekey block (23.46%), followed by Patsaku (18.19%), Khelua (16.49%), Sapekhati (13.06%), Dimow (11.05%), Kalogaon (6.46%), Gaurisagar (5.95%) and Morabazar (5.10%). Similarly, death cases due to AES and JE were highest in Galekey block (26.12%), followed by Khelua, Patsaku, Dimow, Sapekhati, Gaurisagar, Morabazar and Kalogaon. During the study period, the peak of encephalitis cases were recorded in 2011-14 in all the blocks, and later on, there was a decline of encephalitis cases. The highly affected blocks were Galekey, Patsaku and Khelua. Morabazar block found to be low endemic in comparison to other blocks. A maximum of two-four years continuous increase or decrease in the number of cases have been observed during the period of study from the block level disease surveillance. The study also revealed that both positive and death cases of AES and JE resurged in all the blocks in the year 2020 except Morabazar, which showed a decreasing fatality trend during the period of study (Figure 6f).

JE Vaccination

Vaccination is the most cost-effective therapeutic intervention to achieve long-term protection. In 2006, the Government of India launched a JE vaccination campaign for children from 0 - 15 years of age. This was followed by immunization of new cohorts as an integral component of the Universal Immunization Programme with a single dose of live attenuated JE vaccine (SA-14-14-2) in 11 highly endemic districts

of four states (Assam, Karnataka, Uttar Pradesh, and West Bengal). Figure 7 showed the total population and percentage coverage under JE vaccination programme in Sivasagar district of Assam from 2011 to 2020 for the age group of 09-18 months. A total of 112932 individuals have been covered under the vaccination program out of 203361 targeted populations during the period of study (data source: district Immunization Programme, Sivasagar). It was observed that, during the launch of Routine Immunization Programme in 2011-12, the coverage was very poor (13.59%) with one dose only (age above one year). Similarly, during 2012-13 the coverage was also found to be very poor (28.03%). Later on the programme was revised to two doses of JE RI by Gol. The coverage increased in 2016-17, 2017-18, 2019-20 and 2020-21 reported above 70%. The Target population found to be similar in all the years except 2020-21. There was a slight decline in the target population and coverage in the year 2020-21 (Figure 7). The highest percentage coverage was found in 2020-21 (88.77%). Mass JE vaccination campaigns in children aged 1 to 15 years and adults 16 years above were carried out in 2011-12 with target and coverage population sizes of 583330 and 554739 (95.10%), respectively. Similarly, adult (age-group 16-60 years) JE campaign for left out in 2011-12 was carried out during 2014-15 in Sivasagar district of Assam achieving 138719 (77.49%) population coverage out of targeted 179006 population size.

Discussion

North East India is identified as hotspot for Japanese encephalitis, and it is considered a major health problem in Assam. Along with other VBDs, the state of Assam is more vulnerable to JE infection compared to other states of India. Therefore, ASE/JE surveillance is an important and necessary activity to understand the prevalence and warning signals of disease outbreaks. Furthermore, surveillance data is useful in assessing the impact of vaccination and vaccine efficacy.¹⁸ In the present study, we observed that Sivasagardistrict is highly endemic to AES and JE cases. The average annual AES and JE CFRs were 30.80% and 30.61%, which is much higher than the global fatality rate of 20 to 30%.¹⁹ The high rate of mosquito-borne cases in Sivasagar district may be associated with the weather and anthropogenic conditions as well as socio-economic conditions of the people. During the monsoon period (June to September), the agricultural fields are filled with water which provides a suitable breeding ground for mosquito vectors. The district has numerous wetlands and big ponds where migratory birds often harbor, and those birds are one of the main amplifying hosts for the transmission of JEV. Many researchers have reported significant correlations between mosquito vectors and VBD.²⁰ In peninsular and eastern parts of India, pigs are the main vertebrate host of JEV and the major reservoir of JE infection.²¹ Infected pigs act as amplifying hosts. Therefore, pig rearing is an important risk factor of JE transmission in humans. Pig rearing is also a major livelihood for many people in the district. During the 19th Livestock census of 2012 by the Department of Animal Husbandry, Government of Assam, it was estimated that a total of about 1636 thousand pigs were reared in the entire state (Livestock Census 2012, Assam)²² and contributes about 16% of country's total pig population and ranks (Govt of India 2014).²³ Pig has been considered one of the most important livestock in Upper Assam area, particularly in the district of Sivasagar. The population of the district is mostly dominated by the Ahom community, who traditionally rear pigs in their backyard and contributes 5.37 per cent of Assam's total pig population.²⁴ It was observed

that the piggeries are more in the rural population and are unorganized. Hence the chance of human infection is high. The probability of vector mosquito species getting infected with JEV is higher when the infected mosquito population dramatically increased during the rainy season and the human biting rate increases.²⁵ Moreover, lower household income, house type, distance to health sub-centre, knowledge and awareness about mosquito-borne diseases significantly impacted effective controlling of JE.²⁶ It is observed that in Sivasagar district, the number of AES/JE cases declined in the period of study and also the case fatality rate (CFR) of JE also reduced from 45% highest in 2013 to 16.67% in 2020. Similarly, Kumari and Joshi (2012)²⁷ studied the decadal JE fatality rate in the state of Uttar Pradesh and revealed that cases were declined from 33% in 1978–1987 to about 22% in 1998–2009. Similarly, the average case fatality rate of AES and JE in the state of Bihar was found to be 30% and 14% during 2009-14.²⁸ In a recent study, Singh et al. (2020)²⁹ revealed significant improvement in the JE fatality rate from 24.76% in 2005 to only 8% in 2018.

The global incidence of JE cases in Asia and Western Pacific countries predominates in the children age group 0-14 years which constitute about 75% of the total JE cases³⁰. Li et al. (2016)³¹ revealed a similar pattern of diseases prevalence in China. The age of a person acts as an important determining factor in the susceptibility or resistance to diseases, including AES and JE infection. In Sivasagar district of Assam, AES/JE susceptibility was found to be higher in elderly age-group of population. During 2011-2020, only 21.25% of JE cases were reported in the age-group 0-15 years from the study. Aged people above 30 years were found to be more vulnerable during the period of study. Similarly, during 2011-12, high JE cases were reported in the age-group 0-15 years in West Bengal.³² Our study revealed lower CFR in the age-group below 30 years while a high fatality rate was observed in the higher age-group above 30-60 years of age. Lower JE cases in younger age-group may be correlated to the routine vaccination, which started from 2011-12. Due to the high burden of JE cases in the district, mass vaccination campaign was conducted during 2011, and 5.5 lakh populations were vaccinated out of 5.8 lakh targeted population (95%). In 2014, the adult vaccination campaign conducted for the left out during 2011 and a total of 138739 population were vaccinated, covering 77.49% of the targeted population. However, it was revealed that immunization of the adult population and children through routine immunization affected the JE cases in the Sivasagar district of Assam during the period of study. The JE cases were found to be declined from 128 in 2011 to 18 in 2020. Many research reports suggest that vaccination in older people is less effective compared to the younger age-group.^{33,34} Our study also revealed that the male population is more prone to both AES and JE infection in Sivasagar district of Assam during the period of study. More than 60% of the total cases were reported from the male population showing significant differences in female cases. Similar result was reported in mainland China with 60.45% JE cases in male population during the period 2004-14.³⁵ Similarly, high (53.8%) JE cases were reported in male population from the state of Uttar Pradesh during the period from 2013 to 2018.³⁶ However, there was no significant difference between the gender and JE positivity. Medhi et al. (2017)³⁷ reported that about 62.04% of the JE cases from Tinsukia and Sivasagar districts of upper Assam were male population during 2012-14. The reason for the higher rate of AES/JE cases in male populations compared to the female population is

not well established. However, sex is one of the variables that influence the innate and adaptive immune responses resulting in sex-specific adaptability and susceptibility to certain diseases. Differences in the immune system may have resulted in differential AES/JE cases in both sexes. It is also observed that among the elderly age-group (>60 years), JE cases were almost 2-times higher in males than females, which may be correlated to the fact that adult females develop stronger innate and adaptive immune responses than males and, therefore, better resistance to diseases.³⁸

Conclusion

Japanese Encephalitis is a major public health problem in the Sivasagar district of Assam. During the month of July and August highest outbreak of JE were observed in the district. Control of vector populations with Malathion fogging and other insecticides were found to have minimal role in controlling the disease due to the exophilic behavior of *Culex* mosquitoes. The mosquito can breed in larger water bodies, and hence the role of larvicide seems limited. Therefore, it requires proper case management which can reduce the case fatality rate. Moreover, AES/JE surveillance needs to be intensified at the field level to detect the cases and refer to the nearby hospital for better case management. Information, education, and communication also should be intensified to reduce man-mosquito-pig contact. Better management of AES/JE may be done with effective surveillance systems, integrated vector control measures, segregation of pigs from human dwelling, high coverage of JE vaccination increasing, and awareness on prevention measures of mosquito-borne diseases, including Japanese Encephalitis.

Declarations

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Conflict of Interest

Authors declare no conflict of interest

References

1. Erlanger TE, Weiss S, Keiser J, Utzinger J, Wiedenmayer K (2009) Past, present, and future of Japanese encephalitis. *Emerg Infect Dis* 15: 1-7.
2. Campbell GL, Hills SL, Fischer M, et al. Estimated global incidence of Japanese encephalitis: a systematic review. *Bull World Health Organ*. 2011;89(10):766–774, 774A.
3. <https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis>

4. Campbell GL, Hills SL, Fischer M, et al. Estimated global incidence of Japanese encephalitis: a systematic review. *Bull World Health Organ*. 2011;89(10):766–774, 774A.
5. Webb J KG, Pereira SM. Clinical diagnosis of arthropod borne type viral encephalitis in children in North Arcot district, Madras state, India. *Indian J Med Sci*. 1956; 10: 572.
6. Kumari R, Japanese Encephalitis – Transmission dynamics and prevention & control Strategy and outbreak investigation, WHO report, https://www.who.int/docs/default-source/wrindia/japanese-encephalitis/japanese-encephalitis-transmission-control-investigation-presented-by-dr-roop-webinar-ahcf-2020.pdf?sfvrsn=bb590015_2, access on 27.06.2021
7. Hazarika N.C. Project Study on Japanese Encephalitis vaccination at Gogamukh, Assam. Acces at <https://www.indianpediatrics.net/sep1991/1029.pdf> access on 27.06.2021
8. Vajpayee A., Dey P.N., Chakraborty A.K., Chakraborty M.S., Study of the outbreak of Japanese encephalitis in Lakhimpur district of Assam in 1989. *J Indian Med Assoc*. 1992 May;90(5):114-5
9. Health.india.com › Diseases & Conditions
10. www.nvbdc.gov.in
11. Phukan AC, Borah PK, Mahanta J. Japanese encephalitis in Assam, Northeast India. *Southeast Asian J Trop Med Public Health* 2004;35(3):618-22.
12. Bandyopadhyay B, Bhattacharya I, Adhikari S, et al. Incidence of Japanese Encephalitis among Acute encephalitis syndrome cases in West Bengal, india. *Biomed Res Int*. 2013;2013:896749
13. <https://www.sentinelassam.com/top-headlines/assam-becomes-the-most-vulnerable-state-for-japanese-encephalitis-je/>
14. <https://indianexpress.com/article/news-archive/web/assam-launches-vaccination-drive-against-je-to-cover-8-lakh-people-in-one-district/>
15. <http://sivasagar.nic.in/pages/at%20a%20glance.html>
16. <https://www.census2011.co.in/census/district/164-sivasagar.html>
17. National Vector Borne Diseases Control Programme. Clinical Management of Japanese Encephalitis, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India https://nvbdc.gov.in/WriteReadData/l892s/Clinical_Management-JE.pdf, Accessed 27 June 2021
18. Operational Guidelines: National Programme for Prevention and Control of Japanese/Acute Encephalitis Syndrome. Directorate of National Vector Borne Disease Control Program. DGHS, MOHFW, Government of India; 2014. Available from:[http://www.nvbdc.gov.in/DOc/Je-Aes-Prevention-Control\(NPPCJA\).pdf](http://www.nvbdc.gov.in/DOc/Je-Aes-Prevention-Control(NPPCJA).pdf).
19. Campbell GL, Hills SL, Fischer M, Jacobson JA, Hoke CH, Hombach JM, et al. Estimated global incidence of Japanese encephalitis: A systematic review. *Bull World Health Organ* 2011;89:766-774.
20. Borah J, Dutta P, Khan SA, Mahanta J. Association of Weather and Anthropogenic Factors for Transmission of Japanese Encephalitis in an Endemic Area of India. *EcoHealth* 2013;10:129-136 (2013). <https://doi.org/10.1007/s10393-013-0849-z>

21. Datey A, Mohindro Singh L, Rajkhowa U, Prusty BK, Saswat T, Mamidi P, et al., (2020) Molecular epidemiology of Japanese encephalitis virus in pig population of Odisha, Assam and Manipur states of India. *Infection, Genetics and Evolution* 83: 104325. <https://doi.org/10.1016/j.meegid.2020.104325>
22. Livestock Census 2012, Animal Husbandry & Veterinary Department, Government of Assam, available from <https://animalhusbandry.assam.gov.in/information-services/livestock-census> Accessed on 16th August 2020
23. Government of India (2014) 19th Livestock Census 2012 All India Report. Ministry of Agriculture, Department of Animal Husbandry, Dairying and Fisheries, Krishi Bhawan, NEW DELHI, INDIA.
24. Islam R., Nath P., Bharali A. (2016). Constraints perceived by the small scale pig farmers in Sivasagar district of Assam: An analysis. *THE ASIAN JOURNAL OF ANIMAL SCIENCE*. 11. 73-77. [10.15740/HAS/TAJAS/11.1/73-77](https://doi.org/10.15740/HAS/TAJAS/11.1/73-77).
25. Endy TP, Nisalak A. Japanese encephalitis virus: ecology and epidemiology. *Curr Top Microbiol Immunol* 2002; 267: 11-48. http://dx.doi.org/10.1007/978-3-642-59403-8_2
26. Yadav K, Dhiman S, Rabha B, Saikia PK, Veer V (2014) Socio-economic determinants for malaria transmission risk in an endemic primary health centre in Assam, India. *Infect Dis Poverty* 3, 19 (2014). <https://doi.org/10.1186/2049-9957-3-19>
27. Kumari R, Joshi PL. A review of Japanese encephalitis in Uttar Pradesh, India. *WHO South-East Asia J Public Health* 2012;1: 374-95.
28. Kumar P, Pisudde PM, Sarthi PP, Sharma MP, Keshri VR. Status and trend of acute encephalitis syndrome and Japanese encephalitis in Bihar, India. *Natl Med J India*. 2017;30(6):317-320. [doi:10.4103/0970-258X.239070](https://doi.org/10.4103/0970-258X.239070).
29. Singh AK, Kharya P, Agarwal V, Singh S, Singh NP, Jain PK, Kumar S, Bajpai PK, Dixit AM, Singh RK, Agarwal T. Japanese encephalitis in Uttar Pradesh, India: A situational analysis. *J Family Med Prim Care* 2020;9:3716-21.
30. Campbell GL, Hills SL, Fischer M, Jacobson JA, Hoke CH, Hombach JM, et al. Estimated global incidence of Japanese encephalitis: A systematic review. *Bull World Health Organ* 2011;**89**:766-774.
31. Li X, Cui S, Gao X, Wang H, Song M, Li M, et al. (2016) The Spatio-temporal Distribution of Japanese Encephalitis Cases in Different Age Groups in Mainland China, 2004 – 2014. *PLoS Negl Trop Dis* 10(4): e0004611. <https://doi.org/10.1371/journal.pntd.0004611>
32. Bandyopadhyay B, Bhattacharyya I, Adhikary S, Mondal S, Konar J, Dawar N, et al. Incidence of Japanese Encephalitis among Acute Encephalitis Syndrome Cases in West Bengal, India. *Biomed Res Int* 2013;896749. <https://doi.org/10.1155/2013/896749>
33. Wagner A, Garner-Spitzer E, Jasinska J, Kollaritsch H, Stiasny K, Kundi M, et al. (2018) Age-related differences in humoral and cellular immune responses after primary immunization: indications for stratified vaccination schedules. *Sci Rep* 8:9825. <https://doi.org/10.1038/s41598-018-28111-8>
34. Weinberger B. (2018) Vaccines for the elderly: current use and future challenges. *Immun Ageing*. 2018;15:3. [doi:10.1186/s12979-017-0107-2](https://doi.org/10.1186/s12979-017-0107-2)

35. Li X, Cui S, Gao X, Wang H, Song M, Li M, *et al.* (2016) The Spatio-temporal Distribution of Japanese Encephalitis Cases in Different Age Groups in Mainland China, 2004 – 2014. *PLoS Negl Trop Dis* 10(4): e0004611. <https://doi.org/10.1371/journal.pntd.0004611>
36. Singh AK, Kharya P, Agarwal V, Singh S, Singh NP, Jain PK, Kumar S, Bajpai PK, Dixit AM, Singh RK, Agarwal T. Japanese encephalitis in Uttar Pradesh, India: A situational analysis. *J Family Med Prim Care* 2020;9:3716-21.
37. Medhi M, Saikia L, Patgiri SJ, Lahkar V, Hussain ME, Kakati S (2017) 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 Journal of Medical Research*, 146(2): 267-271
38. Klein S, Flanagan K. (2016) Sex differences in immune responses. *Nat Rev Immunol* 16: 626–638. <https://doi.org/10.1038/nri.2016.90>

Figures

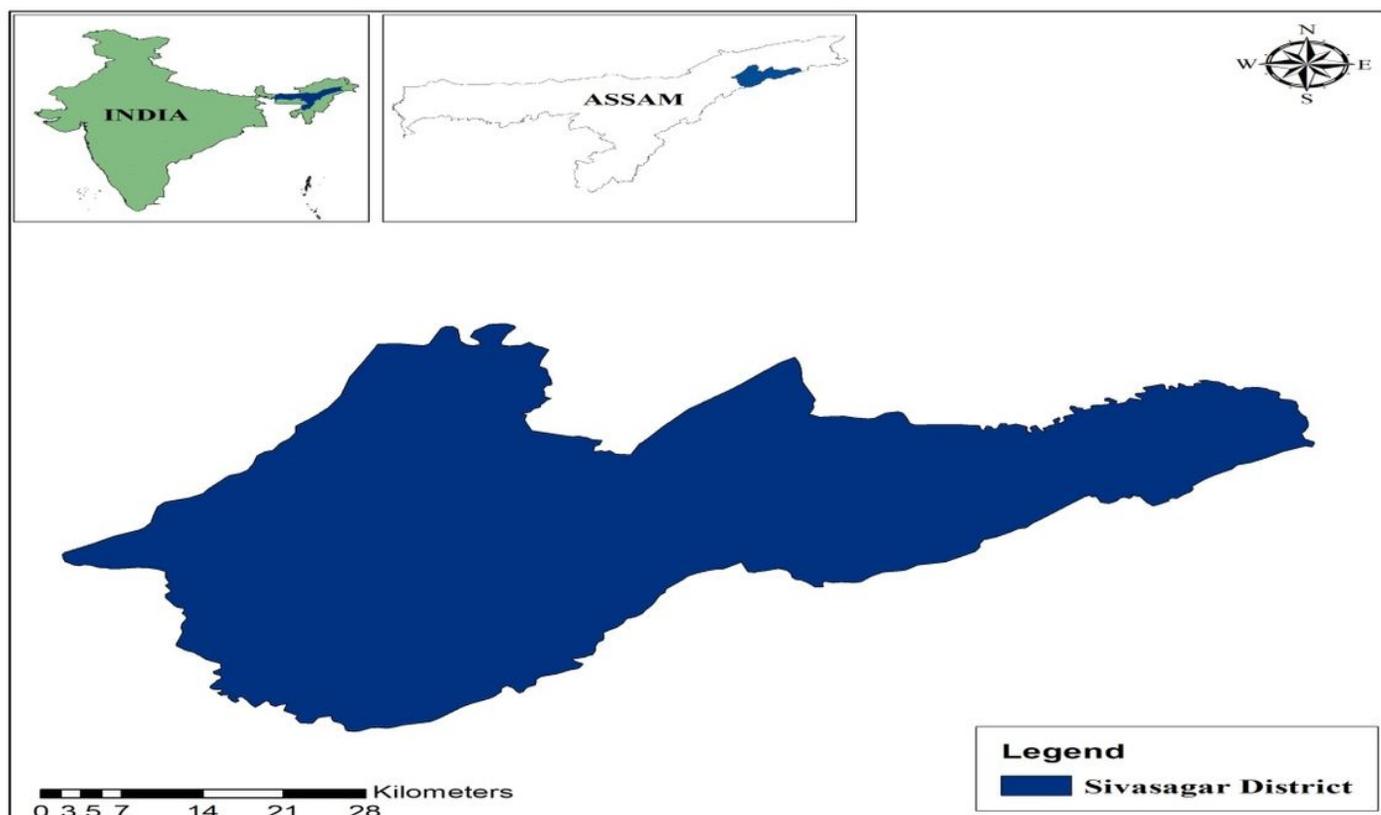


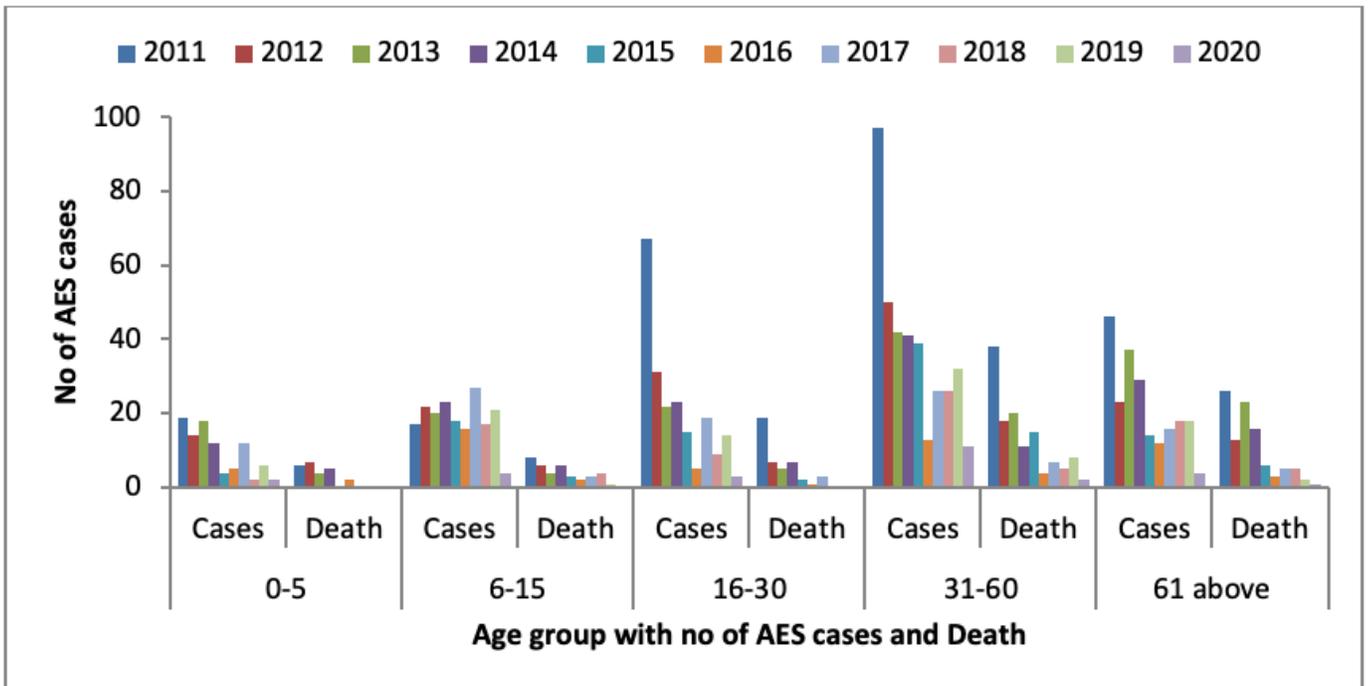
Figure 1

Map of Study Area

Figure 2

Trend of Acute Encephalitis Syndrome (AES) and Japanese Encephalitis (JE) positive cases, deaths, and case fatality rate (CFR).

A



B

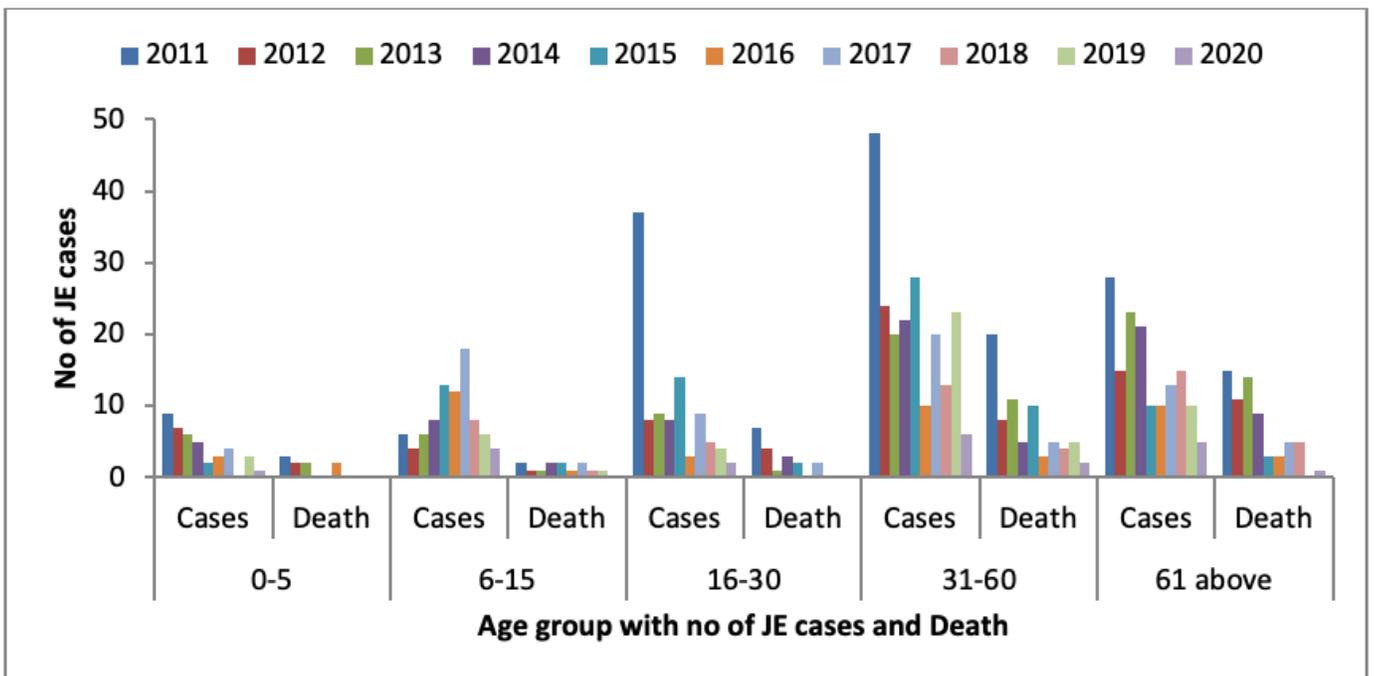


Figure 3

a Age-group and distribution of AES cases in Sivasagar district of Assam from 2011 to 2020. b Age-group and distribution of JE cases in Sivasagar district of Assam from 2011 to 2020.

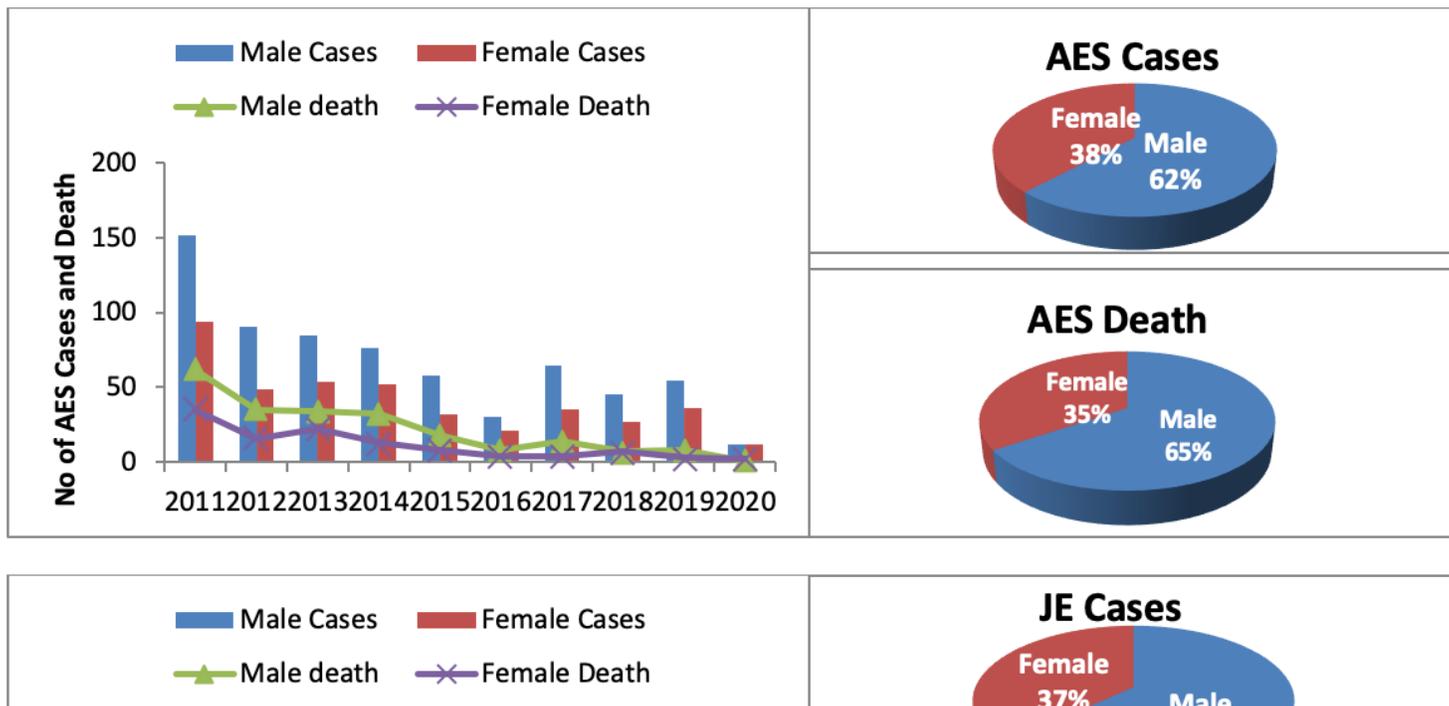


Figure 4

Gender-wise distribution of Japanese Encephalitis cases in Sivasagar District

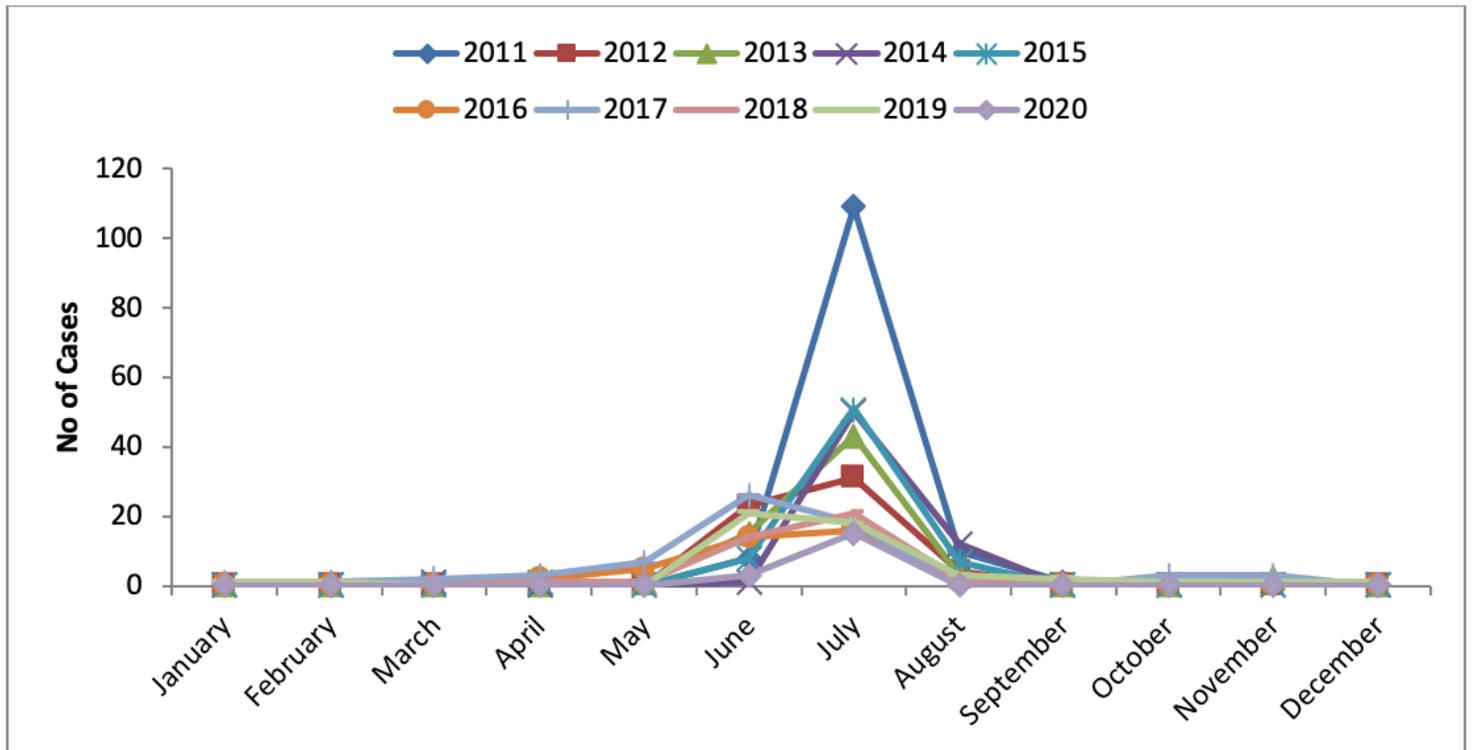


Figure 5

Month-wise incidence of JE cases in Sivasagar district of Assam

Figure 6

Block-wise prevalence of AES/JE cases in Sivasagar district of Assam during the period of 2011-20. (a) Demow, (b) Galekey, (c) Gaurisagar, (d) Kalogaon, (e) Khelua, (f) Morabazar, (g) Patsaku and (h) Sapekhati

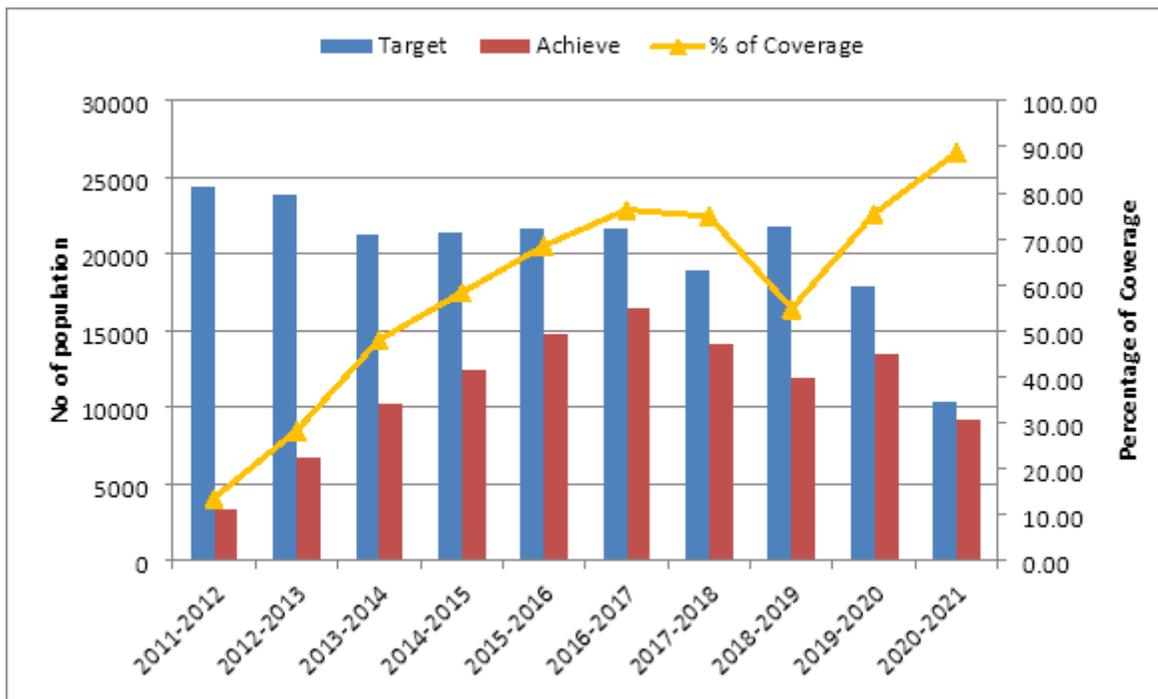


Figure 7

Routine Japanese Encephalitis vaccinations (09-18 months) in Sivasagar district of Assam during the period from 2011 to 2020