Acute Encephalitis Syndrome-The Socio-economic Burden in India

Chairanjib Bhattacharjee*†, Debjit Bhowmik²

1Srikrupa Institute of Pharmaceutical Sciences, Siddipet-502277, Telangana, India
2Himachal Pharmacy College Nalagarh, Solan Dist-174101, Himachal Pradesh, India

Abstract

Acute encephalitis syndrome is a clinical condition caused by infection with Japanese encephalitis virus or other infectious and noninfectious causes. Acute poses a great public health problem in India, occurring both in epidemics and sporadically. Seasonal outbreaks of acute encephalitis syndrome occur with striking regularity in India and lead to substantial mortality. Several viruses, endemic in many parts of India, account for AES. Although Japanese encephalitis virus is a key aetiological agent for AES in India, and has attracted countrywide attention, many recent studies suggest that enteroviruses and rhabdoviruses might account for outbreaks of AES. It is a neurological disorder which affects the brain and the limbic system when a specific strain of virus or a bacteria attacks the body. Encephalitis is an inflammation of the brain tissue. Once the virus enters inside the blood, it starts migrating to the brain tissues and multiplies itself into numbers. As soon as the signal reaches to our immune system, it generates a response to it in the form of inflamed brain or we can say swelled up brain. When this self-generated response and the infection combines, this leads to viral encephalitis and it majorly affects the spinal cord and our central nervous system causing damage to the brain cells through virus-infected blood vessels.

1 Introduction

Acute encephalitis syndrome (AES) is a clinical condition, of which the most common cause is Japanese encephalitis (JE). Though there is deficiency of data on AES and JE from Bihar, the state ranks third in the reporting of JE cases after Uttar Pradesh and Assam. Acute encephalitis syndrome (AES) is a multifactorial clinical condition, the most common cause being Japanese encephalitis (JE). JE is a vector-borne viral disease caused by the JE virus of group B arbovirus (Flavivirus) and is transmitted to humans by the Culicine mosquito. JE affects the central nervous system (CNS), and can cause serious complications and death. The case fatality rate (CFR) is high and those who survive may suffer from neurological sequelae such as convulsions, episodic headache, autonomic disturbance, abnormal behaviour, mood disorder, intellectual deficit, paresis, incoordination of movements, jerky limb movements, speech disorder, cranial nerve palsy, gaze palsy, parkinsonian features, impaired hearing, etc. An estimated 25% of affected children die from the disease, and among those who survive, 30%–40% suffer from physical and mental impairment. Children suffer the highest attack rate due to lack of cumulative immunity from natural infections.

Viral encephalitis is an important cause of mortality and morbidity in children. It may be sporadic like herpes simplex encephalitis (HSE), or epidemic such as Japanese B encephalitis (JE). The etiological agents are varied, and physicians treating such children often feel limited by the lack of availability of diagnostic testing for most of these agents. There are numerous lacunae in our knowledge, problems in epidemiological investigations, lack of diagnostic facilities, as well as difficulties in managing these critically ill children in smaller centers in our country. Acute Encephalitis Syndrome (AES) is a group of Clinical neurologic manifestation caused by wide range of viruses, bacteria, fungus, parasites, spirochetes, chemical and toxins.
The most common causes of acute viral encephalitis are Japanese encephalitis virus, West Nile virus (WNV), Eastern equine encephalitis virus (EEEV), Western equine encephalitis virus (WEEV), Hendra virus (HeV), enteroviruses (ENV), Chandipura virus (CHPV), Nipah (NiV), Kyasanur forest disease (KFD), St. Louis encephalitis virus, Herpes simplex, poliovirus and measles virus. The causative agent of the AES varies with season and geographical location. The outbreak of AES and JE usually coincides with the monsoon and post monsoon period when the density of mosquitoes increases. Encephalitis due to enteroviruses occurs throughout the year as it is water borne disease.

Most of the times, it may be difficult to differentiate Japanese Encephalitis from those caused by other bacteria and viruses, as clinical signs of JE are indistinguishable from other causes of AES. Acute Encephalitis Syndrome (AES) including Japanese Encephalitis (JE) is a group of clinically similar neurologic manifestation caused by several different viruses, bacteria, fungus, parasites, spirochetes, chemical/ toxins etc. The outbreak of JE usually coincides with the monsoon and post monsoon period when the density of mosquitoes increases while encephalitis due to other viruses specially enteroviruses occurs throughout the year as it is a water borne disease.

1.1 History

The history of AES in India has paralleled with that of the Japanese encephalitis virus (JEV) since the first report in 1955 from Vellore, Tamil Nadu. The first outbreak of JEV was reported in Bankura district, West Bengal in 1973. Thereafter, sporadic cases of AES and outbreaks have been the leading cause of premature deaths due to the disease in India. Based on various surveillance reports and outbreak investigations, history of AES in India into 3 phases: (a) period before 1975 when a few cases with JE aetiology were identified; (b) between 1975 and 1999 when more JEV cases were reported with frequent outbreaks that resulted in the development of JE endemic regions near the Gangetic plains and in parts of Deccan and Tamil Nadu; (c) between 2000 and 2010, a dramatic change was observed in the AES scenario, which saw the rise in non-JE outbreaks mostly caused by viruses such as Chandipura virus (CHPV), Nipah virus (NiV), and other enteroviruses. Cases of acute encephalitis syndrome have been observed mostly during April to June in Muzaffarpur, Bihar, particularly in children who are undernourished with a history of visiting litchi orchards, as per a report in National Health Portal of India. Since 1978, outbreaks of the disease with high case-fatality rates have also been occurring in Gorakhpur Division of Uttar Pradesh.

Every year, children in the north Bihar and eastern Uttar Pradesh regions are impacted because of the epidemics. The UP government claimed that the disease claimed at least 187 lives in 2018 against 553 in 2017.

2 Causes of encephalitis

Three groups of viruses are common causes of encephalitis:

1) Herpes viruses, such as chickenpox, EBV (Epstein-Barr virus, which causes mono), and herpes simplex (which causes cold sores).

2) Viruses and other germs transmitted by insects, like West Nile virus (spread through a mosquito bite) and the germs that cause Lyme disease and Rocky Mountain spotted fever (spread through tick bites).

3) Viruses that cause once-common childhood infections, such as measles, mumps, and German measles.

Thanks to immunizations, it's rare today for someone to develop encephalitis from these illnesses.

Less often, encephalitis can be:

- Caused by an infection from bacteria , such as bacterial meningitis
- A complication of other infectious diseases like syphilis
- Due to a parasite, like toxoplasmosis (found in infected cat feces) in people with weakened immune systems

I. Soaring Temperatures: Heat and humidity have been a common factor in the spikes of reported cases of encephalitis in Bihar. The state witnessed high temperatures in the range of 40 degrees Celsius and above in 2019, which has led to multiple heat strokes and an insurgence of reported cases of encephalitis in the state.

II. Malnutrition: Hypoglycemia, or low blood sugar, is a major contributing factor to encephalitis attacks and has a direct relation to malnutrition and lack of proper health programmes in place. The 2019 outbreak is suspected to have erupted from the litchi fruit and has seen a cyclical pattern during the harvest season. Children are more prone to consuming fallen fruits, staying out in the sun without proper food, and getting dehydrated - which could have lead to the outbreak once again.

III. Lack of Awareness: Rural areas have seen the most cases of this virus and can be associated with a lack of awareness and understanding. Most affected and their families are not aware of the threats or prevention and precaution methods, thereby making them more susceptible to such viruses than usual.

You can avoid diseases that can lead to encephalitis, especially with children. Here are a few preventive measures you can take:  

1) Immunisations: Protect your kids from common infections and conditions by getting them immunised according to the schedule recommended by your doctor.
Avoid contact: Take extra care to avoid being around people who are already affected by the virus causing encephalitis.

Maintain hygiene: Ensure your children wash their hands and maintain an antiseptic hygiene regime, especially after coming back from outside.

Avoid Mosquito Bites: Stay indoors after sunset, use mosquito repellents and nets, avoid waterlogged spots in and around your neighbourhood as these can be mosquito breeding sites and wear protective clothing whenever you step outside.

Avoid Tick Bites: Make sure your child is not playing with soil, leaves, vegetation and stray animals. Ensure your pets are tick-free and healthy.

Diagnosis of encephalitis

Doctors use several tests to diagnose encephalitis, including:

- Imaging tests, such as computed tomography (CT) scans or magnetic resonance imaging (MRI), to check the brain for swelling, bleeding, or other problems.
- Electroencephalogram (EEG), which records the electrical signals in the brain, to check for unusual brain waves.
- Blood tests to look for bacteria or viruses in the blood. These also can show if the body is making antibodies (specific proteins that fight infection) in response to a germ.
- Lumbar puncture, or spinal tap, which checks cerebrospinal fluid (the fluid that surrounds the brain and spinal cord) for signs of infection.

Signs and symptoms of encephalitis

Symptoms in mild cases of encephalitis usually include:

- Fever
- Headache
- Poor appetite
- Loss of energy
- A general sick feeling

Serious cases of encephalitis can cause:

- A high fever
- Severe headache
- Nausea and vomiting
- Stiff neck
- Confusion
- Personality changes
- Convulsions (seizures)
- Problems with speech or hearing
- Hallucinations
- Memory loss
- Drowsiness
- Coma

It's harder to spot some of these symptoms in infants. Important signs to look for include:

- Vomiting
- A full or bulging soft spot (fontanel)
- Crying that doesn't stop or that seems worse when the baby is picked up or handled
- Body stiffness

Because encephalitis can happen during or after common viral illnesses, symptoms of these illnesses can start before encephalitis happens. But often, it appears without warning.

Prevention of encephalitis

- Increase access to safe drinking water and proper sanitation facilities.
- Improve nutritional status of children at risk of JE/AES.
- Vector control:
  1. The preventive measures are directed at reducing the vector (mosquito) density.
  2. JE vectors are exophillic and endophagic in nature. The risk of transmission increases when the human dwellings and animal sheds particularly piggeries are situated very close to each other. Piggeries may be kept away (4-5 kms) from human dwellings. When they are situated far from each other, the risk of transmission is reduced.
  3. Personal protection against mosquito bites using insecticide treated mosquito nets.
  4. Clothing reduces the risk of mosquito biting if the cloth is sufficiently thick or loosely fitting. Long sleeves and trousers with stockings may protect the arms and legs, the preferred sites for mosquito bites. School children should adhere to these practices whenever possible.
  5. Household insecticidal products, namely mosquito coils, pyrethrum space spray and aerosols.
have been used extensively for personal protection against mosquitoes. Electric vaporizer mats and liquid vaporizers are more recent additions which are marketed in practically all urban areas.

6. Repellents are a common means of personal protection against mosquitoes and other biting insects. These are broadly classified into two categories, natural repellents and chemical repellents. Essential oils from plant extracts are the main natural repellent ingredients, i.e. citronella oil, lemongrass oil and neem oil.

7. The reduction in mosquito breeding requires eco-management, as the role of insecticides is limited.

8. Vaccination: As per Govt. of India guidelines, 2 doses of JE vaccine have been approved to be included in UIP to be given one along with measles at the age of 9 months and the second with DPT booster at the age of 16-24 months w.e.f. April, 2013.

6 Treatment of encephalitis

Children suffering from encephalitis or AES need care in a hospital in ICU that is Intensive Care Unit to avoid any type of mishap.

- Doctors watch their blood pressure, heart rate, breathing and body fluids to prevent further swelling of the brain.
- Some form of encephalitis can also be treated by giving patient Antiviral drugs.
- To reduce swelling in the brain Corticosteroids are also given.
- Anticonvulsants might be given to a child having seizures.
- Over-the-counter (OTC) medicines, like acetaminophen, can help with fever and headaches.
- Patient is also given anti-inflammatory drugs like Acetaminophen, Ibuprofen and Naproxen Sodium to reduce headaches and temperature.

Most cases of encephalitis or AES get cured or resolved in a few days but some severe case may take few weeks.

Vaccination: As per the guidelines of Government of India, 2 doses of Japanese Encephalitis (JE) vaccine have been approved which is to be included in UIP to be given along with measles at the age of 9 months and the second with DPT booster at the age of 16-24 months w.e.f. April, 2013.

So, we can say that Encephalitis or AES is an infection or inflammation in the brain that can be caused due to virus, bacteria, fungi etc. which results into headache, high fever, seizures, vomiting, coma etc.

ost cases of Encephalitis happen in children, the elderly and people with a weakened immune system from HIV/AIDS, cancer etc. It is also said that in encephalitis inflammation of the brain is caused by an infection or through the immune system attacking the brain in error.

7 Current Scenario of India

Acute Encephalitis Syndrome has heralded the emergence of multiple virulent pathogens, which may result in severe morbidity and mortality. Acute Encephalitis Syndrome (AES) is a major public health concern in India. Large outbreaks of AES affecting particularly children, occur annually in the country post monsoon from July to November. The National Vector Borne Disease Control Programme in India set up country wide surveillance for AES through sentinel sites with a focus on detecting Japanese encephalitis (JEV). Although JEV is the major cause of AES in India (ranging from 5-35%), the etiology in a large number of cases however remains unidentified.

According to the National Centre for Disease Control officials, Acute Encephalitis Syndrome (AES) outbreaks in Muzaffarpur have been reported since 1995. This year the main cause of death in most cases has been attributed to hypoglycemia (low blood sugar level). How is hypoglycemia related to these deaths and what are researchers suggesting? Usually, the disease strikes during monsoon (June-October) but Bihar reportedly showed a high number of affected people during April-June this year.

Acute Encephalitis Syndrome (AES) is considered a very complex disease as it can be caused by various agents including bacteria, fungi, virus and many other agents. In most of the cases reported in India, Japanese Encephalitis (JE) virus is considered the most common cause according to an estimate by Union Health Ministry. As much as 5 per cent to 35 per cent cases reported involve Japanese Encephalitis (JE) virus. The most worrying fact is that the syndrome can also be caused by agents like dengue, mumps, measles, even Nipah or Zika virus. In several cases, the cause of AES remains clinically unidentified.

In India, the numbers of people infected last year mount to as much as 10,485 cases of AES with 632 deaths across 17 states according to the National Vector Borne Diseases Control Programme (NVBDCP). The fatality rate due to Acute Encephalitis Syndrome (AES) is as high as 6 per cent in India, but it rises to 25 per cent amongst children. The state of Bihar, Assam, Jharkhand, Uttar Pradesh, Manipur, Meghalaya, Tamil Nadu, Karnataka, and Tripura are worst affected.

According to Bihar government officials, AES is not a disease but a syndrome and the main cause of death among children due to AES was prolonged hypoglycemia with delayed treatment. A
Changing landscape of acute encephalitis syndrome in India: a systematic review. Natl Med J India. 2012;25:212–220.

2. Mishra MK, Basu A. Minocycline neuroprotects, reduces microglial activation, inhibits caspase 3 induction, and viral replication following Japanese encephalitis. J Neurochem. 2008;105:1582–1595.

3. Kumar R, Basu A, Sinha S, Das M, Tripathi P, Jain A. Role of oral Minocycline in acute encephalitis syndrome in India - a randomized controlled trial. BMC Infect Dis. 2016;16:67.

4. Beig FK, Malik A, Rizvi M, Acharya D, Khare S. Etiology and clinic-epidemiological profile of acute viral encephalitis in children of Western Uttar Pradesh, India. Int J Infect Dis. 2010;14:141-6.

5. Tunkel AR, Glaser CA, Bloch KC, Seijvar JJ, Marra CM, Roos KL. The management of encephalitis: Clinical practice guidelines by the infectious diseases society of America. Clin Infect Dis. 2008;47:393-27.

6. Yong YK, Chong HT, Wong KT, Tan CT, Devi S. Aetiology of viral central nervous system infection, a Malaysian study. Neuroul Asia. 2008;13:65-71.

7. Panagariya A, Jain RS, Gupta S, Garg A, Sureka RK, Mathur V. Herpes simplex encephalitis in north West India. Neurol India. 2001;49:360-5.

8. Potharaju NR. Incidence rate of acute encephalitis syndrome without specific treatment in India and Nepal. Indian J Community Med 2012;37:240-51.

9. Weidmann M, Meyer-Ko¨nig U, Hufert F. Rapid detection of herpes simplex virus and varicella-zoster virus infections by real-time PCR. J Clin Microbiol. 2003;41:1565-8.

10. Niesters HG, van Esser J, Fries E, Wolthers KC, Cornelissen J, Osterhaus AD. Development of a real-time quantitative assay for detection of epstein-barr virus. J Clin Microbiol. 2000;38:712-5.

11. Ramamurthy M, Alexander M, Aaron S, Kannangai R, Ravi V, Sridharan G. Comparison of a conventional polymerase chain reaction with real-time polymerase chain reaction for the detection of neurotropic viruses in cerebrospinal fluid samples. Indian J Med Microbiol. 2011;29:102-9.

12. Piqueur MA, Verstrepen WA, Bruynseels P, Mertens AH. Improvement of a real-time RT-PCR assay for the detection of enterovirus RNA. Virol J. 2009;6:95.

13. Karmarkar SA, Aneja S, Khare S, Saini A, Seth A, Chauhan BK. A study of acute febrile encephalopathy
with special reference to viral etiology. Indian J Pediatr. 2008;75:801-5.

14. Rathore SK, Dwibedi B, Kar SK, Dixit S, Sabat J, Panda M. Viral aetiology and clinico-epidemiological features of acute encephalitis syndrome in eastern India. Epidemiol Infect. 2014;142:2514-21.

15. Roy A, Mandal K, Sen S, Bag T. Study of acute viral meningoencephalitis in children in sub-Himalayan Tarai region: Clinico-epidemiological, etiological, and imaging profile. Indian J Child Health. 2015;2:177-81.

16. Jain P, Jain A, Kumar A, Prakash S, Khan DN, Singh KP. Epidemiology and etiology of acute encephalitis syndrome in North India. Jpn J Infect Dis. 2014;67:197-203.

17. Sundén B, Larsson M, Falkeborn T, Paues J, Forsum U, Lindh M. Real-time PCR detection of human herpesvirus 1-5 in patients lacking clinical signs of a viral CNS infection. BMC Infect Dis. 2011;11:220.