

# Acute Encephalitis Syndrome (AES) as a Cause of Unfortunate Maternal Fetal Demise during the Japanese Encephalitis Epidemic - A Case Report.

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## ABSTRACT

Acute encephalitis syndrome (AES) is defined as the acute-onset of fever with change in mental status and often with new onset of seizures. Japanese encephalitis has been considered as the leading cause of AES in India. JE with pregnancy causes diagnostic dilemma especially in 3<sup>rd</sup> trimester if the patient presents with convulsion and altered sensorium; as in our case. It is often confused with eclampsia. But careful history and clinical investigation is helpful towards correct diagnosis.

**Keywords:** Pregnancy, Acute encephalitis syndrome, Japanese encephalitis.

## INTRODUCTION

Acute encephalitis syndrome (AES) is defined as the acute-onset of fever with change in mental status and often with new onset of seizures. Japanese encephalitis has been considered as the leading cause of AES in India. We are here reporting an unfortunate case of maternal and fetal demise due to AES during JE epidemic in North Bengal and reviewing the literature regarding maternal fetal outcome in JE.

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## CASE REPORT

A 22 years old primigravida was referred to our medical college with history of acute onset fever and convulsion followed by unconsciousness. She had completed 37 weeks of gestation. Her fever was 3-4 days duration and fever was continuous in nature. After she develops convulsion and loses her consciousness, she was taken to the district hospital from where she was referred to our medical college. Her Glasgow coma scale was 5 at the time of admission. Her planter reflex was equivocal and all other reflexes were unresponsive. Her pupil was bilaterally dilated and sluggishly reacting to light. She had no neck rigidity. Her Blood pressure was 120/80, pulse rate was 120/min, respiratory rate was 30/min and temperature was 102°F. Her urine proteinuria was 1+ and capillary blood glucose was 99mg%. Her haemoglobin was 10gm% and blood group was B+. Her HIV and HBsAg status was negative. Her fatal anomaly scan, which was done at 19 weeks of gestation, was normal. Her P/V finding revealed that she was in latent phase of

labour with 2 cm cervical dilatation. Emergency USG of the abdomen was done as there was no fetal heart sound and it was revealed as intrauterine fetal demise. Her blood was collected and sent for anti JE-IgM antibody, which was negative, giving the diagnosis of the acute encephalopathy syndrome (AES). She was managed conservatively with intravenous fluid, infusion mannitol, antipyretic infusion, injection phenytoin, in the high dependency unit. Unfortunately, she died sometime after admission. A post-mortem Caesarean section was performed (PMCS) and a 3.3 kg female fresh stillborn fetus was delivered. There was no meconium stain liquor. Fetal blood was sent for JE-IgM antibody detection, which was negative.

## DISCUSSION

Acute encephalitis syndrome (AES) is defined as the acute-onset of fever with change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and often with new onset of seizures (excluding simple febrile convulsion) in a person of any age at any time of the year.<sup>[1]</sup> It is a major health problem in the eastern part of India especially in sub-Himalayan region. JE has been considered as the leading cause of AES in India.<sup>[1]</sup> Other causes of AES are enteroviruses (ENV), Chandipura virus (CHPV), Nipah virus (NiV), Kyasanur forest disease (KFD), West Nile virus (WNV), Herpes simplex virus in the Indian subcontinent on various outbreaks.<sup>[2]</sup>

The main etiological agent is Japanese encephalitis virus (JEV), a positive-sense, single-stranded RNA virus that belongs to the genus *Flavivirus*, family Flaviviridae (an arthropod-borne virus family) and is closely related to dengue viruses. JE virus is transmitted to humans through the bite of an infected mosquito, primarily *Culex* species (*Culex*

*tritaeniorhynchus*). The virus is maintained in a natural enzootic cycle between mosquito and wild/domestic birds and pigs; where birds act as reservoir host and pig act as amplifying host.<sup>[1]</sup> Humans are incidental or dead-end hosts, because they usually do not develop a level or duration of viremia sufficient to infect mosquitoes.

Most human infections with JE virus are asymptomatic; <1% of people infected with JE virus develop clinical disease with case to infection ratio is 1:200-300. The case-fatality ratio is approximately 20%–30%.<sup>[3]</sup> Acute encephalitis is the most commonly recognized clinical manifestation of JE virus infection. Milder forms of disease, such as aseptic meningitis or febrile headache, can also occur. The incubation period is 5-15 days.<sup>[3]</sup>

JE can cause miscarriage when it causes infection in 1<sup>st</sup> and 2<sup>nd</sup> trimester and can cause intrauterine fetal death in the 3<sup>rd</sup> trimester. There is evidence of JEV transplacental transmission in humans and experimentally in mice.<sup>[4,5]</sup> Intrauterine infection appears to be acquired by the foetus as a result of viraemia after primary maternal infection.<sup>[4,5]</sup> Also certain strain of JEV can cause transplacental transmission in consecutive pregnancies in mice model and.<sup>[6]</sup> Shiraki (1970) has provided evidence that JEV persists in the human brain for 8 to 15 years after the onset of encephalitis. Whether maternal JEV infection can be transmitted to the foetus during consecutive pregnancies is not yet determined but can be a possibility as immune-suppression during pregnancy reactivates persistent JEV similar to mice model.

This is the 1<sup>st</sup> reported case in literature of maternal death due to AES in the 3<sup>rd</sup> trimester. Previously Mathur et al, 1885 described five women who acquired JE in the third trimester with no adverse outcomes.<sup>[7]</sup>

JE with pregnancy causes a diagnostic dilemma, especially in the 3<sup>rd</sup> trimester if the patient presents with convulsion and altered sensorium; as in our case. It is often confused with eclampsia. But careful history and clinical investigations is helpful towards correct diagnosis. History of fever and headache followed by convulsion and coma is most significant. On clinical examination, blood pressure often is normal and urine albumin test is negative to +1.

The most sensitive serologic assays detect JE virus-specific IgM in serum or cerebrospinal fluid by ELISA. The kit was purchased from National Institute of Pune, India. The kit follows IgM antibody captured ELISA technique using specific antigen for JE. JE virus-specific IgM can be measured in the CSF of most patients by 4 days after onset of symptoms and in serum by 7 days after onset.<sup>[8]</sup> False-negative results may occur if the samples are tested too early (e.g. within the first week of illness). This may be the case of our case

where the onset of fever is 4-5 days. In this situation RT-PCR may be useful for early detection of virus from sample.<sup>[9]</sup> A  $\geq 4$ -fold rise in JE virus-specific neutralizing antibodies between acute- and convalescent-phase serum specimens may be used to confirm the diagnosis. The cross-reactivity within the flavivirus group must be considered in making the diagnosis. Following a single infection by one member of the group, antibodies to other members may also appear. Serologic diagnosis becomes difficult when an epidemic caused by one member of the serologic group occurs in an area where another group member is endemic.

There is no specific therapy for JE. The acute illness requires management of a comatose patient who may have intracranial pressure elevations, inappropriate secretion of antidiuretic hormone, respiratory failure, and convulsions. The only practical preventive measures are vector management and personal protection.<sup>[8]</sup>

Two type of inactivated JE vaccine available for commercial use: vero cell culture derived SA-14-14-2 JE vaccine (JEEV by BE, India) and inactivated vero cell culture derived kolar strain, 821564XY, JE vaccine (JENVAC by Bharat biotech).<sup>[10]</sup> Minimum age of vaccination is 1 year with two doses of 0.5 ml each administered intramuscularly 4 weeks interval. The vaccine is recommended only for individual living in endemic region with catch up vaccination needed prior to anticipate epidemic.

## CONCLUSION

Acute Encephalitis Syndrome (AES) as a Cause of Unfortunate Maternal Fetal Demise during the Japanese Encephalitis Epidemic however careful history and clinical investigation is helpful towards correct diagnosis.

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