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Japanese Encephalitis: Profile and Outcome from an Urban Pediatric Institute.

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ABSTRACT

Japanese encephalitis (JE) is a common viral infection encountered in certain endemic regions in India.This is one of the common acute encephalitis in children which carries high mortality and morbidity. Fever, headache, vomiting, abdominal pain, altered sensorium, convulsions, and coma are the common features of JE in children. Higher mortality and morbidity among survivors occurs in children with JE. Difficulty in speech, bizarre involuntary movements, impaired intellect andconvulsions are common sequelae following JE. Vaccine for Japanese encephalitis isavailable for children and adults in endemic areas. Vaccination and mosquito controlare the preventive strategy to reduce the incidence of JE. Though its incidence has decreased following effective vaccination evenin urban health careInstitutes JE is still encountered.

Keywords: Japanese encephalitis, clinical features, mortality, morbidity.

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INTRODUCTION

Japanese encephalitis is a preventable disease, which causes devastating illness with long term sequelae among children. Though reported in regions endemic for the disease,urban referral centers like Chennai do treat childrenwith Japaneseencephalitis. The profile and outcome of children with confirmed JE from an urban tertiary care referral center is discussed in this article. JE is the major cause of viral encephalitis in Asia and accounts for nearly 60,000 cases per year. Highly endemic states in India include west Bengal, Bihar, Karnataka, Tamil Nadu, Andra Pradesh,Assam, Uttar Pradesh, Manipur and Goa. The risk is highest among children aged 1- 15 years, in rural areas in the monsoon and post monsoon season. Case fatality rate is reported to be 30%. 30- 50% develop permanent neurological sequelae. Treatment is mainly supportive. Disease can be prevented by effective vaccination and adequate mosquito control in regions of public health importance. JE is still a disease of epidemiological significance which needs to be addressed aggressively.

METHODOLOGY

This was a retrospective data analysis of all case records of children admitted to the pediatric intensive care unit (PICU) and were confirmed to have Japanese encephalitis. Aim: To understand the clinicalprofile, presentation and outcome of childrenwith Japanese encephalitis. Setting: PICU of a Pediatric tertiary care referral institute at Chennai. Study group: All children admitted and treated with a diagnosis of Japanese encephalitis identified from the case records of the medical record department were studied. Any child admitted with encephalitis in the form of fever, convulsions and altered sensorium and whose serology and /or CSF analysis was positive for Japanese encephalitis were considered as confirmed cases. Children with a positive serology alone without CSF confirmation were excluded. Study parameterswere socio demographic factorslike age, gender, regional distribution and vaccination status.

Clinical presentation included the duration of illness, presenting features, neurological status on admission and hemodynamic status at admission. Course of illness as duration of hospital stay, complications, co infections, need for mechanical ventilationand inotrope support. Complications during hospital stay were alsorecorded. Outcome was defined as recovery to discharge or death.Neurological sequelaeat discharge were recorded. Data was analyzed usingEpicInfo statistical software. Ethical approval was waived as this is a retrospective data collectionfrom case records.

RESULTS

During the period Jan 2009 to July 2015 a total of 21 children were treatedas Japanese encephalitis at the pediatric intensive care unit. All these children were from Chennai, suburban Chennai and nearby districts like Vellore, Tiruvellore, Ponneri, Kancheepuramand Tiruttani. All these children were from poor socioeconomic strata. None in the study group had received JE vaccine in the past. Among the 21 children 12 were males and 9 were females. Age distribution revealed 5 infants,5 were between 2-5 years, 5 were between 6-9years and 6 were between 10-12years. Clinical illness prior to hospitalizationwas less than 24 hours in 2, 24-48 hours in 3 and more than 48 hours in 16 children. Presenting features included fever, altered sensorium, seizures , respiratory distress, focal deficits and hypotonia. 6 of them had non convulsive status epilepticus. Involuntary movements were seen in 20 of the 21 children. Presence of shock, respiratory distress, hepatomegaly and need for ventilation have been shown in table 1. Four children had shock and all of them needed inotropes. CSF was clear in all children. Ig M ELISA for Japanese encephalitis was positive in serum. CSF was positive for JE by PCR. CSF showed elevated lymphocytes in 3 and polymorphs in 3. CSF protein was elevated in 5 children. None of the study group had positive CSF culture or HSV positivity. CT brain revealed features of cerebral edema in 3, Thalamic infarct in two children, features suggestive of meningoencephalitis in 3, hypodensity in the temperoparietal lesion in 3,features of cerebral atrophy in 3 and normal study in 8 children. Among the 18 children who were discharged 2/3rdhad morbidity. 3 had focal neurological deficit, 2 had bizarre involuntary movements , 4 had behavioural disturbances , aphasia in 6, 12 were on anti convulsants at discharge. Hospital stay varied from 3 to 60 days with a mean of 20 days.3 of the 21 children died (14%).

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Table 1: Clinical presentation and other study parameters

Parameter	N (%) (n- 21)
Fever	21(100)
Alert	1(4.8)
Verbal	2(9.52)
Pain responsive	2(9.52)
Unresponsive	16(76.2)
Shock	4 (19.05)
Seizures	17(80.96)
Respiratory distress	5(23.8)
Status epilepticus	10(47.62)
Focal deficits	15(71.43)
Hypotonia	8(38.09)
Hyperreflexia	8(38.09)
Hepatomegaly	17(80.96)
Involuntary movements	20(95.24)
Ventilation support	8(38.09)

DISCUSSION

JE virus, a mosquito-borne flavivirus, is an important cause of encephalitis in Asia JE is a disease of public health importance due to the epidemic potential and high fatality rate [1]. Majority of them are asymptomatic [2]. Less than 1% people with JE virus infection develop the clinical disease. Human transmission does not occur in JE as there is a low degree of viremia. Higher mortality and morbidity in the form of neuro psychiatric manifestations follow JE infection [3]. The clinical disease can be divided into three stages - a prodromal febrile stage, an acute encephalitic stage marked by CNS involvement with fever and a late stage - either recovery or transient / permanent sequelae.

Fever above 38 ºC, chills, muscle pain, headaches accompanied by vomiting. The initial presentation in children may begin with gastrointestinal symptoms: nausea, vomiting, and abdominal pain [4]. Convulsions and altered sensorium in the form of irritability, confusion, drowsiness, lethargy or frank coma may occur in children. Apart from convulsions, weakness and neck stiffness may be present. Rarely acute flaccid presentation has been reported in JE [5]. Focal neurological deficit may a part of the presentation. In this study population focal neurological deficit was encountered in nearly 70 % , hepatomegaly in 75% . CSF analysis in the acute phase may show pleocytosis . But none had pleocytsis in this study group. Extrapyramidal involvement is common during the convalescent phase in children with JE. With JE there was a high occurrence of chorea, athetosis, abnormal posturing, tone abnormalities,brisk reflexes neck stiffness , stereotyped movements are common in the convalescent phase. Higher rate of sequelae occur in children with JE. Major sequelae in the form of frank motor deficits, mental retardation, involuntary movements and/or convulsions were observed. Minor deficits may be scholastic backwardness, behavioural problems and/or subtle neurological signs. Only 30% patients may have complete recovery. Sequelae of the disease were more severe if the initial illness was prolonged [6]. $P < 0.001$, CI 2.45, 12.64), or associated with focal neurological deficits ($P < 0.001$, CI 1.97, 7.02) [6]. Mortality in children with JE has been reported to be as high as 37% in Indian studies [7]. Mortality was significantly related to a short prodromal stage, deep coma, abnormalities in tone and breathing and decerebrate posturing. Overallmortality in this study was 14%.

Evaluation in children with JE includes maintenance of fluid electrolyte balance, adequate hydration, serology for IgM ELISA and CSF analysis for lymphocytic pleocytosis. CSF PCR is confirmatory for JE encephalitis. The positive serology should be interpreted with caution in children who have been given JE vaccination . Serum for JE IgM ELISA, CSF for JE PCR are the laboratory findings to confirm JE encephalitis . 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. Plaque reduction neutralization tests can be performed to confirm the presence of JE virus–specific neutralizing antibodies and discriminate between cross-reacting antibodies from dengue and West Nile viruses. A ≥4-fold rise in JE virus–specific neutralizing antibodies between acute- and convalescent-phase serum specimens may be used to confirm recent infection.

Acute onset of fever with seizures altered sensorium , should make one suspect encephalitis .Viral encephalitis due to JE is common in endemic regions of India. Persistent altered sensorium, presence of bizarre involuntary movements along with the CT brain findings including basal ganglia involvement should make one suspect JE.Usually gray matter is involved in JE. In humans, a characteristic involvement of bilateral thalami can be seen by diffusion-weighted imaging. Magnetic resonance imaging lesions can also be detected in basal ganglia, midbrain, Pons, cerebellum, cerebral cortex, and subcortical white matter, Ammon's horn, and anterior horn of spinal cord.

Management of JE is supportive. This includes Airway, breathing support, maintaining hemodynamic status, anti convulsant therapy, anti-edema measures, drugs to control involuntary movements, nutritional support and physiotherapy. JE is known to cause severe disease in children and high early mortality. A trial with oral ribavirin has not been found to be useful in reducing JE related mortality in children [8]. Children who recover from JE need to be followed up for behavioral disturbances, scholastic backwardness, seizures and other neurological deficit. Acute encephalitis is a disease of major public health concern . A prompt surveillance measure to prevent spread of disease is important. Compared to adult's neck rigidity, convulsions, abnormal behavior, seizures and elevated aspartate transaminase and higher serum bilirubin levels were more common in children. While adults had higher mean elevated protein and WBC in CSF. There was no difference in mortality between adults and children [9].

Vaccination against JE is the single most important control measure in JE endemic states of India.Public health measures for interruption of the zoonotic cycle are another preventive strategy to reduce the incidence of JE. Mouse brain derived and cell culture derived inactivated vaccines are available. SA-14-14-2 vaccine is licensed for use in India. Dose is 0.5 ml subcutaneous as two doses at 9 months and at 18 months. JENVAC is advised as two doses of 0.25 ml at 4 week intervalJE vaccine should not be used as an outbreak response vaccine. Routine JE vaccination is recommended in some of the hyper endemic areas of India. Vaccination is also recommended for travellers to endemic regions, who are likely to stay for 4 weeks or more in rural areas during JE season [10].

JE is still encountered in areas where agriculture is the main occupation and is in the declining trend in areas where routine JE vaccination is being practiced. Though predominantly a disease of rural areas, JE is still being encountered in urban Chennai and the presentation is similar to what is encountered from rural areas. Prevention of mosquito bite and effective vaccination are the best strategy.

CONCLUSION

JE encountered in urban Chennai presents with fever, altered sensorium, convulsions, involuntary movements and hepatomegaly. Gastrointestinal symptoms are not commonly encountered. Almost all children (20 /21) with JE present with involuntary movements. Nearly 38% of children need ventilator support. Mortality was 14%. Among those who were discharged nearly two third had morbidity in the form of seizures, involuntary movements, aphasia and focal deficits.

Points to Remember

- JE, preventable viral encephalitis is still encountered in urban Chennai
- Fever, convulsions altered sensorium and hepatomegaly ---are common in children with JE.
- Presence of CSFpleocytosis, basal ganglia involvement, extrapyramidal involvement is common in JE.
- JE in children is associated with high mortality -14. %
- Two third of the survivors have sequelae, of which involuntary movement is common.

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