

Review Article

Japanese Encephalitis-Emerging Disease in Bangladesh

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Abstract

Viral encephalitis remains a significant public health problem worldwide and one of the most important causes of mosquito borne viral encephalitis not only in Asia but all over the world. Its transmission is either from insect or environmental vectors or from human-to-human contact. It causes severe disease in humans, resulting in death or permanent neurologic deficits among the person who survives. As the risk of Japanese Encephalitis is persisting, implementation of strategies that will strengthen Japanese Encephalitis surveillance systems to understand the disease burden and apply vaccination protocols in national childhood immunization programs in Bangladesh.

Key words: Japanese encephalitis, Japanese encephalitis virus, acute encephalitis syndrome

Introduction:

Japanese encephalitis (JE) virus is the leading cause of viral encephalitis in Asia and western Pacific, where approximately three billion people live.¹ JE is transmitted through a zoonotic cycle. Human are incidentally infected and are dead end host because of transient viremia. From infected host, it spreads through the bite of infected mosquito specially *Culex tritaeniorhynchus*.² Globally, an estimated 30,000 to 50,000 human JE cases occur annually with the case fatality of 10–30%. About 30–50% of survivors develop long-term neurologic and psychiatric sequel, though it is still under reported.¹ There is no specific antiviral treatment available. However, JE is a vaccine-preventable disease.³

Virology:

JE is a member of Flaviviridae of genus *Flavi virus*. It has cross antigenic similarity to dengue, yellow fever and West Nile viruses, Saint Louis encephalitis viruses. It is a spherical shaped, enveloped virus having a +vesensesingle strandednon segmented RNA genome.⁴

Epidemiology, transmission and pathogenesis:

Majority of JEV infections are asymptomatic, less than 1% of people infected with JE virus develop clinical symptoms.² The

incubation period is typically 5-15 days.¹ The clinical features have a broad spectrum, ranging from a mild flu-like illness to a severe meningoencephalitis.¹ When virus transmission occurs to man by an infected vector mosquito, JEV replicates locally, spreads to the regional lymph nodes and replicate there.⁴ After that, they invade to the central nervous system (CNS). JEV is thought to invade brain via vascular endothelial cells by endocytosis.⁵ In the neurons, JEV replicates and matures in the neuronal secretory system, mainly the rough endoplasmic reticulum and Golgi apparatus, eventually destroying them.⁶ Experimental studies in mammalian hosts have shown JEV tropism to neurons in the CNS, indirectly indicating the presence of specific receptors with strong affinity for the virus.⁷ JE is recognized with two epidemiological patterns. In northern Asia such as northern Vietnam, Japan, Taiwan, northern Thailand, Korea, Pakistan, China, Nepal, and northern India where huge epidemic occurs during the summer months, whereas in southern Asia such as Southern Vietnam, Laos, Southern Thailand, Singapore, Indonesia, Malaysia, Philippines, Sri Lanka, and southern India, JE tends to be endemic and cases occur sporadically throughout the year with a peak after the start of the monsoon.⁴

JE virus transmission occurs primarily in rural agricultural areas where rice production and frequent flooding irrigation occurs and the transmission is seasonal in temperate areas of Asia. Human diseases occur mainly during summer and fall. In the subtropics and tropics, transmission can occur year-round, often reaches a peak around rainy season.¹

The virus is maintained in an enzootic cycle between mosquitoes and amplifying vertebrate hosts mainly pigs and wading birds.⁸

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In endemic countries, as Pigs and wading birds are often kept close to humans in farms or in field, they are the most important natural host for transmission to humans. Pigs also exhibits prolonged and high level viremias, and produce many progenies. The mosquito vector of JE differs in different regions. The infection is transmitted exclusively by 10 different species of *Culex*, mostly by *Culex tritaeniorhynchus*. These mosquitoes bite from early dusk until dawn. Only 1 to 3% of the *Culex* mosquitoes are infectious in endemic areas.¹

Bangladesh scenario:

A study on transmission dynamics of JEV in north-western Bangladesh, observed that, among 11,364 pigs in a backyard 30% had evidence of previous JE virus infection.⁹ JE incidence may be substantially reduced through reasonable pig vaccination coverage. Future studies are recommended to understand the contribution of pig infections to JE risk in humans in Bangladesh and the potential impact of pig vaccination on human disease.⁹

In Asia, particularly in Bangladesh, the epidemiology and etiology of encephalitis remain largely unknown. In Bangladesh, JE outbreak was first reported in 1977 in a rural area in Mymensingh district with 22 cases and seven deaths. Cases were confirmed as JE infection by serological testing. Most of the patients were under 15 years of age. Outbreak was thought to be due to local introduction of the virus from an endemic area. However, after two years, serological surveillance revealed a low rate of JE positive antibody.¹⁰ No new cases were documented in that area for two years following the outbreak.¹¹

During 2007-2012, the Institute of Epidemiology, Disease Control and Research (IEDCR) and Institute of Public Health (IPH) of the Government of Bangladesh, in collaboration with WHO, the US Centers for Disease Control and Prevention (CDC), and the International Centre for Diarrhoeal Disease Research, Bangladesh, conducted acute meningoencephalitis syndrome surveillance (AMES) in three tertiary level hospitals (Rajshahi Medical College Hospital, Khulna Medical College Hospital and Chittagong Medical College Hospital) where patients admitted with symptoms suggestive of meningoencephalitis are being tested for several component including JE. During 2007-2012, all serum and CSF samples were tested for JE virus antibody at "National AMES laboratories at institute of Public Health". JE incidence were reported to be 2.7/100,000 population in Rajshahi, 1.4 in Khulna and 0.6 in Chittagong in a study on 2011.¹⁴

This surveillance is replaced by a pilot project recently for introduction of JE vaccine. From the whole country all Encephalitis samples (as many as reported) are coming to central Laboratory for testing from all age groups.

In 2003-2005 icddr, b and the Centers for Disease Control and Prevention (CDC) Atlanta and Ft. Collins, USA began a

prospective, hospital-based surveillance at Dhaka, Mymensingh, Sylhet and Rajshahi to identify the causes of encephalitis in Bangladesh and found that 6% of patients admitted to the hospital with the sign and symptom of encephalitis were infected with JE¹¹. Among 492 patients, 20 (4%) JE cases were positive with two deaths; all JE cases were from rural areas and infected during the period of May–October, predominantly, nearly half, in October. Neurological sequel was observed in one-third of these patients and almost half of them had subjective cognitive function impairment at the six-week follow-up interview.¹⁰ Ten of the first 176 patients (6%) enrolled in the study tested positive for Japanese encephalitis, including 11% (7/63) of patients recruited from Rajshahi Medical College Hospital. Most of the Japanese encephalitis cases found in the current study were in Rajshahi Division, which bordered the areas of known endemic Japanese encephalitis transmission in India.¹² Among the older cases, JE infection in Bangladesh is observed mostly, that is 62%, among the cases of older than 15 years of age which mirrors a similar trend among adults in Nepal and parts of India.¹³

Bangladesh is a country with highest number of populations from Muslim communities. Higher proportion of people is directly involved in agriculture work. Pig raising is not common here. Few indigenous and tribal people living in north-western Bangladesh, commonly raise pigs.¹⁴ The actual pig density is not known, but a recent pig census conducted in three catchment districts of Rajshahi Medical College Hospital identified over 11,000 pigs, which were well distributed throughout the regions.¹

The incidence of JE is increasing due to inadequate control measures and also increases in vector density.¹⁵ Therefore, an overall management of risk factors, control measures, communication and clinical management can minimize JE virus incidences. Vaccination should be recommended for people those are working in agriculture field and also for those would like to visit JE virus endemic regions in a country, especially in the rainy season.¹⁵

World Health Organization has recommended large scale immunization programs in all areas where JE is a public health problem to control JE. But from surveys it became clear that only few economically strong Asian countries have reduced the JE load. The main reason is lack of knowledge on environment, disease burden, piling of human and livestock wastes, poor agriculture and farm yard management, low vector control and poor clinical care of patients and vaccine programs.^{16,17}

JE vaccines:

Currently, the three types of JE vaccines in large-scale use are (i) Live attenuated vaccine (SA 14-14-2 strain, 2 doses) (ii) Inactivated Vero cell-derived vaccines (Beijing-1 strain, 3

doses) (iii) inactivated, Vero cell-derived, alum-adjuvant vaccine (SA 14- 14-2 strain, 2 doses) and (iv) Live chimeric vaccine (with yellow fever 17D as backbone single dose).¹⁸ The percentage of countries that had a JE immunization program increased slightly, from 46% in 2012 to 50% in 2016. Furthermore, countries in the WHO South-East Asia Region are developing a plan for accelerated control of JE by extending vaccination to all areas with any risk of JE transmission.¹⁹ India, Australia, Cambodia, China Taiwan, Japan, Malaysia, South Korea, Sri Lanka, Thailand and Vietnam already introduced JE vaccination.²⁰

Conclusion:

Previous study showed JEV infection clearly as one of an etiology of encephalitis in Bangladesh. Emphasis to be given on JE vaccination program in EPI schedule or among identified endemic region. The evaluation of other etiologies of encephalitis should be continued or initiated.

Vaccination for human and animals can significantly make mortality rate low but risks and effects of regional climate should be taken in consideration. Strengthening of laboratory diagnostic capacity should also need to be improved.

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