Japanese Encephalitis: A Viral Metazoonosis of Growing Public Health Importance

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Abstract

Japanese encephalitis is a viral metazoonosis, which is important from public health as well as economic point of view. The disease is caused by Japanese encephalitis virus, which is neurotropic in nature and primarily affects central nervous system. It is transmitted by the bites of mosquitoes mainly belonging to Culex tritaeniorhynchus. The real magnitude of disease in many Asian countries is not well investigated. However, it is estimated that over 1 billion people are at high risk of acquiring infection due to Japanese encephalitis virus. Currently, there are about 68,000 clinical cases of disease worldwide. More males are affected than females. Maximum cases occur in children. Clinical manifestations include hyperpyrexia, chills, headache, nausea, vomiting, confusion, paresis, paralysis, and coma. Virological, immunological and molecular techniques are employed to confirm the diagnosis of Japanese encephalitis. The disease is a major public health problem in India. Currently, no antiviral drug is available to treat the patient. Environmental sanitation, personal protection, vector control, immunization and surveillance are effective strategies for the control of disease. Further attempts should be made to develop safe, potent and low cost vaccine, which can be easily affordable by poor resource nations to immunize humans as well as pigs to control this emerging vector borne zoonosis of great public health concern.

Keywords

Japanese encephalitis; Metazoonosis; Pig; Public health; Vector; Wild birds

Introduction

Metazoonoses are those zoonoses, which are transmitted biologically by invertebrate vector in which the agent develops, multiplies or both. The examples are babesiosis, chikungunya fever, dengue fever, filariosis, Japanese encephalitis, ilheus fever, Kyasanur forest disease, leishmaniosis, Mayaro fever, plague, Sindbis fever, and trypanosomiasis, yellow fever, and West Nile fever [1]. Among these, Japanese encephalitis is an important metazoonosis, which is of major concern, particularly to Asian countries. The first case of Japanese encephalitis was recognized in Japan in 1871. Since then, the disease was reported from many countries of the world such as Nepal, Bangladesh, Pakistan, China, Taiwan, India, Korea, Malaysia, Laos, Indonesia, Sri Lanka, Kampuchea, Vietnam, Myanmar, Philippines, Siberia, Thailand,
Singapore and Australia [1-6]. The disease is characterized by fever, headache, prostration, neck rigidity, confusion, and encephalitis. The major outbreaks of disease occur every 2 to 15 years. It primarily affects children but persons of any age may be infected [6]. In endemic regions, mortality due to Japanese encephalitis in humans, swine and equines may reach up to 50% [1]. The delay/ inadequate medical care are responsible for high morbidity and mortality of disease in developing nations. As there is no specific antiviral therapy to treat the patient, hence, immunization play a key role to control the disease.

The disease is caused by caused by Japanese encephalitis virus (single stranded RNA), which belongs to Genus Flavivirus and Family Togaviridae [1]. The virus agglutinates the erythrocytes of chick and goose, and is sensitive to ether, urea, and trypsin. Japanese encephalitis virus was first isolated in 1935 during an epidemic in Japan. It is maintained by biological transmission between mosquitoes and vertebrate hosts. Natural infection is demonstrated in herons, egrets, ducks, sparrows, and pigeons. Herons and pigs act as reservoir host and amplifier host, respectively. The disease is transmitted through the bites of infected mosquitoes of Culex species, mainly Culex tritaeniorhynchus, which are very active in the evening and night. Culex tritaeniorhynchus is the principal vector of Japanese encephalitis in many Asian countries including India. The transmission of disease intensifies during rainy season when vector population is abundant [6]. The present communication is an attempt to highlight the growing importance of Japanese encephalitis as a major public health problem, especially in Asian countries.

Clinical Spectrum
Humans

The incubation period of disease is 4 to 14 days. Most persons remain asymptomatic or show mild symptoms. The clinical manifestations in patients include high fever, severe cephalalgia, tiredness, chills, nausea, vomiting, diarrhea, weakness, stiff neck, disorientation, confusion, delirium, convulsion, stupor, paralysis, coma and death [1, 4]. Sudden paralysis affects respiratory system and causes bladder retention problem. Infection in the first or second trimester of pregnancy may lead to fetal death [4]. Death occurs within the first 10 days. Persons who recover from infection often suffer from permanent neurological problems [7].

Animals

Equine: The affected horse shows fever, depression, photophobia, muscular tremors, ataxia, and incoordination [1].

Swine: Disease is asymptomatic in adult pigs. However, abortion in pregnant sow, and neonatal death in piglet are observed [1].

Epidemiology

Japanese encephalitis is a vector borne emerging and re-emerging zoonosis, which causes significant morbidity and mortality in susceptible individuals. The disease is endemic in 24 countries of Asia and Western Pacific regions where more than 3 billion people are exposed to risk of infection [6]. Globally, 68,000 clinical cases of Japanese encephalitis occur each year with 13,600 to 20,400 deaths [6]. In Asia, the incidence of Japanese encephalitis, which causes almost 30,000 human cases and 7000 deaths annually, is related with irrigation of rice field [8]. Disease can be a risk to travelers who visit rural endemic areas. The people living in rural areas, rice field workers, pig raisers, paddy growers, and military persons are at a greater risk of acquiring infection due to Japanese encephalitis virus. Outbreaks of disease usually occur shortly after the rainy season in temperate zones and year round in tropical regions. Culex tritaeniorhynchus is the principal vector of disease transmission, which breeds in rice fields. The virus is maintained in nature by bird-mosquito-bird and pig-mosquito-pig cycle. The role of pigs as an amplifying host in the maintenance and transmission of Japanese encephalitis is well documented. It is imperative to undertake additional studies to elucidate the role of other livestock and wild birds as amplifier host/reservoir host of Japanese encephalitis.

Since 1954 when the first case of Japanese was diagnosed in India, it became a major public health problem with 7500 cases occurring every year [5]. The disease is widespread in India and is reported in epidemic form from many states such as Assam, Manipur, West Bengal, Bihar, Uttar Pradesh, Tamil Nadu, Kerala, Goa, Pondicherry, and Andhra Pradesh. The disease in sporadic form has been recognized in Madhya Pradesh and Maharashtra. The case fatality rates ranges between 25 to 50 %. A massive outbreak of Japanese encephalitis occurred in Gorakhpur,
India in 2005, in which 5737 persons were affected and 1344 died [1]. In Northern India, transmission is noticed from May to October whereas in Southern India, it occurs throughout the year. In most of the epidemics, the incidence of disease was higher in males than females. Maximum cases occurred in children below 10 years of age.

**Diagnosis**

Clinical signs are not very characteristic to make the diagnosis of Japanese encephalitis. Hence, it is imperative to seek laboratory help to confirm an unequivocal diagnosis of disease. Isolation of virus can be attempted from cerebrospinal fluid, blood and brain by inoculation in infant mice, tissue culture to confirm the diagnosis. Other techniques such as demonstration of antibodies (compliment fixation, haemagglutination, and enzyme linked immunosorbent asssay), antigen detection (indirect fluorescent assay, immunoperoxidase) and genome detection (reverse transcriptase polymerase chain reaction) are also useful in diagnosing Japanese encephalitis [1]. In endemic area, the virus can also be isolated from the mosquitoes. It is important to mention that clinical specimens should be collected from patients showing fever and altered sensorium. Disease should be differentiated from other viral encephalitis. Early diagnosis is imperative to start supportive therapy to have good prognosis of disease.

**Prevention and Control**

Japanese encephalitis is the most common form of encephalitis in Asia. Currently, no effective medications are available to treat the patients. However, the patient management should focus on supportive care, which include such as control of fever, convulsions, airway management and maintenance of fluid and electrolyte balance [1]. Persons who are going for outdoor work should use protective clothing and apply anti-mosquito repellent cream to avoid mosquito’s bites. Four types of vaccines namely, live attenuated vaccine, inactivated Vero cell derived vaccine, inactivated mouse brain vaccine and live recombinant vaccine are available [6]. Presently, live attenuated SA 14-14-2 vaccine is commonly used in endemic areas [6]. The detail information on vaccines for Japanese encephalitis can be obtained from the review article of Mac Arthur and Holbrook (2011). Travelers spending more than one month in endemic area should take vaccination. During an outbreak of disease, it is advisable to stay in well screened room, or use bed net, and spray insecticides in room. Environmental sanitation, vector control, water management in paddy fields, keeping the piggeries 4 to 5 km away from human dwellings, surveillance, immunization and health education are crucial to combat the disease. [9] has recommended that vaccination should be extended to all countries where Japanese encephalitis is a public health problem. It is suggested that in endemic areas, swine and horses should also be immunized with live attenuated and inactivated vaccines [6]. It is hoped that monitoring the viral activity in sentinel animal such as pig in endemic area may be useful to predict the epidemic of disease so that effective strategies can be planned to preventive the epidemic of this life-threatening vector borne viral zoonosis.

**Conclusion**

Japanese encephalitis is the leading cause of encephalitis with significant morbidity and mortality in Asian countries. Humans accidentally get infection by the bite of infected Culex mosquitoes, and act as dead end host, as life cycle of virus cannot continue in humans. Mortality rate in some epidemics may be 50 %. Most symptomatic infections in endemic areas occur in young children and elderly people. Major outbreaks are usually coincided with heavy rainfall and or floods. Immunization is the most effective strategy for the prevention of disease. As Japanese encephalitis has a great impact on the pig industry, it is advised to vaccinate the pigs in endemic areas to break the cycle of pig-mosquito-pig cycle in nature. The risk factors, ecology of virus and molecular epidemiology of disease need to be further studied. It is emphasized that Japanese encephalitis should be immediately notified so that preventive measures are taken to control the disease.

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**References**


