ISSN 2349-7823

International Journal of Recent Research in Life Sciences (IJRRLS)
Vol. 4, Issue 4, pp: (8-18), Month: October - December 2017, Available at: www.paperpublications.org

A Review on Japanese Encephalitis

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Abstract: **Japanese encephalitis is a viral disease which is endemic to the South, Southeast Asia and Asia Oceania regions. Japanese encephalitis (JE) virus is a member of the family Flaviviridae, genus Flavivirus Only a single serotype of JE virus has been identified and subtypification has been described. It is a zoonosis – an animal disease that can spread to humans. This disease is primarily transmitted by evening biting *Culex* mosquitoes that feed on infected birds, pigs and other mammals passing the infection to humans living and working in rural areas around rice paddies and irrigation systems. Over the years active vaccination campaigns in endemic countries have led to a decrease in the number of reported cases. Currently, there is no cure and treatment is mainly supportive for JEV. Though the patients are not infectious, but further mosquito bites should be avoided. Many antiviral agents have been investigated but none of these have convincingly improve the outcome of JEV. In this review, the current knowledge of the epidemiology and the pathogenesis of this deadly disease have been summarized.**

Keywords: **Japanese encephalitis, culex and flaviviridae.**

1. INTRODUCTION

Japanese encephalitis (JE) is an important zoonotic disease having serious public health implications. The disease has been known since the early twentieth century. This disease is distributed throughout the temperate and tropical zones of Asia. The virus infects pigs, horses, bovines, dogs, goats, sheep, bats, reptiles and various species of birds. The virus was isolated for the first time in the world from a post-mortem of human brain in Japan in 1933. In India Japanese Encephalities (JE) is prevalent since mid 1950's. In India, the first endemic case of Japanese encephalitis was identified in the state of Tamilnadu in 1955 (Tiwari *et al.,* 2012)**.** The first outbreak of encephalitis was observed in West Bengal in 1973, where 325 cases of deaths were reported out of 763 cases of encephalitis (Bandhopadhyay *et al.,* 2013). In 1976 and 1978 encephalitis outbreak dominated again in West Bengal where 1500 cases was recognized out of which 700 patients died (Bandhopadhyay *et al.,* 2013). Uttar Pradesh experienced its first epidemic in 1979 and the disease has continued there with 1,716-3,894 cases per year (Kakker *et al.,* 2012). In 2005, another severe epidemic with 5,737 cases and 1344 deaths has been reported in Gorakhpur in Uttar Pradesh (Parida et al.,2006). Another outbreak occurred in 2006, with 2320 cases and 528 deaths , during 2007, with 3,024 cases and 645 death (Tiwari *et al.* 2012). In year 2011, around 891 people, including 508 in Uttar Pradesh alone 200 in Bihar 11 in delhi died due to encephalitis (Kakker *et al.* 2012). Epidemic of Japanese encephalitis in Andhra Pradesh, during 1999, caused 178 deaths out of 873 affected peoples (Upadhya *et al.,* 2012). In Maharashtra JEV outbreak reported since 1995 (Thakare *et al.*,1999). In Karnataka, an out break took in the month of August 2004 to July 2005, 85 deaths out of 110 cases (Anuradha *et al.,* 2011). The earliest serological evidence of JE virus activity was identified in India in 1952 (Smithburn et al,1954).The disease has been recognized in India in 1956 (Carey et al, 1969.) The disease was recorded in India predominantly from rural areas but reports were there from sub urban areas also. Reported incident has generally been higher in males than in females. But sub clinical infections have occurred equally in both sexes. Large number of sub clinical infections occurs each year during the transmission season. Diagnoses can be made at primary health centre level based on clinical symptoms only. Therefore, there is a need to develop simple tests for use at the peripheral level both for diagnosis and for epidemiological surveys (Chaudhuri et al 1987). Outbreaks of JE have occurred in different part of India from time to time closely associated with monsoon and agricultural practices.

In Haryana, epidemic of JE was reported in 1990 and it was the first epidemic of encephalitis in the northwest region (Sharma and Panwar, 1991). Then again, in 1994 there was a report of 40 JE cases in Karnal and Kurukshetra districts (Kar and Saxena, 1998). In 1999, JE was diagnosed in Sonipat district (Katyal et al.,2000). In 2003, there was a report of 86 cases with 53 deaths in the state (Rao et al., 2005).

2. ETIOLOGY

JE is caused by Flavivirus of family Flaviviridae which is a single stranded, enveloped RNA virus. It has three proteins envelope protein, core protein and membrane protein. There are five genotypes I to V, based on the nucleotide sequence of the *envelop* (*E*) gene. Genotype I and III were found mainly in northern temperate "epidemic" regions and genotypes II and IV were found in southern "endemic" regions. Until 2007, all known Indian JEV strains belonged to genotype III, recently, genotype I has been isolated from the Gorakhpur region, India.

TRANSMISSION:

JEV is an arthropod-borne virus (arbovirus) that is transmitted in an enzootic cycle among mosquito vectors and vertebrate hosts, particularly pigs and birds; and humans become infected when bitten by an infected mosquito (rosen 1986; Weaver and Barrett,2004). Horses are the primary affected domestic animals of JE though essentially a dead-end host; other equidae (donkeys) are also susceptible. Pigs act as important amplifiers of the virus producing high viraemias which infect mosquito vectors , Mosquitoes: *Culex* spp., *Culex tritaeniorhynchus.* The natural maintenance reservoir for JE virus are birds of the family Ardeidae (herons and egrets), Although they do not demonstrate clinical disease they do generate high viraemias upon infection (Flohic *et al.,* 2013). Humans are vulnerable to the disease and this disease is a primary public health concern in Asia. Humans, horses, and other non-avian vertebrates are considered incidental dead-end hosts because they do not produce a level of viremia sufficient to infect new mosquitoes (Solomon and Vaughn,2002; Vaughn and Hoke,1992). In addition to its mosquito-specific horizontal transmission, JEV is also vertically transmitted to the progeny of infected mosquitoes through eggs(Dhanda et. al.,1989;Rosen et. al.,1989). Other subclinically infected animals which likely do not contribute to spread include: cattle, sheep, goats, dogs, cats, chickens, ducks, wild mammals, reptiles and amphibians.

PATHOGENESIS:

Japanese Encephalitis (JE) is a major cause of viral CNS infection. JEV pathogenesis is still unclear (Yang et al.,2011). Since the variation exists in neuro-virulence and peripheral pathogenicity among JE virus strains. When the infected mosquito bite, the virus enters into the reticulo-endothelial system and invades the central nervous system after the transient period of viremia following distribution in hypothalamus, hippocampus, substantia nigra and medulla oblongata regions of brain via vascular endothelial cells by the mechanism of endocytosis which involves cholesterol and clathrin mediated pathways, referred to as lipid rafts acting as portals for virus entry (Das et al.,2010). There is replication of virus in neurons and matures in the neuronal secretary system. Nearly 33% of JE infected patients die due to neurocysticercosis (NCC), suggesting that itmay somehow predispose to JE (Desai et al., 1997). During acute stages congestion, edema, hemorrhagic symptoms are found in brain. Pathological changes in the neural tissues have also been reported in lymphoid organs and immune cells such as spleen and kupffer cells respectively.

3. CLINICAL SIGNS

Equine: Incubation period is 8 to 10 days. The disease is usually subclinical. There is fever, impaired locomotion, stupor, teeth grinding, blindness, coma, death (rare) (Gulati *et al.,* 2011).

Swine: Incubation period is unclear. Exposure early in pregnancy is more harmful and there is stillbirth or mummified fetuses. In piglets there are neurological signs, death and in Boars there is infertility, swollen testicles (Lindahl *et al.,* 2014).

In man: A Prodromal Stage - It lasts for 1 to 6 days. It can be as short as less than 24 hours or as long as 14 days.

An Acute encephalitic Stage:

Begins by the third to fifth day. The symptoms include fever, convulsions, altered sensorium, unconsciousness, coma, stiff neck, muscular rigidity, tremors, abnormal movements of limbs and speech impairment (kakoti *et al.,* 2013).

A Late Stage: This stage is characterised by the persistance of signs of CNS injury such as mental impairment, increased deep tendon reflexes, paresis, speech impairment, epilepsy, abnormal behavior (kakoti *et al.*, 2013).

4. DIAGNOSIS OF JE

The diagnosis of JE become difficult particularly in theose areas where two or more related species of flaviviruses co-circulate. Because of high degree of cross-reactive antibody it becomes a challenge for serological assays to detect JE and distinguish it from other flaviviruses. Japanese encephalitis should be suspected in horses with fever and symptoms of CNS disorder. The primary signs in pigs are the birth of litter with large number of stillborn or weak piglets in temperate region. The disease is most common in summer and early autumn.

The ideal assay for JE should have a high degree of sensitivity and specificity (Endy and Nisalaka, 2002). A variety of diagnostic tests are available:

Virus detection methods:

Culture/virus isolation:

There are a variety of methods for isolation of JE virus , the classical being intracerebral inoculation of clinical specimens in suckling mice. Normally 1-2 days old suckling mice are inoculated intracerebrally with 0.02 ml of a suspension of clinical material. Mice are observed twice a day for the first signs of encephalitis which occur approximately 3-10 days after inoculation (OIE, 2004). Staining is to be performed for confirmation of JE virus. Shell vial culture assay, a centrifuge enhanced tissue culture for isolation of flaviviruses has been developed (Rangaiah *et al*., 2006). Various cell cultures that are being used more recently include primarily chicken or duck embryo cells, lines of Vero, LLCMK2, C6/36, and AP61 cells (Rice, 1996). However, isolation of virus from clinical specimens is generally considered a rare occurrence (Shope and Sather, 1979) probably because of low viral titers, rapid production of neutralizing antibodies, and the logistic difficulty in transportation of specimens in developing countries and frequent freezing and thawing of clinical material. Sensitive mosquito inoculation techniques have been described for isolation of JEV (Gajanan *et al*., 1995). Identification of JEV in culture substrates was traditionally carried out by the complement fixation test and agar gel diffusion. The neutralization test, monoclonal-based immunofluorescence technique, and enzyme immunoassay are in use (Yang *et al.,* 2006).

Antigen detection:

Various assays for antigen detection in JEV suspected specimens are reverse passive haemagglutination, immunofluorescence and staphylococcal coagglutination tests using polyclonal or monoclonal antibodies (Tiroumourougane *et al*., 2002). A powerful technique to diagnose fatal cases of JE is JE antigen staining in tissue specimens when serology or viral isolates are not available (Endy and Nisalaka, 2002).

A sensitive, quantitative, short time and reproductive focus assay is available for JEV. After 2 or 3 days of incubation of cell culture plates, the infected cells are treated with anti-JE virus serum and complement and subsequently stained with tryphan blue (Kuroda and Yasui, 1985).

Serological Assays:

Haemagglutination Inhibition (HI):

HI is the standard procedure for detection of antibodies against JEV (OIE, 2004). The value of the HI assay is in that it can be performed with minimal laboratory equipments, reagents and expense. The nonspecific inhibitors of haemagglutination are removed from sera using acetone, ether or kaolin prior to performing the HI assay. The HI titer is taken as the highest serum dilution that causes complete inhibition of agglutination (Clarks and Casals, 1958). A 4-fold increase in the JE specific HI titer between paired sera is indicative of a JE infection (Endy and Nisalaka, 2002). This test has been used for detection of JEV prevalence in pigs (Ogata *et al.*, 1973; Chang *et al*., 1974) and equines (Joshi *et al*., 1998). HI assay has been modified to be done by filter paper disc method where a titer of 1:20 and above is taken as positive (D'Souza *et al*., 1978). The results obtained with the serum on filter paper disc absorbed with blood are comparable to those obtained with the serum (D'Souza *et al.*, 1978). Wu *et al.* (1999) used sucrose acetone purified TaGAr01 strain of JEV from infected suckling mice brain as an HI antigen and treated the serum sample in acetone before

conducting the test. Horimoto *et al.* (1987) tested cattle serum sample for JEV antibodies using commercial antigen of JEV strain JaGAr01. They also used 16 units of the HA antigen and antibody titer of more than 1:10 was considered as positive. Kumanan *et al.* (2002) used JEV antigen prepared from mouse brain infected with Nakayama strain of JEV and goose erythrocytes and HI antibody titer of 320 and above was considered as positive since single serum samples were used. Pandey *et al.* (1982) used JEV strain P20778 and used 8 HA units of JE antigen and antibody titer of 1:20 and above was considered as positive. Babu *et al.* (1994) treated the serum samples using chilled acetone and absorbed with goose RBC and serum was considered as positive if it inhibited 8 HA units of antigen at a dilution of 1:20 or more. Yang *et al.* (2006) prepared viral antigen for HI using a sucrose acetone extraction method from the brain of a suckling mice infected with the JEV Nakayama strain.

Neutralization tests:

JE virus produces cytopathic effect (CPE) in certain cell lines such as cultured hamster kidney cells and chick embryonic fibroblast monolayer cultures (Kissing, 1957; Diercks and Hammon, 1958; Porterfield, 1959). Handerson and Taylor (1959) developed a method to detect plaques of arboviruses using an agar overlay staining with neutral assay. Yoshioka *et al.* (1965) developed plaque reduction neutralization assay (PRNT) for JEV using cultured chick embryonic fibroblasts and demonstrated a good correlation with HI antibody titers. This technique was subsequently adapted to the green monkey kidney cell line and Vero cells and was found to be more sensitive than HI. Widjaja *et al.* (1995) studied prevalence of neutralizing antibodies against JEV in horses using PRNT.

Joshi *et al.* (1998) used HI and SNT to demonstrate post epidemic JE antibodies in porcine, cattle, goat and horse. Ting *et al.* (2001) used PRNT for detecting and quantifying JE neutralizing antibodies. Lian *et al.* (2002) used SNT for detection of antibodies against JE virus in the Cerebrospinal fluid (CSF) of horses. Mehendale *et al.* (1996) isolated the virus by using C6/36 cell culture. Yang *et al.* (2006) used KV1899 (Korean strain) of JEV virus grown in TF104 cell lines in minimum essential medium (MEM) containing 5% foetal calf serum (FCS). They have used virus suspension containing 200 TCID50/0.1 ml and they considered titer of >4 as positive. Kuroda and Yasui (1985) used JaGA01 virus strain and propagated in suckling mice brain. In addition, they have grown the virus in Vero cells, LLCMK2, L-929, HEL cells and BHK-21 cells grown in MEM containing 10% FCS.

Enzyme linked immunosorbent assay (ELISA):

The ability to detect IgM during acute JE virus infection provides a highly specific antibody based assay without the problems of cross reactivity that IgG antibodies display for other flaviviruses. As IgM does not cross the blood brain barrier, its detection in CSF is associated with intrathecal production of IgM by CSF leukocytes and has been demonstrated to be diagnostic for JE virus infection of the CNS (Solomon *et al.*, 1998). IgM antibody capture ELISA (Mac-ELISA) is the method of choice to demonstrate virus specific antibody in both blood and CSF. However, when serum IgM antibodies are used for confirming JE, the co-presence of IgG antibodies should be demonstrated by another serological assay. Avidin biotin system (ABC Mac-ELISA) (Chow *et al*., 1992), biotin labeled immunosorbent assay to sandwich ELISA (Chang *et al.*, 1984), nitrocellulose membrane based IgM capture dot enzyme immunoassay (Mac DOT) (Solomon *et al.*, 1998) and antibody capture radioimmunoassay (Burke *et al.*, 2006) are some of the newer modifications of Mac-ELISA that have been used in antibody detection.

Quantitative and qualitative study of ELISA to detect IgM and IgG antibodies against JEV has been done in horse sera (Ihara *et al*., 1997) and swine sera (Burke *et al*., 1985; Jia *et al.*, 2005; Yang *et al*., 2006). ELISA has been found to detect and differentiate both IgM and IgG antibodies to JEV in the sera (Ohkubo *et al.*, 1984). In another study, an indirect ELISA was examined for its potential use in the rapid monitoring of the JEV and the results were compared with those from HI and SNT. The comparative analysis had that the results of I-ELISA showed significant correlation with the conventional HI and SNT (Yang *et al*., 2006).

Solomon *et al.* (1998) developed nitrocellulose membrane based IgM capture dot enzyme immunoassay. It is rapid, simple, requires no specialized equipments and can distinguish JEV from dengue. Konishi and Yamaoka (1982) developed rapid ELISA of whole blood for detection of antibodies to JEV and compared it with the HI test. The rapid system gave a correlation coefficient of 0.916 and qualitative agreement of 96.1%. Ravi *et al. (*2006) developed rapid IgM capture ELISA for the diagnosis of JE.

Latex agglutination test:

Jia *et al.* (2002) developed and applied the latex agglutination test (LAT) to detect serum antibodies against JEV. Here, the attenuated JEV was cultured in BHK-21 cells. In addition, it was purified and concentrated with PEG. A suitable concentration of JEV antigen was used to sensitize latex to prepare the latex antigen. The antigen thus prepared is used for agglutination test to detect the antibodies of JEV.

Single radial haemolysis test (SRH):

The SRH originally developed for the assay of antibodies to influenza virus haemagglutinins has been successfully employed in the assay of antibodies to flaviviruses. It is very simple test and is highly specific. Crude extraction of infected mouse brain can be used as antigen in the case of flaviviruses (George and Pavri, 1986).

Nucleic acid based assays:

Polymerase chain reaction is based on the ability to amplify small amounts of RNA or DNA to detectable levels using molecular primers, a polymerase enzyme and a thermocycler (Paranjpe and Banerjee, 1998; Endy and Nisalaka, 2002). TaqMan reverse transcription (RT)-polymerase chain reaction (PCR) assay has been developed for rapid detection and quantification of the viral RNA of various JEV strains. The detection of sensitivity of the real time reverse transcriptase loop mediated isothermal amplification (RT-LAMP) for JEV was one PFU (plaque forming unit), similar to that of conventional reverse transcription-polymerase chain reaction (RT-PCR). The RT-LAMP is able to detect the target product within 1 hour by only reacting reverse transcriptase and Bst DNA polymerase in a single tube at an isothermal temperature (Hiroko and Komiya, 2006, Parida *et al.*, 2006)

Real-time polymerase chain reaction (PCR) assays provide sensitivity and specificity equivalent to that of conventional PCR combined with Southern blot analysis, and since amplification and detection steps are performed in the same closed vessel, the risk of releasing amplified nucleic acids into the environment is negligible. In general, both PCR and amplified product detection are completed within an hour or less, which is considerably faster than conventional PCR detection methods. By reverse transcriptase PCR, the viral genome can be amplified directly from tissue or blood(Diagana et al.,2007;Swami et. al.,2008). A novel nested reverse transcription-polymerase chain reaction (RT-PCR)-based kit is described for detecting JEV, in which all reagents are lyophilized in reaction tubes and control RNA is included in each reaction to monitor false negative results(Jeong et. al.,2011).

Another study described and evaluated a reverse transcription loop-mediated isothermal amplification (RT-LAMP) assay for detecting JEV. The sensitivity of the JEV RT-LAMP assay was in concordance with that real-time RT-PCR, and it was more sensitive than that of conventional RT-PCR. The JEV RT-LAMP was highly specific; no cross-reactivity was found with dengue-2 virus, rabies virus, norovirus, astrovirus, and human enterovirus 71. The JEV RT-LAMP assay was simpler and less time-consuming compared to the conventional RT-PCR and real-time RT-PCR. The results suggest that the RT-LAMP assay can be applied as a practical molecular diagnostic tool for JEV infection and surveillance(Chen et. al.,2011).

TREATMENT:

To date, treatment of JE is essentially supportive. A severe case should be managed in an intensive care unit. Supportive measures include maintenance of airways, breathing and circulation, hydration, electrolyte status, and control of pyrexia and convulsions. Raised intracranial tension should be controlled with mannitol infusion (0.25 to 1.0 gm/kg every 4–6 hours), intravenous furosemide or intermittent positive pressure ventilation to keep arterial carbon dioxide tension between 25–30 mm of Hg.

Minocycline, a tetracycline drug with antibacterial and neuroprotective properties, has recently been shown to be effective against the JE virus in an animal model (Tiwari *et al.*, 2012).

PREVENTION AND CONTROL:

Control is through early case detection and treatment.

Vector Control

a) Reduction of breeding source for larvae

b) Reduction in man-mosquito contact

c) Control of adult mosquitoes

Prevention through JE vaccination

▶ Vaccines

❖ ICMR in collaboration with Bharat Biotech on OCT 6, 2013 launched the first indigenous vaccine to prevent Japanese encephalitis in children. So far, India used to import the vaccine from China.

❖ The Vero cell-derived purified inactivated Japanese encephalitis vaccine–JENVAC, which was approved by the DCGOI, pioneers as the first vaccine ever to be manufactured in a public-private collaboration.

❖ The virus strain for this vaccine was isolated in Kolar (Karnataka), during the early 1980s and was characterized by National Institute of Virology based in Pune. The strains were then submitted to Bharat Biotech for further vaccine formulation.

▶ The biggest advantage of JENVAC over live attenuated vaccines is that vaccine could be administered even during an epidemic as it is an extremely purified and inactivated vaccine. It achieved all its primary and secondary endpoints in the age-group of 1 to 50, following 1 to 2 doses of vaccination.

▶ Phase III trials revealed 98.7% sero-protection 28 days following the first dose, and 99.8% sero-protection 28 days following the second dosage.

▶ The results proved that JENVAC can be administered as a single dose at times of epidemics when mass vaccinations are required, and it can also be administered in 2-doses during routine immunisation as part of the National immunisation programme.

Live attenuated vaccine:

▶ The only live attenuated JE vaccine currently available is the one derived from SA-14-14-2 strain, produced by Chengdu Biologicals (Chengdu TECBOND Biological Products Co, Ltd, Chengdu, People's Republic of China).

▶ This vaccine is being used in the public sector in the People's Republic of China (since 1998), Nepal (since 1999), and India (since 2006).

▶ An Indian study found vaccine efficacy to be 94.5% after 6 months. Safety profile has been good, with only 5%–10% of recipients developing transient fever, local reactions, rash, or irritability.

▶ This vaccine was imported by the government of India from the People's Republic of China after the Uttar Pradesh epidemic of 2005.

▶ SA-14-14-2 strain inactivated vaccine

▶ The IC51 Vaccine – IXIARO® – manufactured by Intercell AG (Vienna, Austria) and distributed by Novartis Vaccines is a new generation formalin inactivated vaccine prepared from the SA-14-14-2 strain grown in vero cells.

▶ This is the only JE vaccine to have received US Food and Drug Administration approval for use in adults 17 years of age or older.

▶ In May 2013, US Food and Drugs Administration approval for use also in children aged 2 months through 16 years was accorded. This vaccine, produced with Austrian collaboration, is available in India as JEEV (Biological E. Ltd., Hyderabad, India).

▶ It was licensed in the US on the basis of its ability to induce neutralizing antibodies and also on safety evaluations in almost 5,000 adults. Among adults administered two primary doses of this vaccine 28 days apart, 96% developed protective neutralizing antibodies (Firbas *et al.*, 2015).

▶ Local symptoms of pain and tenderness were the most commonly reported symptoms. In children, fever was the most commonly reported systemic reaction.

▶ No studies of IXIARO® in pregnant women have been conducted.

▶ The Advisory Committee on Immunization Practices, USA recommends the JE vaccine for travelers who plan to spend a month or more in endemic areas during the JE virus transmission season.

▶ The primary immunization schedule for IXIARO® is two doses administered intramuscularly on days 0 and 28.

▶ The two-dose series should be completed a week or more before travel (Firbas *et al.*, 2015).

Mouse brain killed vaccine:

▶ The earliest vaccine to be used was the inactivated vaccine derived from mouse brain originally produced by BIKEN (Kyoto, Japan) and marketed in the US as JE-VAX.

▶ Since the vaccine was derived from neural tissue, a risk of neurological events (acute disseminated encephalomyelitis) did exist.

▶ A new pattern of adverse reactions in the form of urticaria, angioedema, respiratory distress, and collapse due to hypotension has been reported since 1989, mostly among travelers vaccinated in Australia, Europe, and North America.

▶ Rates for these reactions varied from 0.7–104/1,000.

▶ These safety concerns led to suspension of vaccine production and all remaining doses expired in 2011(WHO, 2014).

P3 strain inactivated vaccine:

▶ The cell culture-derived, formalin inactivated JE vaccine based on the Beijing P-3 strain is another vaccine in wide use in the Chengdu, People's Republic of China since the 1960s.

▶ Primary immunization of infants resulted in about 76%–90% protection, but immunity was relatively short-lived.

▶ The relatively low efficacy and need for repeated booster doses led to the vaccine being replaced by the live attenuated vaccine.

5. JE VACCINATION IN INDIA

In india JE vaccination campaign was launched during 2006, in which 11 of the most sensitive districts in Assam, Karnataka and Uttar Pradesh were covered. Altogether, 86 JE endemic districts in the states of Assam, Andhra Pradesh, Bihar, Haryana, Goa, Karnataka, Kerala, Maharashtra, Tamil Nadu, Uttar Pradesh, andWest Bengal have been covered. Reorientation training course on JE case management is a continuing process. In Andhra Pradesh, Assam, Haryana, Karnataka, Tamil Nadu, Uttar Pradesh, and West Bengal such orientating training courses were carried out during 2008 and 2009 (NVDCP, 2009).

6. CONCLUSION

JE is a disease which is still on the increase in many parts of Asia. It is a zoonosis with its natural cycle in pigs, birds, and mosquitos and man is an incidental dead-end host. It tends to occur in epidemics and outbreaks especially affecting poor rural rice growing, pig rearing people in Asia. The disease presents a severe encephalitis with compact clinical course, high mortality and high disability rate in survivors. Diagnosis is usually made by presence of IgM antibody in CSF. Treatment to date is essentially supportive. The mainstay of prevention is by human vaccination. The main vaccines in use presently are the live attenuated SA-14-14-2 strain derived Chinese vaccine and the killed SA-14-14-2 strain derived vero cell vaccine. The later is US Food and Drug Administration approved for travelers to endemic areas. Increasing incidence and recent outbreak of Japanese encephalitis in India, indicates the failure of present vaccination and immunization program, controlled by Indian government. In India, immunization of children has been carried out in different regions but reoccurrence of Japanese encephalitis in those area and lack of surveillance system in other parts of country has been showing where we are and what we have done to protect from this endemic disease. Researches for the effective treatment of Japanese encephalitis are being carried out all over the world. Recombinant vaccines are found to be promising agent to cure and immunize people against Japanese encephalitis but, their use is presently limited by significant limitation.

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