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A REVIEW ON NIPAH VIRUS

Veterinary Science

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ABSTRACT

In 1998, Nipah Virus which is a paramoxyvirus related to Hendra virus, first occurred in Malaysia. Clinical manifestations caused by the virus vary from asymptomatic infection to fatal encephalitis. No outbreaks of Niipah virus (NiV) had been observed in Malaysia since 1999, however India and Bangladesh continue witness the outbreaks. While the outbreak in Malaysia and Singapore was primarily associated with the contact with pigs, in India and Bangladesh the major route of transmission is consumption of contaminated date palm sap and human-to-human transmission. The main reservoir of NiV is bats that transmit disease to humans and animals. Presently, as there are no specific drugs or vaccines available for the treatment of NiV, supportive care and prophylactic measures should be the major strengths of management.

KEYWORDS

Nipah Virus, Fruit bats, Zoonoses, Pigs

INTRODUCTION

In the South-East Asia region of World Health Organization, Nipah virus (NiV) is considered as an emerging infectious disease of public health importance. NiV, which belongs to genus henipavirus in the family Paramyxoviridae, is a negative sense, enveloped and single-stranded RNA virus (Chattu *et al*., 2018). The virus and disease has acquired its name from the village called 'Sungai Nipah' from Malaysia where the virus was identified during an outbreak among pig farmers in 1999 (Annonym, 1999). Animal-to-human as well as human-to-human route of transmission have been documented (Chattu *et al*., 2018). More than 600 cases of human infections were documented between 1998 and 2015. Subsequent outbreaks with high case fatality have observed in India and Bangladesh. While 106 fatalities (38%) were reported out of a total of 276 cases in Malaysia, significantly higher case fatality rates of 43-100% were reported in later outbreaks in India and Bangladesh (WHO, 2018). Clinical manifestations of NiV infection in humans ranges from asymptomatic one to acute respiratory syndrome and fatal encephalitis. The broadly distributed fruit bats from the family, Pteropodidae are the natural reservoirs of the virus (Yob *et al*., 2001). Transmission of NiV from bats to humans occurs via various routes such as inhalation, contact or via consumption of foods contaminated with NiV (Chua *et al*., 2002). NiV is transmitted through both zoonotic route which includes transmission form bats to humans, or from bats to pigs, and then from pigs to humans and human-to-human route. Currently, the treatment of NiV is only supportive because no vaccines or antiviral drugs are available for NiV disease (WHO, 2018). Prevention strategies for the disease at present focus on improving the awareness about the disease in the affected area.

HISTORICAL PERSPECTIVE

NiV was not recognized until 1999 when an outbreak in Kampung Sungai Nipah, Malaysia in pig farmers was discovered. In Peninsular Malaysia and Singapore, NiV infection in humans was first identified during a large outbreak with 276 reported cases between September, 1998 and May, 1999. It was the first evidence of occurrence of NiV in humans (Chua *et al*., 2003). After three years, a genetically distinct NiV independently emerged in both India and Bangladesh. Since then, human NiV outbreaks have been reported almost every year. In 2014 in the Philippines, a virus assumed as NiV caused a disease outbreak in horses and humans. NiV was first detected in 2001 in Bangladesh and outbreaks have occurred nearly every year in Bangladesh with intermittent outbreaks of disease in Eastern part of India bordering to Bangladesh. Two outbreaks of NiV encephalitis in 2001 and 2007, in the eastern state of West Bengal, bordering Bangladesh, have been documented in India. A high case fatality rate (70%) was reported during two outbreaks with 50 deaths out of total seventy-one cases (Chattu *et al*., 2018).

A strong seasonal pattern and a limited geographical range are the characteristics of Nipah outbreaks in South-East Asia region (Chattu *et al*., 2018). All the outbreaks of the disease have occurred in winter and spring i.e. between December and May. Numerous factors such as the breeding season of bats, rise in virus shedding by the bats and the harvesting season of the date pal sap could be associated with the seasonal pattern of the disease (WHO, 2018).

RESERVOIR

Fruit bats belonging to the genus Pteropus have been recognized as natural reservoirs of NiV. In Malaysia, NiV has been isolated from the brain and spinal fluid of victims of NiV infection and also from the environmental samples of bat urine and incompletely consumed fruit (Chua *et al*., 2000; Chua *et al*., 2002). In Cambodia, Nipah virus has been isolated from Lyle's flying fox (*Pteropus lylei*) (Reynes *et al*., 2005). The viral RNA has also been found in saliva and urine from from *Pteropus lylei* and Horsfield's roundleaf bat (*Hipposideros larvatus*) in Thailand (Wacharapluesadee *et al*., 2005). Antibodies against Nipah-like virus have been detected in sera collected from fruit bats in India, Indonesia, and Timor-Leste (Heymann *et al*., 2008).

TRANSMISSION

The virus is shed in the excretion and secretion of infected bats such as saliva, urine, semen and excreta; however fruit bats are symptomless carriers. In pigs, the NiV is highly contagious and it is spread by coughing. When the disease was first identified in Malaysia in large outbreak in 1999, it was discovered that the direct contact with infected pigs was the predominant mode of transmission of disease (Goh *et al*., 2000). During 1998-1999 outbreak, out of total infected population, ninety percent were pig farmers or had contact with pigs.

Loss of natural habitats of bats has been reported as the reason of emergence of bat-related viral infection communicable to humans and animals. The bats get stressed and hungry because their habitat is destroyed by the human activities which lead to weakening of bat's immune system. Due to this, the virus load in bats increases and the amount of virus shed by the bats through their saliva and urine also goes up (Halpin *et al*., 2000).

In 2001, focal outbreaks of NiV in Bangladesh and India were documented in 2001. Indirect transmission of NiV to humans can be attributed to the consumption of fresh date palm sap which is perhaps contaminated by fruit bats during the winter season (Luby *et al*., 2006). Drinking of date palm sap is common among many South-East Asian countries including India, Bangladesh, Thailand, and Indonesia as well as in the Philippines and Malaysia. While consuming date pal sap, fruit bats contaminate it with their saliva, urine and feces. By this means, NiV is thought to be transmitted from infected fruit bats to humans (ICDDR B, 2010). Human-to-human transmission of NiV has been documented during 2001 outbreak in India. 33 hospital visitors and health workers developed illness after being exposed to patients hospitalized with NiV infection during the outbreak in the region of Siliguri, which suggested nosocomial infection (Chadha *et al*., 2006). Furthermore in 2004, solid evidence suggestive of human-to-human transmission of NiV was found in Bangladesh (Chattu *et al*., 2018).

CLINICAL PRESENTATION AND DIAGNOSIS

After the incubation period of 5 days to 2 weeks, symptoms similar to influenza such as fever and muscle pain are developed. Inflammation

of brain resulting in disorientation or coma occurs in some cases. But, even incubation period of two months have been observed during the outbreak in Malaysia (Goh *et al*., 2005). Encephalitis can be seen in acute cases or can initiate in later stages. Patients who recover from acute episode of encephalitis can have relapse. Magnetic resonance of the brain plays crucial role in distinguishing between encephalitis caused by Nipah virus from other encephalitis as well as it is essential in identifying between acute and late onset and a relapsed form of the disease.

The majority of patients who survived the disease had few or no sequelae. Still, roughly 20% of patients suffered from neurological deficits, neuropsychiatric sequelae, and gait/movement disorders. Relapsing encephalitis, which can reoccur weeks to years after symptomatic infection of NiV and even after asymptomatic phase, is the most interesting complication and sequelae of Nipah virus infection. Till now, more than 20 cases of relapsing encephalitis due to NiV have been documented. Out of 20, one of the case had relapse of encephalitis 11 years after an asymptomatic infection.

DIAGNOSIS

Because the initial sign and symptoms of NiV infection are non-specific, the diagnosis is often not suspected as NiV infection during the time of presentation. This may delay the exact diagnosis of disease and also outbreak detection becomes more challenging in such situations. Thus, timely and effective control measures and outbreak response activities can get hampered. Moreover, the accuracy of laboratory results can be affected by clinical sample quality, quantity, type of sample, timing of collection and the time required to transfer samples from patients to laboratory (32).

The diagnosis of NiV infection can be done with the clinical history in the acute and convalescent phase of the disease. RT-PCR from samples including bodily fluids and detection of antibodies via enzyme linked immunosorbent assay (ELISA) are the main two tests for diagnosis of NiV infection. Isolation of virus by cell culture is another method to diagnose NiV infection.

Internationally, NiV is categorized into biosecurity level 4 agent (5). Laboratory present at the ICMR institute, National Institute of Virology, Pune is well equipped to diagnose NiV cases in India.

CLINICAL MANAGEMENT

Even though the disease is one of the priority diseases on the WHO R&D Blueprint, no drugs and vaccines specific for NiV infection have been discovered. Intensive supportive care is the suggested mode of clinical management during severe neurological and respiratory complications (32).

Antiviral drug such as Ribavirin is indicated in young children suffering from severe respiratory infection. Convalescent plasma is administered in cases of severe disease when treatment with established record of efficacy and safety is not available. Like many other viral severe diseases, as for other severe diseases of viral origin, aggressive supportive care may help; aggressive supportive care should be the priority in treatment to increase the chances of survival of the patient.

PREVENTION STRATEGIES

1. REGULATING NIV IN DOMESTIC ANIMALS

At present, no vaccines are available against NiV in animals. Thorough and regular cleaning and disinfection of pig farms can be considered as prophylactic measure in reducing incidence. The animal premises should be quarantined immediately if an outbreak is suspected. Culling of infected animals with deep burial or incineration of carcasses is required to lower the risk of disease transmission to humans.

2. REDUCING THE RISK OF INFECTION IN PEOPLE

When no vaccine is available against the infection, the only way to decrease the incidence of infection in people is to increase the awareness in people about risk factors and educating them about transmission of disease and the measures they can take to alleviate the exposure and reduce infection from NiV.

3. REGULATING THE INFECTION IN HEALTHCARE SETTINGS

People working in healthcare sectors who care for patients suspected or suffering from NiV, or handling samples or specimens from them, should follow standard infection control precautions at all times for all patients. Because human-to-human transmission and particularly nosocomial transmission is documented, in addition to standard precautions contact and droplet precautions should be used. Only trained staff working in well-equipped laboratory should handle the samples taken from animals and humans suspected with Niv infection.

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