Nipah Virus: Outbreaks, Diagnosis and Prevention

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Abstract
Nipah virus, an emerging zoonotic virus that causes severe and often lethal respiratory illness and encephalitis in humans has been in limelight due to the recent outbreak in India in the year 2018. It is a member of the family paramyxoviridae and belongs to genus Henipavirus. It causes a range of illnesses in humans ranging from asymptomatic infection to fatal encephalitis. As this virus has a potential to cause morbidity and mortality in humans and has major economic and public health impacts, the World Organisation for Animal Health has made it a notifiable disease of importance for international trade. The natural hosts of this virus are fruit bats of pteropodidae family. This virus can be transmitted to humans from animals (bats, pigs), and also human to human transmission is reported. Because of its potential to cause a public health emergency and the absence of efficacious drugs and/ or vaccines, it has been added by WHO to the list of blueprint priority diseases.
Keywords: Nipah virus, outbreak, respiratory illness, WHO, treatment and control

Introduction

Nipah virus is a member of genus Henipavirus, family paramyxoviridae (Eaton *et al.*, 2007). It is an enveloped, single stranded, negative sense RNA virus. Other species in this genus are Hendra virus and Cedar virus. This virus owes its name to Sungai Nipah, a village in Malaysian peninsula where pig farmers suffered from encephalitis due to infection by this virus (Marsh *et al.*, 2012). This group is characterized by a wide host range as compared to other members of the family. India has become a hotspot for livestock diseases, including zoonotic diseases owing to the rapid growing human population, increased human- animal interactions and poor sanitation.

Nipah virus is inactivated at 60°C for 60 minutes. It is susceptible to common soaps and disinfectants such as alcohol, ether and sodium hypochlorite but has the ability to survive for longer periods in favourable conditions, like for days in contaminated fruit juice and in fruit bat urine (WHO, 2009). Bats have been identified as reservoir of zoonotic viruses like Ebola, Marburg, SARS and Melaka viruses. Nipah virus has emerged as one of the most important bat borne pathogens discovered in recent times (Leroy *et al.*, 2005; Towner *et al.*, 2007; Li *et*

*al.,*2005and Chua *et al.,*2007). Since its first outbreak in 1998, it has led to several outbreaks and claimed many human lives.

Historical background

Nipah virus was first recognized in the year 1998-99 during an outbreak among pig farmers in Kampung, Sungai Nipah, Malaysia. Over a period of 35 weeks from September 1998 to May 1999, several human cases of viral encephalitis were reported and it was suspected to be already circulating Japanese encephalitis among pig farmers, creating a scare in the country. 105 cases died among the 265 reported. This disease was named after Kampung Sungai Nipah (Nipah River Village), where the first viral isolate was obtained and therefore named as NiV. The chronology of outbreaks due to Nipah virus is summarized in **Table** 1.

Table 1. Year wise list of Nipah virus outbreaks reported along with the number of cases and fatalities (WHO-SEARO, 2012 and Aditi and Shariff, 2019).

Year	Country	Cases	Deaths	Case fatality
2018	India	18	17	94%
2013	Bangladesh	24	21	87%
2012	Bangladesh	12	10	83%
2011	Bangladesh	44	40	91%
2010	Bangladesh	16	14	88%
2009	Bangladesh	4	1	25%
2008	Bangladesh	11	9	82%
2007	India	5	5	100%
2007	Bangladesh	18	9	50%
2005	Bangladesh	12	11	92%
2004	Bangladesh	67	50	75%
2003	Bangladesh	12	8	67%
2001	Bangladesh	13	9	69%
2001	India	66	49	74%
1999	Singapore	11	1	9%
1998-99	Malaysia	265	105	40%

Transmission

Macrochiroptera (fruit bats) of the family pteropodidae are the natural hosts for Nipah virus (Bothma, 2018). These fruit bats are widely distributed in tropics and subtropics of Asia, Australia, Indonesia, Madagascar and a number of islands in both Indian and Pacific oceans (Young *et al.*, 1996 and Olso *et al.*, 2002). The main natural reservoirs identified for this virus are Indian flying fox (*Pteropus giganteus*) and short nosed Indian fruit bat (*Cynopterus sphinx*). Serological evidence has shown that circulation of this virus is extended to a wide range of insectivorous and frugivorous bats.

During the initial outbreaks in Malaysia and Singapore, direct contact with sick pigs or their contaminated tissues was the cause of human infections and it was thought to have occurred *via* respiratory droplets, contact with throat or nasal secretions from pigs, or contact with the tissue of sick animal (WHO, 2009).

Consumption of fruits or fruit products contaminated with saliva or urine from infected bats was found to be most likely source of infection in outbreaks in Bangladesh and India (Luby *et al.*, 2012). This virus has been found in urine and uterine fluids of wild pteropid bats. It has also been experimentally isolated from urine, uterus and kidney of infected bats. This virus is also found in fruit or juice contaminated with bat urine or saliva. Contaminated drinking water and aborted fetuses or other fluids/ tissues of parturition are other sources of infection. Role of other animals as source of virus is less clear (Luby *et al.*, 2012). No person to person transmission was reported in outbreaks from Malaysia and Singapore. Conversely, person to person transmission has regularly been reported from India and Bangladesh (CDC update, 1999).

Signs and symptoms

Humans: Incubation period is variable, mostly 4 days to 2 weeks, but at times may even extend up to 60 days (Luby *et al.*, 2012 and Chua, 2003). Human infection ranges from asymptomatic infection, acute respiratory infection (mild to severe) to fatal encephalitis. To start with, the infected persons develop flu like symptoms like high fever, headache, myalgia, weakness and sore throat. These symptoms are followed by dizziness, drowsiness, altered consciousness and neurological signs together indicating acute encephalitis. Encepahalitis and seizures occur in severe cases only and they progress to coma within 24-48 hrs. In Bangladesh strain patients have experienced atypical pneumonia and severe respiratory problems including acute respiratory distress (Hossain *et al*., 2008).

Most of the patients who survive acute encephalitis make a full recovery but long term neurological deficits have been reported in about 20% of cases. Case fatality rate varies from 40% to 100% as reported in various outbreaks

Animals

Nipah virus outbreaks have been reported in pigs and other domestic animals like horses, sheep, cats, dogs and goats. Most of the pigs had no symptoms but some of them developed acute febrile illness, labored breathing and neurological symptoms. There is limited clinical information existing for other species (WHO, 2009 and Uppal, 2000).

Laboratory diagnosis

Because of its highly infectious nature, special precautions need to be undertaken in the collection, submission and processing of samples. The important tests which can be used to diagnose this virus are:

- Enzyme-linked immunosorbent assay (ELISA)

- Serum neutralization tests
- Polymerase chain reaction (PCR)
- Virus isolation by cell culture

Serological tests: ELISA can be used for detection of IgG and IgM. But there is problem of false positives with ELISAs and as a result the positive reactions have to be confirmed by serum neutralization tests (World Organization for Animal Health, 2010). The sera that completely block the cytopathic effect (CPE) are designated as positive (World Organization for Animal Health, 2010).

PCR: PCR has an advantage of not propagating live infectious virus. Real time PCR from throat and nasal swabs, cerebrospinal fluid, urine, and blood should be performed in the early stages of disease (World Organization for Animal Health, 2010).

Virus isolation: Cell culture is done using African green monkey kidney (Vero) and rabbit kidney (RK-13) cells. The sample for isolation is transported at 4ºC if done within 48 h or else frozen if a delay of more than 48 h is expected. Cytopathic effect usually occurs within 3 days. In absence of CPE, two 5-day additional passages are recommended to confirm negative results (World Organization for Animal Health, 2010).

Treatment

Even after being on the priority disease on the WHO R&D blueprint, there is still is no specific drug or vaccine available for this infection. Intensive supportive system is recommended to treat severe respiratory and neurologic complications (Bothma, 2018).

Prevention and control

Although no vaccine at present is available to prevent this viral disease, the research for the development of vaccines is ongoing (McEachern *et al.*, 2008). Therefore, the prevention of this viral infection relies on avoiding exposure to sick pigs and bats in endemic areas and avoiding drinking raw date palm sap (CDC Update, 1999). Because of the serious human health implications, all field investigations should take the necessary steps to prevent the infection which includes veterinary investigations on all clinically suspected cases especially pigs (Giangaspero, 2013). In case of a suspected outbreak the animal premises needs to be quarantined immediately. Culling of infected animals with close supervision of burial may be important to decrease the risk of transmission to people (Bothma, 2018).

Surveillance tools should include reliable laboratory assays for early detection of disease in communities and livestock. Raising awareness of transmission and symptoms is most important in reinforcing the infection control practices to avoid human to human nosocomial infections (CDC Update, 1999).

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