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NIPAH Virus Infection - A Review Article

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ABSTRACT

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Nipah virus (NiV) is an emerging zoonotic disease with high case fatality rate. Infection is spread to humans from the natural reservoir host (bats) through intermediate hosts like pig or through fruits contaminated by bat saliva or urine. Currently there is no treatment and vaccine for the disease. So early identification of the outbreak, and personal protective measures are important to prevent the transmission of the disease.

Keywords: Nipah, Epidemic, Virus

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INTRODUCTION

Nipah virus infection is a rare zoonotic disease caused by Nipah virus of the *Paramyxoviridae* family. *Pteropus* bats (fruit eating species, popularly known as flying foxes) are supposed to be the natural hosts of the virus.[1] Among the genus *Pteropus*, the Indian Flying Fox (*Pteropusgiganteus*) and the relatively smaller Greater short-nosed fruit bat or Short-nosed Indian fruit bat (*Cynopterus sphinx*), which are widespread and very common species in South Asia, have been identified as the main natural reservoir. So far Nipah virus has not been isolated from insectivorous bats. There is no apparent disease in fruit bats.[2] Bats have also been recognized to be important reservoir of other zoonotic viruses, including Ebola, Marburg, SARS and Melaka viruses.[2]

So far, the disease has been reported only in Malaysia, Singapore, Bangladesh and nearby districts in India. In May 2018 there was a new outbreak in Kerala state in India with a higher case fatality rate. Nipah virus infection was identified in Kerala state on the very second person hit by the outbreak.

HISTORY

NiV was first identified in Kampung Sungai Nipah (Nipah River Village), Malaysia during an outbreak of disease in 1998. On this occasion, pigs were the intermediate hosts.[3] NiV was transmitted from pigs to humans, causing 265 human cases in Malaysia, with 105 deaths.[4] Most of the affected humans were pig farmers.[5] The Malaysian government had to kill 1.1 million pigs to stop the spread of the disease.[4] However, in subsequent NiV outbreaks in Bangladesh and India, there were no intermediate hosts.[3] The outbreak also spread to neighbouring country Singapore during March 1999 where 11 abattoir workers handling pigs from infected farms in Malaysia developed the disease. But there was only one fatality.

1n 2001 Nipah outbreak occurred in West Bengal of India and Bangladesh. Bangladesh reported outbreaks almost every year after that. Indian reported another outbreak in 2007. Seventy-one cases with 54 deaths were reported in the two outbreaks.[6] The last outbreak occurred in Kerala, India during May-June 2018. So far, NiV has infected 626 people resulting in 374 deaths.

MICROBIOLOGY

The Nipah virus belongs to the genus Henipavirus in the Paramyxoviridae family **(figure 1)**. Hendra virus (HeV) and Cedar virus are the other two recognized species of the genus *Henipavirus.*[2]

The virus is inactivated by 60°C for 60 minutes. It is stable between pH 4.0 and 10.0. It survives for

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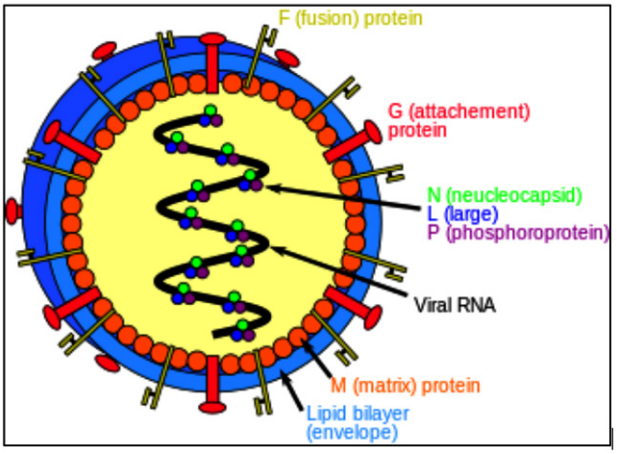

Figure 1. **Structure of Nipah Virus**

long periods in favourable conditions, for days in fruit bat urine and contaminated fruit juice. It is susceptible to common soaps and disinfectants. Lipid solvents, such as alcohol and ether, and sodium hypochlorite solutions were used effectively in outbreaks for disinfection.[2]

Pathogenesis

Endothelial cells have been identified as an important target of infection; however, it is unknown how the virus spreads to the central nervous system (CNS).[7]

Transmission

Fruit bats are the natural reservoirs of the disease. In the initial outbreaks in Malaysia and Singapore, most human infections resulted from direct contact with sick pigs or their contaminated tissues.[2]

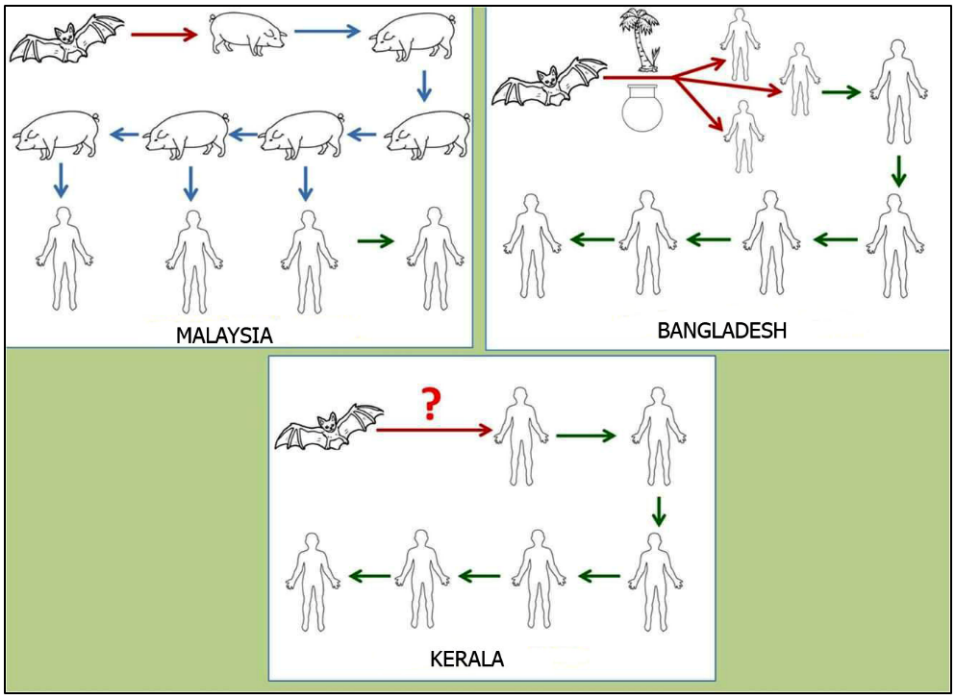

Figure 2. **Transmission of Nipah Virus**

While the outbreak in Malaysia had progressed from the natural host (fruit bats), to amplification host (pig) and finally to humans, in the subsequent outbreaks no amplification host was needed. In the Bangladesh and India outbreaks, consumption of fresh date palm sap contaminated with fruit bat urine or saliva containing NiV was the cause of the outbreak **(figure 2)**. There was also person to person transmission including a hospital setting in India where 75 % of cases occurred among hospital staff or visitors.[1,2,8] Nipah cases tend to occur in a cluster or as an outbreak, although 18 % of cases in Bangladesh were isolated.[1]

Nipah virus has also been shown to infect dogs and cats, but it is not yet known whether it infects chickens.[5] No source was yet identified in the latest outbreak in Kerala even with extensive search. Wildlife studies have shown that the virus was widely distributed in at least 10 genera and 23 species of bats in a large part of Asia and Africa.[1]

CLINICAL FEATURES

The median incubation period of the disease was 9 days (range, 4-21 days).

Fever, headache, altered mental status, severe weakness,cough, respiratory difficulty, vomiting, and convulsions were the most common signs and symptoms.

In Malaysia and Singapore, respiratory symptoms were reported less frequently.[8] High prevalence of respiratory symptoms, like cough, could have contributed to the transmissibility of Nipah virus infection from person to person that was observed in Bangladesh and Siliguri but not in Malaysia.[8] In Siliguri, India, patients were normotensive at admission but became hypertensive before death[1].

Asymptomatic infection was reported in 8% of laboratory-confirmed

Table 1. Outbreaks

Year	Country	State or District	Cases	Deaths	Case fatality
1998-1999	Malaysia	Perak, Selangor, Negeri Sembilan states	265	105	40%
1999	Singapore	Singapore	11	1	9%
2001	India	Siliguri district, West Bengal	66	49	74%
2001	Bangladesh	Meherpur district	13	9	69%
2003	Bangladesh	Naogaon district	12	8	67%
2004	Bangladesh	Faridpur and Rajbari districts	67	50	75%
2005	Bangladesh	Tangail dstrict	12	11	92%
2007	Bangladesh	Thakurgaon, Naoga and Kushtia districts	18	9	50%
2007	India	Nadia district, West Bengal	5	5	100%
2008	Bangladesh	Manikgonj, Rajbari and Faridpur district	11	9	82%
2009	Bangladesh	Rajbari, Gaibandha, Rangpur and Nilphamari districts	4	1	25%
2010	Bangladesh	Faridpur, Rajbari, Gopalganj and Madaripur districts	16	14	88%
2011	Bangladesh	Lalmonirhat, Dinajpur, Comilla, Nilphamari and Rangpur districts	44	40	91%
2012	Bangladesh	JoypurhatRajshahi, Natore, Rajbari and Gopalganj districts	12	10	83%
2013	Bangladesh	Gaibandha, Jhinaidaha, Kurigram, Kushtia, Magura, Manikgonj, Mymenshingh, Naogaon, Natore, Nilphamari, Pabna, Rajbari and Rajshahi districts	24	21	87%
2014	Bangladesh	Manikganj, Magura, Faridpur, Rangpur, Shaariatpur, Kushtia, Rajshahi, Natore, Dinajpur, Chapai Nawabganj, Naogaon districts	18	9	50%
2015	Bangladesh	Nilphamari, Ponchoghor, Faridpur, Magura, Naugaon, Rajbari districts.	9	6	67%
2018*	India	Kozhikode, Malappuram districts, Kerala	19	17	89%
Total			626	374	60%

(2)(9)(10) *As of June 2, 2018

cases in Malaysia. Although cases of mild illness were identified, there was no evidence of asymptomatic Nipah virus infection in Bangladesh during the outbreaks.[8]

Among the people who died, death occurred after a median of 6 days (range, 2–36 days) after the onset of illness.[8] Most people who survive acute encephalitis make a full recoverywithout residual neurological consequences, but around 20% are left with persistent convulsions and personality changes.[2]

The case fatality rate of Nipah infection ranges from 0-100 in various outbreaks and average case fatality rate is 60% **(table 1)**.

Respiratory Infection

Nipah Virus is shed mainly by nasopharyngeal and tracheal secretions in the early phase of the illness and can be detected in bronchiolar epithelial cells. Histological changes in the lungs of NiV cases include pulmonary edema, necrotizing alveolitis with haemorrhage, and aspiration pneumonia. Nipah Virus infection of the respiratory epithelium results in the induction of inflammatory cytokines which result in the recruitment of immune cells and can progress to an Acute Respiratory Distress Syndrome (ARDS)-like disease.[7]

Prognostic Markers

Patients who died were more likely than survivors to have altered mental status, difficulty breathing, documented temperature >37.8 deg C, and abnormal (diminished or extensor) planter reflexes.[8] In Bangladesh, the higher case-fatality rate could be related to suboptimal health care.[8] But there is no explanation to the high case fatality rate in Kerala where the health care system is comparable to developed countries.

Diagnosis

Attempts to isolate virus and real time polymerase chain reaction (RT-PCR) from throat and nasal swabs, CSF, urine and blood should be performed in the early stages of disease. Antibody detection by ELISA (IgG & IgM) can be used later.[9]

Majority of patients will have normal glucose level and raised protein in CSF. Normal WBC count and normal chemical parameters in CSF do not rule out Nipah virus infection in patients with encephalitis.[8]

For isolation and propagation of NiV, biosafety level-4 (BSL-4) facilities are needed. However, primary virus isolation from suspected samples may be conducted under BSL3 conditions under stringent guidelines to ensure operator safety.

In India, recently established full-fledged BSL4 lab at National Institute of Virology (ICMR), Pune has got all the preparedness for diagnosis of NiV that takes care of any eventuality in the country.[1]

Differential Diagnosis

Differential diagnosis includes other Viral encephalitis including Japanese Encephalitis, Rabies, Herpex Simplex Encephalitis.[9]

Treatment

There are currently no antiviral drugs available to treat Nipah virus infection for either people or animals.[2] Ribavirin an antiviral drug has been used with conflicting results.[11] The therapeutic use of a neutralizing human monoclonal antibody, the m102.4, which recognizes the receptor binding domain of the NiV G glycoproteins, appeared promising in a ferret animal model.[2]

Prevention

There is no vaccine against Nipah virus.[2] In case an outbreak of Nipah is suspected quarantine of animal premises should be done. Care should be taken while handling sick animals and while taking care of ill people. The samples collected from people and animals suspected to be Nipah should be carried out by trained staff with standard precautions.[12]

END NOTE

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Conflict of Interest: None declared

Editor's Remarks: A recent outbreak of Nipah Virus occurred in North Kerala and was detected very diligently resulting in rapid epidemiological control. The details of the outbreak are compared with the previous series in this article. An article with contemporary interest.

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