

Review Article

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## Nipah Virus (Niv): 21<sup>st</sup> Century Novel Emerging Zoonotic Virus with Pandemic Potential

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### ABSTRACT

Nipah virus (NiV) is a paramyxovirus (genus Henipavirus) whose wildlife reservoir is bats of the genus *Pteropus*. The emergence of pandemic potential of NiV is due to the fact that one or more pigs were infected from bats, and the virus then spread efficiently from pig to pig, then from pigs to people. Characteristics of Nipah virus that increase its risk of becoming a global pandemic includes: humans are already susceptible; many strains are capable of limited person-to-person transmission; as an RNA virus, it has an exceptionally high rate of mutation and that if a human-adapted strain were to infect communities, high population densities and global interconnectedness would rapidly spread the NiV. The disease transmission from pigs acting as an intermediate host during Malaysian and Singapore outbreaks has changed in NiV outbreaks in India and Bangladesh, transmitting the disease directly from bats to human followed by human to human. It is apparent from the presence of the virus and antibodies in the fruit bats of the region and 13 years of continuous NiV outbreaks in humans in Bangladesh that it is the potential threat to the Indian subcontinent. The present century of NiV epidemic reported in Kozhikode and Malappuram district of Kerala last year. NiV haunts one more epidemic in the Ernakulam district of Kerala this year. Due to the lack of vaccines and effective antivirals, Nipah encephalitis poses a great threat to public health. This paper describes the potential of Nipah virus to cause an expanding pandemic threat, epidemiological patterns observed to date and suggests measures that should be taken for surveillance, provide early warning for veterinary and human public health authorities, prevention and infection control

#### Keywords

Nipah virus,  
*Pteropus*,  
NiV outbreaks,  
Pandemic threat

#### Article Info

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#### Epidemiology

First Nipah virus (NiV) outbreak in India occurred in Siliguri district of West Bengal in

2001, where direct transmission of the NiV virus from bats- to- human and human- to- human was reported in contrast to the role of pigs in the Malaysian NiV

outbreak. Nipah virus (NiV) derives its name from Kampung Sungai Nipah; a village in Malaysia from where it was first reported with acute encephalitis for those workers handling pigs in 1998-99. The mortality rate in the first 265 identified human cases was 40%. The recent epidemic in May 2018 in Kerala for the first time has killed over 17 people in 7 days with high case fatality and highlighted the importance of One Health approach.

The recently emerging zoonotic Nipah virus (NiV) comes under *Henipavirus* in the subfamily *Paramyxovirinae*. NiV is a single-stranded negative-sense RNA virus, pleomorphic ranging from 40 to 600 nm in diameter covered by a lipid bilayer envelope. The virus has three important internal proteins, Nucleocapsid proteins (N), Phosphoproteins (P) and large polymerase proteins (L).

The envelope has two types of spikes called Fusion proteins (F) and receptor-binding Glycoproteins (G). While fusion proteins are responsible for the fusion of the viral membrane with the host cell membrane enabling the release of viral contents into the cell, the glycoproteins generally bind to Ephrin B2 surface proteins. The Matrix proteins (M) responsible for the structural integrity and the budding of virus particles.

In nature, the virus is maintained in the bats-pigs cycle. Pigs act as intermediate as well as amplifier hosts. In addition to pigs, other animals like cats, dogs, goats, and horses have also been shown to be positive for anti-NiV antibodies, but their role in transmitting infection in humans has not been established.

Frugivorous (fruit-eating) bats of *Pteropus* genus are the main natural reservoir hosts of the virus. The bats shed the virus in their secretions and excretions. The humans acquire the infection by coming in contact with bat

excreta or saliva or consuming partially eaten or licked fruits by bats. Human to human spread has been recorded on many occasions. Once the virus is transmitted to pigs, they are highly infectious to other pigs and humans. The virus is seldom present in pig's urine. Outbreak investigations identified consumption of raw date palm sap as the primary route of transmission of Nipah virus from *Pteropus* bats to people (Iuby *et al.*, 2013)

The consumption of date palm sap (which is also known as toddy, kallu, tuak and tuba in other countries) is popular in a number of Southeast Asian countries, including Bangladesh, India, and Indonesia. Fruit bats also consume date palm sap and can contaminate it with saliva, urine, and faeces. This is the means by which NiV is thought to be transmitted from infected fruit bats to humans.

There is strong evidence that the emergence of bat-related viral infection communicable to humans and animals has been attributed to the loss of natural habitats of bats. As the flying fox habitat is destroyed by human activity, the bats get stressed and hungry, their immune system gets weaker, their virus load goes up, and a lot of virus spills out in their urine and saliva.

Deforestation and urbanization of some areas in Bangladesh have contributed to greater overlap between human and bat habitats. By promoting human-bat interactions, this overlap can increase the risk of "spillover" events, with NiV crossing the species barrier and infecting people.

### **Major outbreaks**

The present century of NiV epidemic reported in May 2018 which involved two northern districts of Kerala State, India resulted in 16

fatal cases. The epicenter of this outbreak was in Kozhikode district with a few cases recorded in the adjoining Malappuram district. Bats are the main reservoir hosts involved in transmitting NiV in Bangladesh and India, unlike Malaysia and Singapore where the infection was mediated through infected pigs.

The latest haunts of NiV reported in June 2019 which involved a 23-year-old student found positive in the Ernakulam districts of Kerala. The Kerala government said a list of 311 people who had interacted with the student had kept under medical observation.

### **Clinical prognosis**

#### **Humans**

The incubation period is usually 4 to 14 days long.

Patients will have a fever, headache, dizziness, and vomiting, abnormal doll's eye reflex, pupillary reflexes, vasomotor changes, myoclonic jerks, seizures which developed into a picture of severe encephalitis.

Neurological involvement is diverse and multifocal, including aseptic meningitis, diffuse encephalitis, and focal brainstem involvement.

A unique and interesting feature of NiV infection is the development of relapse and late-onset encephalitis, some of which occurred months or years after the acute illness.

Case fatality rates range from 40% to 100%.

In the Malaysian outbreak, Ribavirin was given orally or intravenously to patients with NiV encephalitis. The mortality rate was reduced up to 36% when the infected patients were treated with ribavirin

In the Singapore outbreak, acyclovir was given to all NiV encephalitis patients and only one death reported due to NiV infection,

But the role of acyclovir drug is still unclear.

In a recent in vivo study, Favipiravir viral RNA-dependent RNA polymerase inhibitor (T- 705) antiviral showed promising results when tested on NiV infected golden hamsters.

The experimental monoclonal antibody, m102.4, which targets the ephrin-B2 and ephrin-B3 receptor binding domain of the *Henipavirus* G envelope glycoprotein is a potent cross-reactive neutralizing antibody *in vitro*.

#### **Pigs: (Porcine respiratory and neurologic syndrome, Barking pig syndrome, One mile cough)**

Pigs manifest respiratory and neurologic symptoms and present with a typical barking cough which is recognized as a tell-tale sign of NiV infection in pigs.

Young pigs show epistaxis, dyspnea and characteristics coughing and older animals showed neurological signs such as ataxia, paresis, seizures, and muscle tremors.

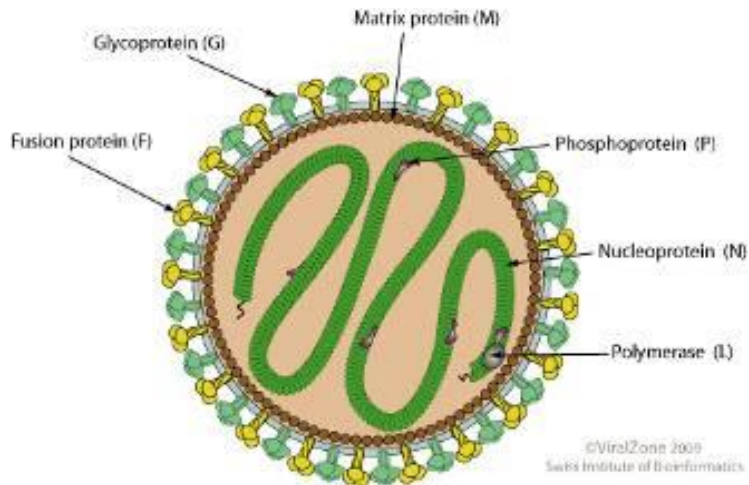
Naturally infected pigs developed tracheitis and bronchointerstitial pneumonia with hyperplasia of the airway epithelium.

A concurrent disease in pigs was characterized by a febrile respiratory illness, epistaxis, coughing in young and older pigs showed neurological signs.

Some progress in developing a protective vaccine called ALVAC Canarypox vectored Nipah F and G vaccine was quoted to be a promising vaccine for swine with a potential for humans as well.

## Epidemiology

Year	Place
1998	Kampung Sungai Nipah, Malaysia
2001	Siliguri, West Bengal, India
	Meherpur, Bangladesh
2007	Nadia, West Bengal, India
	Thakurgaon, Bangladesh
2014	Tinalon, Philippines
	Midtungok, Philippines
2018	Kozhikode, Kerala, India
	Malappuram, Kerala, India
2019	Ernakulam, Kerala, India



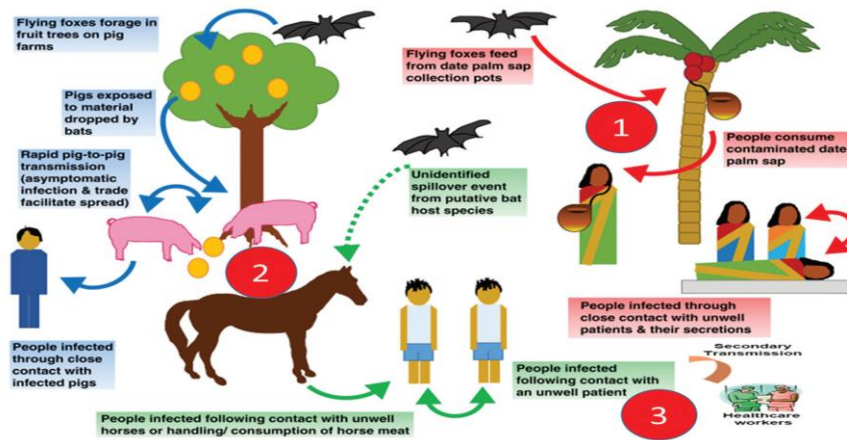
## *Pteropus* bat Natural reservoir: Nipah virus



### Transmission of NiV: Bats to Human via consumption of raw date palm sap.

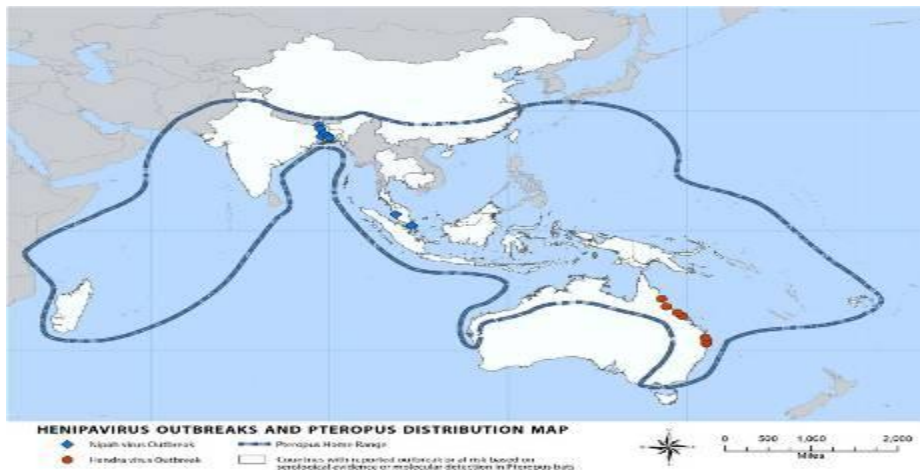


Schematic representation of three modes of Nipah virus spread: (1) bat- to- human, (2) animal- to- human, and (3) human- tohuman (including nosocomial)



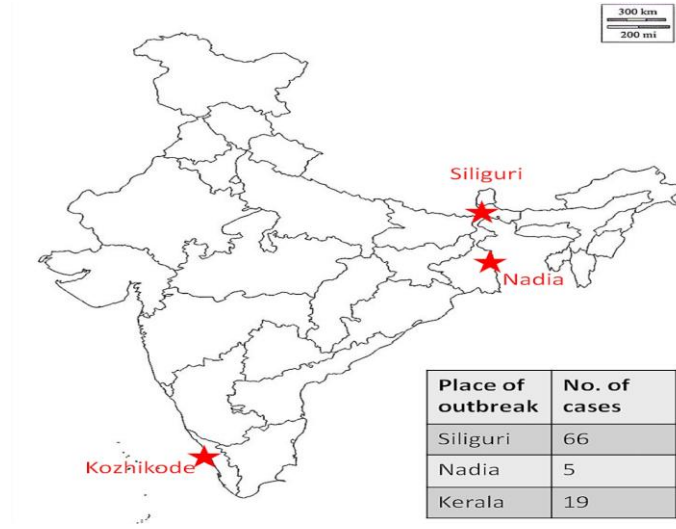
(Chattu *et al.*, 2018)

Map of *Henipavirus* outbreaks and distribution of *Pteropus* bats. Adapted from Nipah virus distribution map, Centers for Disease Control and Prevention ([www.cdc.gov/vhf/nipah/outbreaks/distribution-map.html](http://www.cdc.gov/vhf/nipah/outbreaks/distribution-map.html)).





### NiV Outbreaks in India



(Soneja *et al.*, 2019)

### Usage of PPE while working



Candidate vaccines using a vesicular stomatitis virus vector are the most advanced, having demonstrated protection in hamsters, ferrets, and African green monkeys.

A recombinant subunit vaccine formulation protects against the lethal NiV challenge in cats.

#### Diagnosis

The virus can be isolated from kidneys, CSF and other body tissues including liver.

ELISA

RT-PCR

Sequence analysis

Immunofluorescent tests

Virus neutralization tests

Ferrets have been used as a laboratory model for Nipah virus infection and pathogenesis.

## Prevention

### Biosafety Issues of Nipah Virus

For those who have to work in the field or on farms where Nipah infection is suspected, personal protection, such as masks, goggles, gloves, gowns, and boots, is advocated together with hand-washing and disinfection of equipment.

Strict quarantine procedures and the slaughter of all swine from affected facilities. Adherence to appropriate biosecurity and quarantine procedures within facilities, as with other contagious diseases, is of more importance in prevention of spreading of disease. An active surveillance and slaughter program of commercial pig population successfully eliminated the virus swine population.

With its high virulence, animal-to-human, and human-to-human spread, significant morbidity and mortality, resultant fear and panic and tremendous economic losses caused, it fulfills some criteria to be considered a potential agent for bioterrorism and is thus listed as Category C agent on a list of Bioterrorism Agents by Centers for Disease Control and Prevention (CDC) and any handling has to be done in BSL-4 facilities.

The Historical devastation of zoonotic diseases, the high case fatality rate of human Nipah infection and its recognition as a stage III zoonotic disease suggest that scientists, the public health community and policymakers should respect the pandemic risk of Nipah virus.

Mass education at all levels about the NiV, avoidance of contact with bats and pigs and their secretions and excreta and ensuring that these animals do not lick or contaminate

foods, drinks, and drinking water supplies. People should be advised not to consume any vegetables or fruits partially eaten by bats.

Drinking of date palm sap contaminated by bats should be discouraged.

Nipah virus emerged as a zoonotic virus, causing severe morbidity and mortality in both humans and animals and destroyed the pig-farming industries and it continues to cause human fatalities in recent outbreaks in Kerala also. As the reservoir host, *Pteropus* bat is widespread, and NiV has been found in bats in various countries, the potential for outbreaks to occur in new regions remains significant. The interest in NiV has remained limited to small research communities and affected countries but its control needs more than research and diagnostics.

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