

# Nipah: A Deadly Emerging Zoonosis

Emerging zoonotic diseases are posing an unprecedented risk to both human and animal health with their lingering adverse economic impacts, especially in developing countries. With the dawn of the 21<sup>st</sup> century, the pandemics of SARS-CoV and influenza A virus (H1N1) perplexed the global public health agencies and created a public health emergency situation worldwide. In sequence, the epidemics of the Ebola virus in West Africa, the Zika outbreak of Brazil, and the MERS-CoV outbreak of Saudi Arabia, baffled the public health agencies about what is coming next to tackle. More recently, the outbreak of Nipah virus in the Kerala state of India, which claimed 17 lives out of 19 cases, again highlights the potential of deadly strike by these zoonotic pathogens. However, the much appreciated efforts by the Kerala healthcare system successfully contained the Nipah outbreak by rapid response through proper tracking and exchange of information in real time among various public health experts. The lessons from this Nipah outbreak firmly advocate the concept of the One Health approach for tackling these deadly pathogens.

Zoonoses are diseases or infections that are naturally transmissible from vertebrate animals to humans and vice versa. Of the total identified 1415 species of infectious organisms known to be pathogenic to humans, zoonotic agents constitute 868 (61%) species<sup>1</sup>.

Humans, animals and microbes have co-existed for millennia and shared, at times, many deadly plagues. However, unsustainable anthropogenic activities during the last few decades have been reported to be linked with many of the emerging and re-emerging infectious diseases and in many scenarios these factors propelled the momentum of small outbreaks to the status of large epidemics and pandemics. The main factors responsible for these emerging epidemic and pandemic threats include rapid globalisation, international travel, extensive commercial trade, changes in land use patterns, intensive farming practices, change in human demography and behaviour patterns, change in food habits, climate change leading to natural disasters; and breakdown of public health measures<sup>2</sup>.

The emerging infectious diseases are those that have recently increased in incidence, geographic range, or host range. It has been estimated that of a total of 175 diseases considered to be emerging, 132 (75%) are zoonotic in origin<sup>1</sup>. Many of these emerging zoonoses are highly infectious with significant mortality rates (e.g., severe acute respiratory syndrome coronavirus (SARS-CoV), influenza A virus (H1N1) pdm09, Ebola, Crimean-Congo haemorrhagic fever, Middle-East respiratory syndrome coronavirus (MERS-CoV), Nipah etc.). The recent Nipah outbreak in the Kerala state of India with a case fatality rate of 89.5% (17/19) again proved to be a lethal salvo from the Pandora's box of deadly zoonoses.

The Nipah virus is a single-stranded RNA virus belonging to the *Paramyxoviridae* family, which includes other important

viruses affecting humans (e.g., measles, mumps etc.) as well as animals (e.g., Rinderpest, Newcastle disease, etc.). Traditionally, the viruses of the *Paramyxoviridae* family are considered to have a narrow host range with low mortality rates<sup>3</sup>. The various ecological and anthropogenic factors have led to the emergence of two highly pathogenic novel paramyxoviruses; Hendra virus and Nipah virus. In 2002, the International Committee for Virus Taxonomy (ICTV) approved the establishment of the genus *Henipavirus* due to distinct genetic and molecular features<sup>4</sup>. The outbreaks of these emerging zoonoses could be attributed to the spillover of diverse and novel paramyxoviruses that circulate in wildlife reservoirs to other terrestrial mammals, including humans.

To date, three major outbreaks of Nipah virus have been reported with significant mortality rate and adverse economic impacts.

## Brief Description of Major Nipah Outbreaks

**1. Malaysian outbreak:** The first outbreak of Nipah was reported during 1998 in Malaysia, where the virus was isolated from a fatal human case in Sungai Nipah, Malaysia; therefore the virus has been named as Nipah<sup>5</sup>. The epidemiology of outbreak is correlated with the slash-and-burn of forest area of Borneo and Sumatra as well as the effect of El Nino, which eventually led to a mass exodus of fruit bats which later settled to orchid plantations near intensively-farmed piggery<sup>6</sup>. The rapid transportation of infected pigs to five states of Malaysia and Singapore resulted in 265 human cases with 105 deaths<sup>7</sup>. During March 1999, Nipah virus caused febrile illness in 11 abattoir workers (including one death) in Singapore following close contact with pigs imported from Malaysia. Finally, the outbreak had been contained by employing various public health measures including culling of more than 1 million pigs<sup>8</sup>.

**2. Outbreak in Bangladesh and India:** The second major outbreak of Nipah virus was observed during 2001 in the Meherpur area of Bangladesh, but it could not be investigated until 2003, when another cluster of febrile illnesses with neurologic features occurred in adjoining villages in the Naogaon district, resulting in 8 deaths<sup>9</sup>. At the same time the outbreak was also reported in Siliguri, India (adjoining area to Bangladesh). The primary route of bat-to-human transmission was linked to the consumption of contaminated date palm sap. In addition, nosocomial transmission of infection to healthcare workers was also reported during the outbreak<sup>10</sup>.

**3. Outbreak in Kerala, India:** The most recent Nipah outbreak was promptly reported with the diagnosis of 26-year-old Mohammed Sabith as an index case on 17th May, 2018 at Kozhikode, Kerala. As per records, Sabith contracted the virus from fruit bats and later the transmission of disease was observed from person to person and to healthcare workers, which claimed 17 lives out of 19 cases. However, the robust public health system of Kerala managed to contain the outbreak within a short period of 21 days with 17 casualties<sup>11</sup>.

## Reservoir Host and Transmission Cycle

**Reservoir Host for Nipah Virus:** The *Pteropid* fruit bats have been considered as the reservoir of Nipah virus. The bats can

harbour the viruses without any overt clinical signs and can directly or indirectly spill over to other animals (e.g., pigs during the Malaysian outbreak) or humans (e.g., bats – date palm sap – human during the Bangladesh outbreak).

Major pathways of virus spillover have been described in Figure 1.

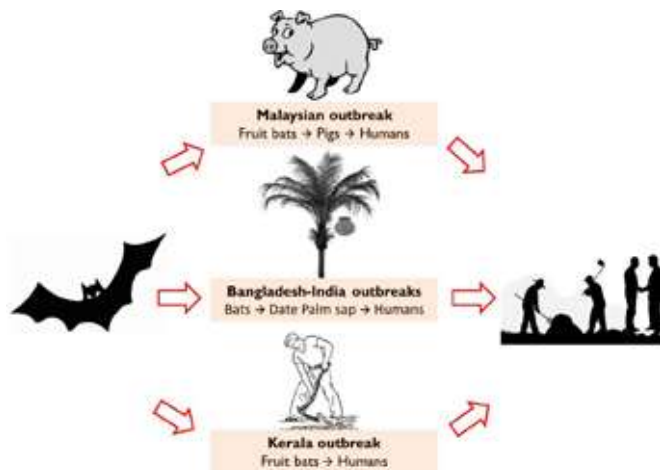


Figure 1: Transmission pathways for Nipah outbreaks

### Disease in Human and Animals

The virus shows broad species tropism due to the fact that it uses ephrinB2/B3 molecules as their entry receptors, which are highly conserved amongst all mammals<sup>2</sup>.

### Disease in Humans:

The incubation period of the disease varies from four days to two months (more than 90% of cases at two weeks or less)<sup>13</sup>. Generally, the patient shows unspecific symptoms including mild fever, vomiting, headache and dizziness.

A high level of acute respiratory distress syndrome was observed in the Bangladesh and Indian outbreaks (in 50–67% cases) as compared to the Malaysian outbreaks (14–29% of cases)<sup>14</sup>.

Later, the signs of severe encephalitis get prominent, which include:

- Reduced level of consciousness
- Prominent signs of brain-stem dysfunction
- Neurological involvement – diverse and multifocal

Moreover, in some of the cases, the development of relapse and late-onset encephalitis has been observed after months/years of acute illness. The high mortality rate is due to encephalitis or respiratory involvement.

### Disease in Animals:

Pigs and other domestic animals (horses, goats, sheep, cats and dogs) were found to be seropositive during the Malaysian outbreak<sup>15</sup>. It should be noted that animals may incubate the virus for up to 18 days and although asymptomatic, are infectious during this period.

The pigs remained infectious during the incubation period (4 to 14 days), whereas limited clinical information exists for other animal species. Most of the pigs remained asymptomatic, however, some cases developed acute febrile illness, laboured breathing, loud non-productive cough (barking pig syndrome and one-mile cough) and neurological

symptoms such as trembling, twitching and muscle spasms. The mortality among pigs was found to be low, except in young piglets<sup>16</sup>.

### Diagnosis of Nipah

Nipah infection in humans and animals can be confirmed by virus isolation, nucleic acid amplification tests and various serological tests.

- Isolation and propagation of virus requires BSL-4 facilities
- Serological tests: the most commonly used serologic assays are ELISAs
- Molecular diagnostic tests like real-time PCR can be used for virus detection

### Treatment Measures

The treatment of Nipah is largely supportive, and may include:

- Anticonvulsants
- Treatment of secondary infection
- Mechanical ventilation and rehabilitation
- Use of monoclonal antibodies in severe cases
- Empiric treatment with ribavirin

### Prevention and Control

Early detection of outbreak and installing preventive measures as soon as possible is very important to contain the outbreak. Medical and veterinary professionals, along with ecologists, should increase the awareness of the disease, particularly in reference to hosts and mode of transmission of the virus in the true spirit of a One Health approach.

### Preventive Strategies

#### a) At farm level

- Suitable interventions to prevent the infection either by direct contact with bats or by feeding contaminated fruits to farm animals
- Avoid the construction of animal shelters nearby fruit trees which could attract bats
- Reduce overcrowding in farms to avoid rapid spread of disease

#### b) Prevent food contamination

- Consumption of contaminated fruits and sap should be avoided
- Use of physical barriers to prevent access of bats to date palm sap

#### c) Prevent human-human spread

- Avoid close contacts with infected individuals
- Use of proper personal protective equipment (PPE)
- Proper hand hygiene
- Consult physician in suspected cases

### Conclusion

The way the Kerala healthcare system handled the recent Nipah virus outbreak of 2018 holds crucial lessons to tackle the emerging lethal zoonoses. Early detection of outbreak and installing preventive measures as soon as possible are crucial strategies, as treatment options for the disease are limited. The medical and veterinary professionals along with ecologists should come together in the spirit of a One Health approach for tackling these deadly pathogens. The inter-sectoral collaborations among national and global health agencies to share diagnostics and surveillance services for adopting rapid action to tackle these emerging infections is the need of the hour.



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