Original Article

# Nipah Virus: A Zoonotic Disease Causing Fatal Encephalitis

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## Abstract

The Review aims at giving the overview of the Diagnosis, treatment, transmission and past outbreaks of Nipah Virus (Henipavirus). Nipah virus is a Zoonotic virus that was emerged in the year 1990 which caused disease outbreaks in animals and Human beings. It was first emerged in Malaysia and Singapore in 1998-1999 which resulted in large outbreak of encephalitis with high amount of death in people and also respiratory disease in pigs which served as amplifying hosts. The most common symptoms of NiV infection in several species of mammals and also in people, are a severe systemic and often deadly neurologic or respiratory disease. The hosts of NiV are several species of pteropid fruit bats. NiV has previously caused outbreaks in Bangladesh and India nearly annually since 2001, making NiV important transboundary biological threats. NiV animal models have been developed previously which have helped in facilliating an understanding of pathogenesis and guided the successful development of both active to passive Immunization. It has the capacity or ability to infect Human beings directly from natural reservoirs or from other various susceptible animals

**Keywords:** Antiviral, Transmission, Pteropid, Pathogenesis, Vaccine, Nipah.

## INTRODUCTION

Nipah Virus is a Bat borne paramyxovirus that is the prototypic members of the Genus Henipavirus. The Henipavirus was outbreak in the mid, 1990s, causing over from their natural bat hosts and causing serious disease outbreak in Humans and livestock [1, 2]. Nipah virus was first found in Malaysia and subsequent outbreaks have been occurred in Bangladesh and India [2, 3]. In total, there have been estimated 582 human instances of Nipah virus and of these 54% had been fatal [4, 5].

Their vast species of tropism and potential to motive deadly respiratory or neurological ailment in people and animals make them necessary transboundary organic threat [6, 7]

Recent experimental findings in animals have proven that a human monoclonal antibody concentrated on the viral G glycoprotein is an advantageous postexposure remedy in opposition to Nipah virus infection. [8, 9]

In addition, a subunit vaccine based on the G glycoprotein of Nipah virus affords safety in opposition to Nipah virus challenge. The vaccine has been developed for use in horses and in the first safety vaccine in opposition to the Biosafety degree four (BSL-4) agent to be licensed and commercially deployed. [20, 38]

Together, these advantages offer achievable techniques to tackle Nipah virus contamination of farm animals and person-to-person transmission was reported during that outbreak. [18] The first time Nipah virus was discovered in the year 1999 following an outbreak of disease in pigs and people in Malaysia and Singapore. This outbreak resulted in nearly 300 human cases and more than 100 deaths, and that caused strong economical impact as more than 1 million pigs were killed to help in controlling the outbreak. [22]

### Spreading of the Virus across the World

There have been no other known outbreaks of NiV in Malaysia and Singapore since 1999, outbreaks have recorded after that in some parts of Asia since then in the countries such as Bangladeh and India. The Virus has been shown to spread from person to person in these outbreaks which raises the concerns that the potential for NiV is to cause a Global Pandemic in the upcoming near future. [28]

The Fruit bats that are infected can spread the disease to people or other animals, such as pigs. People can become infected if they are in close contact with an infected animal. [27] The disease can also spread through coming in contact of body fluids of the infected animals. Once if it spreads in people then the chances of it spreading from person to person are also high. [30]

- Nipah virus (NiV) can spread to people from:
- Direct contact with infected animals, such as bats or pigs, or their body fluids (such as blood, urine or saliva)
- By consuming food products that are contaminated by body fluids of infected animals such as date palm sap or other such fruits

- By coming in close contact with a person which is infected with NiV or their body fluids [30]

In the first outbreak of NiV, people were infected by coming in close contact with infected pigs. The NiV strain which was appeared in that outbreak was initially transmitted from Bats to Pigs, it was very subsequent within pig populations. [27] It then spreaded in the people who were working in close contact with the pigs which were infected. The people working in close contact with the infected pigs started falling ill.

However, person-to-person spread is reported regularly in countries such as Bangladesh and India. This is most commonly seen spreading in the families and caregivers of Healthcare workers and in Healthcare settings. [16]

Transmission also occurs from exposure to food products which are likely to be in contamination by infected animals. The Infection can also be seen spreading due to the consumption of raw date palm sap or fruit which is contaminated with saliva or urine from infected bats. [20]
Some cases of NiV infection have also been reported amongst the people who climb trees where bats often roost. [15]

### Signs and Symptoms

Infection with Nipah virus (NiV) can cause mild to svere disease, including swelling of the brain (encephalitis) and gradually after some period of time it can cause death if not taken proper care. [24]
Symptoms appear typically in 4-14 days after coming in exposure with the virus. The disease in initial stage generally includes signs of respiratory illness, which includes cough, sore throat and difficulty in breathing. [29] After the initial phase, it leads to the phase of brain swelling which is also known as Encephalitis, in this phase the symptoms include disorientation, mental confusion and also drowsiness which then progresses rapidly to coma within 24-48 hours. [30]

### Symptoms may include following:

- Fever
- Headache
- Cough
- Sore throat
- Difficulty breathing
- Vomiting

### Severe symptoms may follow, such as:

- Disorientation, drowsiness or mental confusion
- Seizures
- Coma
- Brain swelling (encephalitis)

Death may occurs in average 40-75% of cases. Long-term side effects in survivors of Nipah virus infection has noted various changes in personality such as persistant convulsions. [27]
Infection can lead to death even after months or years later the exposure to NiV virus.

## DIAGNOSIS

Nipah virus can be diagnosed through various means even during the illness and after recovery. There are various different tests which are available to diagnose the NiV infection.[29] Laboratory testing can be conducted during the early stages of illness by using RT-PCR ( Real time polymerase chain reaction) from throat and nasal swab cerebrospinal fluid, urine and blood. [33]
Later the testing for antibodies can be conducted using an enzyme-linkes immunosorbent assay (ELISA). [44]

- The early diagnosis can be a little bit challenging due to non-specific early symptoms for the illness. However, early detection and diagnosis are important to increase the chances of survival and recovery in the infected individuals, to stop the transmission of the disease in other people. [37]

## TREATMENT

Currently there are no such licensed treatments available for Nipah virus (NiV) infection. Treatment is limited to supportive care and rest and also proper hydration and treatment of the symptoms as per they occur. Although, there are various Immunotherapeutic treatments which are currently under development and evaluation for treatment of NiV infections. [20]

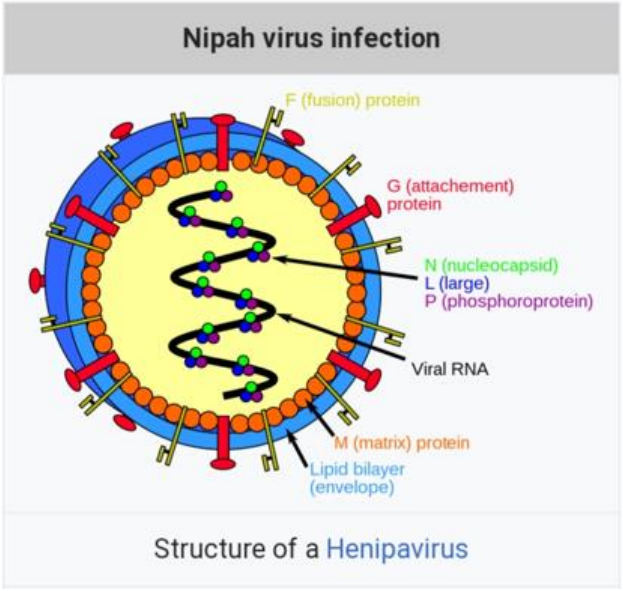


**Fig –** Structure of Henipah Virus

- One Monoclonal antibody, 102.4, which underwent successful phase 1 clinical trials and was applied on a compassionate basis. In addition, the antiviral treatment

In Malaysia, in the initial NiV outbreak, drug named ribavirin was used but its efficacy is unclear efficacy in people is unclear. [22, 23]

## PREVENTION

In areas where NiV outbreaks have occurred, people should:

- Practice handwashing regularly with soap and water
- Avoid contact with sick bats or pigs
- Avoid areas where bats are known to roost
- Avoid contact with the blood or body fluids of any person known to be infected with NiV [32]

As NiV can spread from person-to-person, standard infection control practices and proper barrier nursing techniques are important for able to prevent the infections that are caused from hospital where the patient is suspected NiV infection. [33] In future, there can also be risk of spreadin the NiV infection in near areas, such as regions where flying foxes live. [36]The flying foxes are a type of species of bats which are currently found in Cambodia, Madagascar, Indonesia, Philippines and Thailand. People that are visiting this places should also consider taking the same precautions as the people living in the areas where this viral infection is actively transmitted or the areas where the outbreaks have occurred. [39]

### Broader prevention steps also include:

- Increasing surveillance of animals and people in areas where NiV is known to exist.
- Increasing research on the ecology of Fruit bats to understand where they live and how they spread the virus to other animals and people.[38]
- Evaluation of novel technologies or methods to minimize spread of the virus within bat populations.[40]
- Improving the tools that are used to detect virus early in communities and livestocks.
- Making Protocols for healthcare settings on standard infection control practices to prevent person-to-person spread. [43,39]
- Raising awareness about the signs, symptoms and risk of NiV in populations which are at higher risks due to Geographical locations and various other factors. [25]

## PAST OUTBREAKS

- It was found that the name originated from Sungai Nipah, a village in the Malaysian Peninsula where pig farmers became ill with encaphilitis in 1999.[44]
- Three years later, a genetically distinct NiV independently emerged in India as well as in Bangladesh, where human NiV outbreak events have been reported nearly every year
- A putative NiV also caused an outbreak of disease in horses and people in the Philippines in 2014.[45]
- To date, there is no reported evidence of NiV outbreaks in humans emerging in any other country than Malaysia, Singapore, Bangladesh, India and Philippines

- On 19 May 2018, the Kerela Health Department reported three deaths due to Nipah virus infection in Chenagroth in Perambra block of Kozhikode district in South Indian State of Kerela. [45]
- As of 23 May 2018 and since the beginning of the outbreak, following more investigations and contact tracing, a total of 13 people have tested positive for NiV in Kozhikode and Malappuram districts.
- Of the 11 deaths reported so far, three have been reported from Malappuram district of Kerela and the others from Kozhikode district.
- This was the first time of NiV infection reported in Kerela state and third known NiV outbreak in India. Last outbreak was reported in 2007.
- A total of 276 cases were reported with 106 fatalitis (38%) in Malaysia.
- Case fatalitis in later outbreaks in India and Bangladesh were associated with significantly higher case fatality rates of 43 to 100%. [28,44]

## NATURAL HOST: FRUIT BATS

Fruit bats of the family Pteropodidae – particularly species belonging to the Pteropus genus- are the natural hosts for Nipah virus. Fruit bats don't seem to have any diseases. Henipaviruses are thought to have a similar geographic range to that.

The evidence of henipavirus infection in pterosaurs supported this theory. Bats from Australia, Bangladesh, Cambodia, China, India, Indonesia, Madagascar, Malaysia, Papua New Guinea, Thailand and Timor-Leste. [26]

## CONCLUSION

NiV has emerged as a deadly zoonotic disease. Bats the natural reservoirs of the virus, are wonderful at virus dissemination and human outbreaks proceed to be said usually. Due to the worldwide distribution of the bats, outbreaks in new areas are probably to occur. The high case of fatality charge and acute course of sickness make the infection hard to diagnose. This is further compounded by the lack of easily available low-cost diagnostic tests.[37] Effective treatment and prophylaxis are unavailable due to lack of research in human topics because the normal burden is small and the direction of contamination is acute. The recent outbreak in India highlights the opportunity of the manageable spillover in the areas the place presently regarded threat factors do not exist now.[50] A higher grasp of bat ecology and the motives of spillover events, the development of high quality cure and prophylaxis for people and animals and strengthening of the surveillance to prevent the outbreak is required to prevent the outbreak is required to curb the danger posed by means of NiV.[49]

## REFERENCES


1. Clayton BA, Wang LF nad Marsh GA (2013) Henipaviruses: an updated review focusing on the pteropid reservoir and features of transmission. Zoonoses and Public Health 60, 69-83. – PubMed
2. Marsh GA et al. (2012) Cedar virus: a novel henipavirus isolated from Australians bats. PLoS Pathogens 8, e1002836. – PMC – PubMed
3. WHO (2018) WHO | Nipah Virus Infection. World Health Organization: Available at http://www.who.int/csr/disease/nipah/en/ (Accessed 17 June 2018).
4. Luby SP (2013) The pandemic potential of Nipah virus. Antiviral Research 100, 38-43. – PubMed
5. Chatterjee P (2018) Nipah virus outbreak in India. The Lnacet 391, 2200.
6. Chua KB (2003) Nipah virus outbreak in Malaysia. Journal of clinical Virology 26, 265-275. – PubMed
7. Luby SP and Gurley ES (2012) Epidemiology of henipavirus disease in humans. Current Topics in Microbiology and Immunology 359, 25-40. – PubMed
8. Chua KB et al. (1999) Outbreak of Nipah virus infection among abattoir workers in Singapore. The Lnacet 354, 1253-1256. – PubMed
9. Paton NL et al. (2000) Case-control study of risk factors for human infection with a new zoonotic Paramyxovirus, Nipah virus infection among abattoir workers in Singapore. The Lancet 354, 1253-1256. –PubMed
10. Parashar UD et al. (2000) Case-control study of risk factors for human infection with a new zoonotic Paramyxovirus, Nipah virus, during a 1998-1999 outbreak of severe encephalitis in Malaysia. The Journal of Infectious Diseases 181, 1755-1759. –PubMed
11. Uppal PK (2006) Emergence of Nipah virus in Malaysia. Annals of the New York Academy of Sciences 916, 354-357. –PubMed
12. Field H et al. (2001) The natural history of Hendra and Nipah viruses. Microbes and Infection 3, 307-314.- PubMed
13. Rahman SA et al. (2010) Characterization of Nipah virus from naturally infected Pteropus vampyrus bats, Malaysia. Emerging Infectious Diseases 16, 1990-1993. – PMC –PubMed
14. Institute of Epidemiology, Disease Control and Research (IEDCR). Available at http://www.iedcr.org/ (Accessed 8 October 2018).
15. Yadav PD et al. (2012) Detection of Nipah virus RNA in fruit Bat (Pteropus giganteus) from India. The American Journal of Tropical Medicine and Hygine 87, 576-578. – PMC –PubMed
16. Rahman M and Chakraborty A (2012) Nipah virus outbreaks in Bangladesh: a deadly infectious disease. WHO South-East Asia Journal of Public Health 1.
17. Luby SP et al. (2006) Foodborne transmission of Nipah virus, Bangladesh. Emerging Infectious Diseases 12, 1888-1894. -PMC – PubMed
18. Salah Uddin Khan M et al. (2010) Use of infraded camera to understand bats access to date palm Sap: implications for preventing Nipah virus transmission. Eco Health, 7, 517-525. – PubMed
19. Chowdhury S et al. (2014) Sereological evidence of henipavirus exposure in cattle, goats, pigs in Bangladesh. PLoS Neglected Tropical Diseases 8, e3302. – PMC – PubMed
20. Gurley ES et al. (2007) Person-to-person transmission of Nipah virus in a Bangladeshi community. Emerging Infectious Diseases 13, 1031-1037. – PMC – PubMed
21. Homaira N et al. (2010) Nipah virus outbreak with person-to-person transmission in a district of Bangladesh, 2004. Emerging Infectious Diseases 11, 1594-1597. -PMC-PubMed
22. Harcourt BH et al. (2005) Genetic characterization of Nipah virus, Bangladesh, 2004. Emerging Infectious Diseases 49, 1743-1748. – PMC-PubMed
23. Luby SP et al. (2009) Transmission of human infection with Nipah virus. Clinical Infectious Diseases 49, 1743-1748. -PMC – PubMed
24. Hegde ST et al. (2016) Investigating rare risk factors for Nipah virus in Bangladesh: 2001-2012. Eco Health 13, 720-728. – PMC – PubMed

25. NIPAH Virus Disease Guidelines:: National Centre for Disease Control (NCDC). Available at http://www.ncdc.gov.in/index4.php?lang=1&level=0&linkid=113&lid=228 (Accessed 17 June 2018).
26. Chadha MS et al. (2006) Nipah virus-associated encephalitis outbreak, siliguri, India. Emerging Infectious Diseases 12, 235-240. – PMC-PubMed
27. Arankalle VA et al. (2011) Genomic characterization of Nipah virus, West Bengal, India. Emerging Infectious Diseases 17, 907-909. -PMC – PubMed
28. Ching PKG et al. (2015) Outbreak of henipa virus infection, Philippines, 2014. Emerging Infectious Diseases 21, 328-331. -PMC – PubMed
29. Abdullah S and Tan CT (2014) Henipavirus encephalitis. Handbook of Clinical Neurology 123, 663-670. – PubMed
30. Siva S, Chong H and Tan C (2009) Ten year clinical and sereological outcomes of Nipah virus Infection. Neurology Asia 14, 53-58.
31. Sejvar JJ et al. (2007) Long term neurological and functional outcome in Nipah virus infection. Annals of Neurology 62, 235-242. –PubMed
32. Hossain MJ et al. (2008) Clinical presentation of Nipah virus infection in Bangladesh. Clinical infections Diseases 46, 977-948. – PubMed
33. Goh KJ et al. (2000) Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. New England Journal of Medicine 342, 1229-1235. – PubMed
34. Harcourt BH et al. (2001) Molecular characterization of the polymerase gene and genomic termini of Nipah virus. Virology 287, 192-201. – PubMed
35. Lo MK et al. (2012) Distinct and overlapping roles of Nipah virus P gene products in modulating the human endothelial cell antiviral response. PLoS ONE 7, e47790. – PMC –PubMed
36. Wong KT et al. (2002) Nipah virus infection: pathology and pathogenesis of an emerging paramyxoviral zoonosis. The American Journal of Pathology 161, 2153-2167. – PMC –PubMed
37. Liebl DJ et al. (2003) Mrna expression of ephrins and Eph receptor tyrosine kinases in the neonatal and adult mouse central nervous system. Journal of Neuroscience Research 71, 7-22. – PubMed
38. Zimmer M et al. (2003) Ephb-ephrinB bi-directional endocytosis terminates adhesion allowing contact-mediated repulsion. Nature Cell Biology 5, 869-878. – PubMed
39. Bossart KN et al. (2008) Functional studies of host-specific ephrin-B ligands as Henipavirus receptors. Virology 372,357-371. – PubMed
40. Weingartl H et al. (2005) Invasion of the central system in a porcine host by Nipah virus. Journal of Virology 79, 7528-7534. – PMC – PubMed
41. Park M-S et al. (2003) Newcastle disease virus (NDV)- based assay demonstrates interferon-antagonist activity for the NDV V protein and the Nipah virus V, W, and C proteins. Journal of Virology 77, 1501-1511. – PMC –PubMed
42. Virtue ER, Marsh GA and Wang L-F (2011) Interferon signaling remains functional during henipavirus infection of human cell lines. Journal of Virology 85, 4031-4034. – PMC –PubMed
43. AbuBakar S et al. (2004) Isolation and molecular identification of Nipah virus from pigs. Emerging Infectious Diseases 10, 2228-2230. – PMC – PubMed
44. Hughes JM et al. (2007) Emerging viruses: coming in on a wrinkled wing and a prayer. Clinical Infectious Diseases 44, 711-717. – PMC – PubMed
45. Hume AJ et al. (2007) Emerging viruses: coming in on a wrinkled wing and a prayer. Clinical Infectious Diseases 44, 711-717. – PMC – PubMed
46. Guillanme V et al. (2004) Specific detection of Nipah virus using real time RT-PCR (TaqMan). Journal of Virology Methods 120, 299-237. – PubMed
47. Chang L-Y et al. (2006) Quantitative estimation of Nipah virus replication kinetics in vitro. Virology Journal 3, 47. -PMC- PubMed
48. Daniels P, Ksiazek T and Eaton BT (2001) Laboratory diagnosis of Nipah and Hendra virus infections. Microbes and Infection 3, 289-295. – PubMed
49. Crameri G et al. (2001) Establishment, immortalisation and charecterisation of pteropid bat cell lines. PLoS ONE 4, e8266. – PMC – PubMed
50. Mire CE et al. (2013) Single injection recombinant vescicular stomatitis virus vaccines protects ferrets against lethal Nipah virus disease. Virology Journal 10, 353.-PMC- PubMed