

A REVIEW: ON NIPAHVIRUS(NiV): EPIDEMIOLOGY, PATHOLOGY, TREATMENT

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Abstract

Nipah virus infection is a new disease found mainly in Southeast Asia. This virus is carried around by fruit bats from the Pteropus. Guess what? These bats seem to be just fine, but they can pass on this infection. The first time people heard about the Nipah virus was back in 1998-1999 when there were big outbreaks in Malaysia among pigs and people. It looks like the virus jumped from bats to pigs around 1996, and then it spread among the pigs. At first, nobody noticed it because the sickness didn't seem too serious and looked like other diseases pigs can get. Sadly, the Nipah virus moved from pigs to pig farmers & workers at slaughterhouses in Malaysia & Singapore, leading to severe sickness—often deadly—like encephalitis in over 250 people. Even some other animals like cats, dogs, and goats got sick too! To stop the outbreaks in Malaysia, more than a million pigs were killed. And guess what? In some high-risk areas, they even banned pig farming for good.

Keywords

Nipah virus, person-to-person transmission bats; Egyptian fruit bats; experimental infection; Nipah virus

Introduction

Nipah virus (NiV) is a really serious kind of Paramyxovirus. It's one of the ten important germs on the World Health Organization's list of diseases that need research—made back in 2018. This virus isn't just a problem for humans; it also makes animals sick, which hurts farmers' wallets a lot. The Pteropus fruit bat is thought to be the natural home for this sneaky virus.

Since it was found in Malaysia back in 1998, NiV has caused big health problems in Southeast Asia. Because of this, it's on the World Health Organization's list of urgent diseases that need more study and better solutions.

In India, things got tricky between 2001 and 2007 when the first outbreak happened in Siliguri, West Bengal. Another outbreak popped up later on in Nadia too! In 2018 there was a new case from Kerala's Kozhikode district connected to fruit bats once again. The death rate was super high there—91%.

Just recently—from September 12 to September 15, 2023—the Ministry of Health and Family Welfare in India announced six confirmed Nipah virus cases in Kozhikode district, including two deaths. The first case didn't have an obvious source of infection. But the others were family members & hospital contacts linked to the first case. By September 27, they traced 1288 contacts linked to these cases—including healthcare workers—who are now being closely watched for 21 days. Since September 12, 387 samples were tested; six came back positive for Nipah virus while the rest were negative! Thankfully though, since September 15, no new cases have shown up.

About pathogen

Nipah virus (NiV) is a paramyxovirus (Henipavirus genus, *Paramyxovirinae* subfamily, *Paramyxoviridae* family, order Mononegaviruses), an emerging virus that can cause severe respiratory illness and deadly encephalitis in human. This virus doesn't have any perfect shape.

It is to be 40 to 600 nm in diameter. This RNA virus is nonsegmented single-stranded and possesses a helical symmetry. There were 6 basic genes nucleocapsid, phosphoprotein, matrix, fusion glycoprotein, attachment glycoprotein, and long polymerase are present in the RNA genome as mentioned in fig.1. the virus has its own viral matrix protein and it's covered by the lipid membrane. [12012]

The virus was attached to the host cell with the help of the G protein via interaction with the mammalian protein family, ephrin b1, b2, or b3. The virus was liberated into the host cell with the help of the fusion protein. Nipah virus can survive 3 days in some fruit juices or mango fruit, and 7

days in artificial date palm sap.

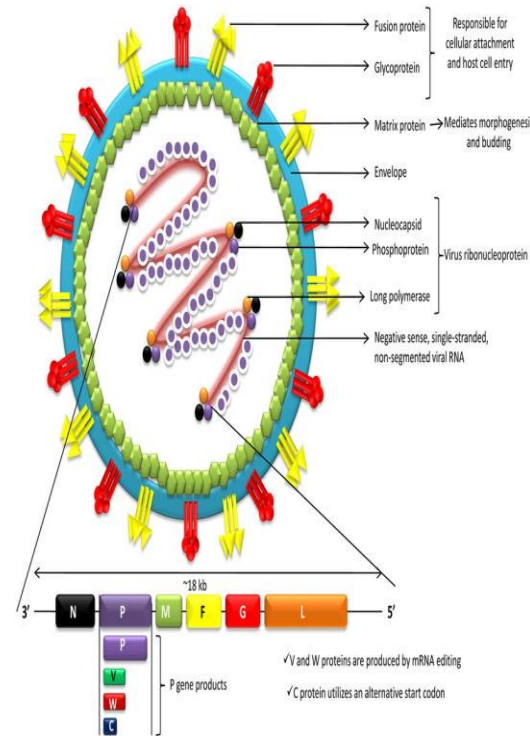


Figure 1. Nipah virus structure. Gene products. N, P, and L proteins constitute the viral ribonucleoprotein

Mode of transmission

The pathogen affects the animal first and then transmits to the human. The pathogen affects the bats. The affected bat is the main source of transmission of this pathogen. The affected bat species transmit it through the food and faces that come in contact with animals like horses and pigs this is the second phase of transmission which can transmit pathogens higher rate. Mostly due to the contact with this animal, the pathogen was transmitted to humans. It spreads throughout humans faster than animals through breathing and physical contact. As a reservoir host for several high-risk pathogens, including Nipah, rabies, and Mar bug viruses, bats serve. Such viruses are not associated with any remarkable pathological changes. The virus has

crossed its species barrier frequently to several other species including man through spilled-over transmission, but with limited transmission from person to person thereafter, from bats.[18]

In Bangladesh, during May-December 2004 the detailed interview of NiV infection survivors, medical practitioners, and caretakers-based research was conducted. And it shows that there were 2 types of transmission: animal-to-man and man-to-man. The spiritual strategies were looked for the correction of illness due to Some communities thought that NiV infections were due to supernatural or mystic powers The result of the investigation suggested spreading the awareness camp for collaborative prevention and control measures.[18]

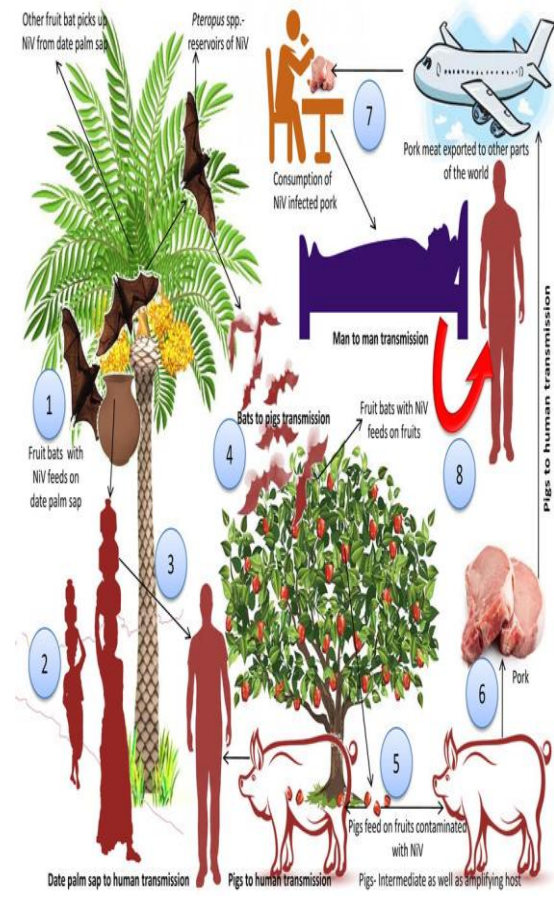


Figure 2. Transmission of the Nipah virus. 1. Fruit bats act as natural reservoirs of Nipah viruses. Fruit bats with NiV feed on date palm sap. Viruses can survive in solutions that are rich in sugar, viz., fruit pulp. 2. Virus

transmitted to humans through the consumption of date palm sap. 3. Fruit bats of Pteropus spp. NiV reservoirs visited such fruit trees and got the opportunity to naturally spill the drop-containing virus in the farm to contaminate the farm soil and fruits. 4. Pigs and other animals consume contaminated fruits. Pigs act as intermediate as well as amplifying host. Combination of close surroundings of fruiting trees, fruits-like date palm, fruit bats, pigs and human altogether form the basis of emergence and spread of new deadly zoonotic virus infection like

Nipah. 5. Pork meat infected with NiV are exported to other parts. 6. Consumption of infected pork can act as a source of infection to human. 7. Close contact with NiV affected human can lead to spread of NiV to other persons]

Saliva and Urine are the roots of virus transmission from human to human. So contaminated fruit or saps by the infected animal is also be source of transmission of the infection. [12010]

Also, some unconventional ways, such as sexual transmission through semen, are concerning. It is due to decreasing control over microorganisms that were previously more manageable, which is progressively surfacing in various regions of the world. In recent the gripping to look for its relation of the NiV to the semen. The Nipah virus RNA was reported to be present in the semen after the onset of symptoms of infection, while there was early elimination of the virus in the blood and urine [*nipa virus and semen*].

Histopathology

Samples collected during autopsies of patients who tested positive for the Nipah virus revealed significant damage to blood vessels, specifically showing signs of endothelial damage and vasculitis, particularly in arterioles, capillaries, and venules. The brain was the organ most severely affected, but other organs, including the lungs, heart, and kidneys, also showed involvement.

The vasculitis was characterized by necrosis (death of tissue) in the vessel walls, thrombosis (blood clots), and infiltration of inflammatory cells such as neutrophils and mononuclear cells. Additionally, the formation of syncytial cells (cells that have fused) was observed

in the endothelium of affected blood vessels in both the brain and lungs, as well as in Bowman's capsule of the glomerulus in the kidneys. Zones of microinfarction and ischemia were commonly found surrounding or adjacent to vasculitis blood vessels. In the brain, many neurons had eosinophilic cytoplasmic and nuclear viral inclusions, as is seen in association with other paramyxovirus infections [13].

Symptoms

The incubation period of the virus in humans is nearly 2 weeks to 2 months. The initial symptoms include high fever, headache, nausea, and vomiting. Also, abnormal eye reflexes, vasomotor abnormalities, seizures, and myoclonic jerks, which indicate brainstem dysfunction, are the symptoms shown by the NiV. Also, neurological symptoms, including aseptic mentality, localized brain tem involvement, and extensive encephalitis, were expressed by affected individuals.

A psychological symptom such as depression, personality issues, and difficulty speaking and focusing is shown by the patient. In some cases, patients may experience relapses and late-onset encephalitis that can last for months or even years after the illness [3]. Coma and death result from these diseases within a



few days. **Epidemiology and overall outbreak in the world**

Outbreak in India

In India, in 2001, the first case was found, and NiV independently emerged there; it was transmitted from human to human in the state of West Bengal. 66 patients were affected by NiV, and 45 patients died. Also, in District Hospital and later infected, 11 patients were hospitalized. Again in 2007, the minor breaks with 5 cases and 100% fatality. Over the border from the Nipah belt in Bangladesh. After a gap of 11 years in May 2018 again in Kozhikode and Malappuram in the state of Kerala, although a southern state on the west coast that is geographically isolated from that area was formerly affected and where date palm sap intake is not

widespread.

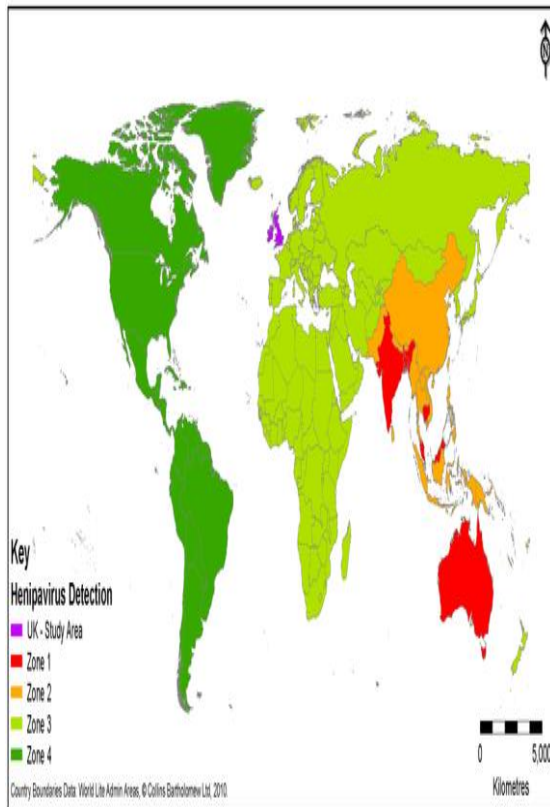


Figure 1. Identification of risk zones for Nipah virus. Zone 1: countries with outbreaks of nipa viruses or where Nipah virus have been isolated from fruit bats. Zone 2: country that borders a Zone 1 country and Pteropus fruit bats are distributed in the country. Zone 3 indicates all other countries in Eurasia, and Africa and Australasia, which includes countries that have detected antibodies to Nipah virus in fruit bats. Zone 4: North and South America, which share no bat species with the “Old World” and no Nipah virus have been isolated or antibodies detected. Doi: 10.1371/journal. Pone. 0027918.g003

In 2019, again in Ernakulam District of Kerala, a 21-year-old male student of engineering college Thodupuzha, Idukki District, Kerala, was admitted to a private hospital with a history of 10 days at Thrissur. And also had a health history of high-grade intermitted fever and

headache, which later involved gait imbalance and irritability. There were multiple small infarcts in the cerebellum, medulla oblongata, and pons in a magnetic resonance imaging (MRI) scan. Suspecting NiV infection, the sample of the urine, blood, CSF, and throat swab is sent to the

ICMR-National Institute of Virology, Pune on 3 June 2019. The NiV sequence detected was 99.70% identical to the sequence retrieved from all samples of the student against NiV positive. NiV outbreak declared by the Ministry of Health and Family Welfare, Government of India. Using the provided data of testing transferred toward other institutes for acknowledgment on 4 June 2019[2]

In Singapore and Malaysia

Febile encephalitis due to NiV has been reported in 246 patients between 1998 and 1999 and in farmed pigs during the same period as an epidemic with neurological as well as respiratory signs. Farmers associated with pig farming and abattoir workers were found to be in the high-risk group, and the human mortality was about 40%. NiV infection has not been reported directly in men or pigs in Indonesia, but exposure of Pteropus vampire bats to NiV has been reported. Thus, in Indonesia, there is every possibility of disease spreading from the carrier bats to pigs or men. The presence of anti-NiV antibodies in serum indicated an early exposure of bats to the virus. In India, a sero-surveillance study conducted over 41 pteropid fruit bats in the North Indian region showed seropositivity in twenty bats.

In Malaysia in 1999, human cases of Nipah viral encephalitis were initially confused with Japanese encephalitis or

Hendra-like viral encephalitis. However, the Ministry of Health confirmed that NiV was the causative agent of the infection in pigs and humans, and morbidity was higher in the Negri Sembilan region of Malaysia. The genome of the NiV was sequenced at the CDC, Atlanta, Georgia, USA. The Ministry of Health declared a total of 101 human deaths, and approximately 900,000 pigs were culled. Researchers confirmed that Nipah infections in pigs and men that occurred in peninsular Malaysia in 1998–1999 spilled over from Chiropteran bats (Yob et al. 2001). In Peninsular Malaysia, an epidemiological study was conducted for three years to assess the seroprevalence of anti-NiV antibodies and the presence of virus among *Pteropus vampyrus* and *P. hypomelanus* bats of different age groups and physiological status.

In Bangladesh, outbreaks of the Nipah virus were initially confirmed only by the presence of anti-NiV antibodies in serum samples. However, after 2004, researchers started genetic characterization of the Nipah virus by detecting viral nucleic acid. Till the year 2010, overall 9 outbreaks have been recorded in Bangladesh. The raw date palm was the source of infection in the outbreak recorded during the year 2011. Such a finding is further strengthened by the fact that raw date palm consumption was common in patients with fatal infection (65% mortality rate). Another outbreak in 2011 in a remote town named Hatibandha in the Lalmonirhat district, northern Bangladesh, reported 15 deaths due to NiV infection. Studies performed in pigs in Ghana suggested that serum antibodies against Henipahviruses, including Hendra and Nipah viruses, and

viral nucleic acid were also present in another.

Treatment

In 1998 and 1999, there were major outbreaks of the Nipah virus in Malaysia. During this time, doctors treated seriously ill patients with a medicine called ribavirin, which turned out to be quite effective. It reduced the death rate by about 36% compared to patients who didn't receive ribavirin or were treated before it was available. However, there are still no vaccines or approved treatments for the Nipah virus, which is a big concern.

Interestingly, both the Nipah and Hendra viruses have similar proteins that help them attach to host cells. This means they might use the same receptors on our cells to enter, indicating that there's still a lot to learn about these viruses.

Scientists at the NIAID Rocky Mountain Laboratories tested an experimental Nipah vaccine on three African green monkeys. After 29 days, they infected these monkeys and three unvaccinated control monkeys with the Nipah virus. Over 17 days, the control monkeys got sick within three to five days, and tests showed they were shedding the virus in their urine and mucus.

In contrast, the vaccinated monkeys stayed healthy and showed no signs of the virus in their samples. Remarkably, the vaccinated monkeys developed Nipah-specific antibodies just 14 days after vaccination, well before they were exposed to the virus. The research team had previously conducted a similar successful study with hamsters.

Participants in the UK have recently received doses of the ChAdOx1 NipahB vaccine at the University of Oxford. This trial is a crucial first step in developing a

vaccine against the Nipah virus, a serious illness mainly found in Southeast Asia, which can be fatal in up to 75% of cases. This milestone comes as the global health community observes the 25th anniversary of the first Nipah outbreaks. Since the virus was first identified in 1998, there have been no approved vaccines or treatments. Because of its high death rate and how it spreads, the Nipah virus is considered a major concern for potential pandemics. This vaccine trial is a key effort to find a way to prevent local outbreaks and prepare for future global health threats.

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has started an early-stage clinical trial for a new vaccine to prevent Nipah virus infection. This experimental vaccine is made by Moderna and developed with help from NIAID's Vaccine Research Center. It uses messenger RNA (mRNA) technology, which is also used in some COVID-19 vaccines. The Phase I study is taking place at the NIH Clinical Center in Bethesda, Maryland.

Nipah virus is a zoonotic disease, meaning it spreads between animals and humans, with fruit bats being the main carriers. The first outbreak occurred in 1998 in Malaysia and Singapore, leading to 265 cases and 105 deaths, which also harmed the local pig farming industry. Since then, there have been yearly outbreaks in Asia, especially in Bangladesh and India. The virus can cause symptoms ranging from mild to severe, quickly progressing to brain swelling, coma, or death. About 40% to 75% of people infected may die. While most infections come from animals, it can also spread between people. Right now,

there are no approved vaccines or treatments for Nipah virus infection..

“Nipah virus is a serious pandemic threat because it can mutate easily, affects many types of animals, can spread between people, and has a high death rate,” said Dr. Anthony S. Fauci, director of NIAID. “There is a strong need for a Nipah virus vaccine.”

Earlier this year, NIAID released a Pandemic Preparedness Plan to focus on studying viruses that could cause pandemics, prioritizing research on important pathogens like Nipah. This trial is the first to use this approach since the plan was published.

The experimental mRNA-1215 Nipah virus vaccine will be tested in a trial to check its safety, how well people tolerate it, and how effectively it generates an immune response in 40 healthy adults aged 18 to 60. Participants will be divided into four groups of 10. Each group will receive two doses of the vaccine through shoulder injections, spaced four or 12 weeks apart.

- Group one will receive two injections of 25 micrograms (mcg).

- Group two will get two 50-mcg injections.

- Group three will receive two 100-mcg injections.

- The dose for the fourth group will be decided based on results from the first three groups, and they will receive two injections 12 weeks apart.

Participants will be monitored through clinical observations and blood tests at various times during the study, and they will be followed by clinical staff for a year after their last vaccination.

This is the first-in-human trial of the ChAdOx1 NipahB vaccine, being developed by researchers at the

University of Oxford's Pandemic Sciences Institute.

Conclusion and future direction:

The Nipah virus (NiV) is a disease that mainly spreads from fruit bats to humans. It is a serious public health concern because it has a high death rate and can also spread from person to person. Understanding where the virus comes from shows that it is often linked to farming and environmental changes that increase contact between humans and bats. Symptoms of NiV can vary widely, from no symptoms at all to severe respiratory issues and brain inflammation. This highlights the importance of early detection and being prepared for public health emergencies. Right now, there are no specific antiviral treatments for Nipah virus infections. Care mainly focuses on relieving symptoms and providing intensive support for severe cases. Research is ongoing to find antiviral drugs, monoclonal antibodies, and vaccines, which are urgently needed to combat possible outbreaks. As we learn more about the virus and how it spreads, it's crucial to take a team-based approach that includes monitoring the virus, raising community awareness, and researching treatment options. Strengthening public health systems is vital to reduce the risks of diseases that jump from animals to humans and to ensure quick responses to new infectious threats.

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