

CD Alert

National Centre for Disease Control,
Directorate General of Health Services, Government of India

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Nipah Virus Disease

INTRODUCTION

Nipah virus disease (NVD) is an emerging zoonotic infectious disease caused by Nipah virus (NiV) belonging to the genus Henipavirus of the family Paramyxoviridae. It was first recognized in a large outbreak of 276 reported cases in Malaysia and Singapore from September 1998 to May 1999. Nipah cases in humans tend to occur in a cluster or as an outbreak especially in close contacts and care givers. CDC identifies it as a Category C bioterrorism agent and WHO identifies it as bio risk hazard group 4 pathogen. Currently there is no known treatment or vaccine available for either humans or animals. Active surveillance, meticulous contact tracing, isolation and quarantine of suspected and confirmed cases, preventive measures through effective IEC/IPC & Infection Control Practices are mainstay for outbreak management.

HISTORICAL BACKGROUND

Nipah virus was named after one of the affected Malaysian villages, Sungai Nipah. It mainly affects pigs and humans. When it first appeared in 1998 in Malaysia, it caused significant damage to the local swine industry as well as the loss of over 100 human lives. It was subsequently imported to Singapore via live pigs during March 1999 and led to 11 cases, with 1 death among abattoir workers. Dr Chua Kaw Bing from the University of Malaya, Malaysia, discovered the new virus

on 18 March 1999. Since its discovery in 1999, the outbreaks of NiV have been reported from five countries including India.

GLOBAL AND INDIAN SCENARIO

Since its discovery, there have been almost 726 cases of NVD and 427 deaths reported globally with cases mainly from the Southeast Asia region. Of these, 46% of cases have been reported from Bangladesh, Malaysia (36.5%), India (13.5%), Philippines (2.5%), and Singapore (1.5%). In Bangladesh, Nipah virus infection outbreaks are seasonal, corresponding with the harvesting season of date palm sap from November to March.

In India, initial NiV outbreaks in humans were reported from West Bengal in 2001 and 2007. More recently since 2018, cases have been reported from Kerala as localized outbreaks.

Current outbreak has occurred in the Kozhikode district of Kerala. Till date, a total of 6 cases have been reported out of which 6 were confirmed and 2 deaths were reported (1 suspect and 1 confirmed).

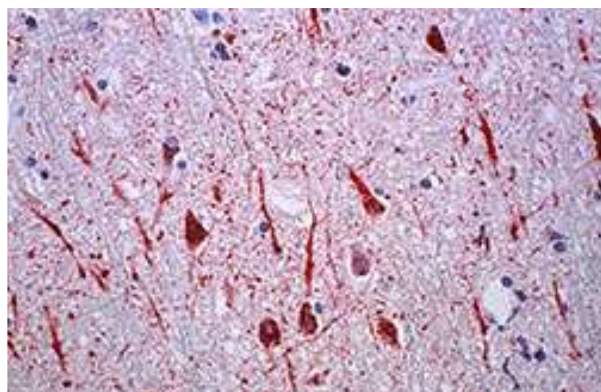
First death case was a 47-year-old male from Maruthonkara village of Kozhikode District who had visited Kuttiady towns for a wedding function developed symptoms around 22nd August 2023 and succumbed to death on 30th August.

Details of Nipah virus cases so far in India are shown in Table on page 2.

Duration	Cases	Deaths	CFR (%)	Remarks
Jan-Feb 2001	66	45	68	Investigations revealed possible Epidemiological linkages in 43 cases and person to person transmission in Siliguri, West Bengal
Jan-Apr 2007	5	5	100	Nadia District, West Bengal
Apr-May 2018	19	17	89.4	Kerala (Kozhikode and Malappuram)
2019	1	0	0	Kerala (Ernakulum)
2021	1	1	100	Kerala (Kozhikode)
2023* Current Outbreak	6	2	33.33	Kerala (Kozhikode)

EPIDEMIOLOGY

Agent: Nipah virus is a member of Paramyxoviridae family classified under genus Henipavirus. Henipaviruses are pleomorphic (varying in shape from spherical to filamentous) and vary in size from 40 to 1900 nm. NiV genome consists of non-segmented negative sense single-stranded RNA.



Nipah Virus Image Source: CDC

NiV viruses are classified into clades based on phylogenetic analysis of G gene (1809 bp) and N gene (1599 bp). Clades based on G gene classify NiV into NiV-Malaysia (NiV-MY- contains isolates from Malaysia and Cambodia) and NiV-Bangladesh (NiV-BD- includes isolates from Bangladesh and India). Based on N gene, some of the Thailand isolates classify as NiV-BD and some as NiV-MY. The genetic epidemiology of NiV is an evolving field.

Environmental Survival

NiV can survive from 3-7 days in fruit juices or simulated date palm sap at 22 °C under

laboratory conditions. In fruit bats urine, it has a half-life of 18. It can be completely inactivated by heating at 100° for more than 15 minutes. NiV is also sensitive to soaps, detergents, formalin and sodium hypochlorite.

Host Characteristics

The natural host of the virus is believed to be Pteropid fruit bats (flying foxes). Affected hosts like pigs, humans and possibly dogs have been reported with clinical illness caused by Nipah virus. Serologic evidence of Henipavirus has been found in several common farm animal cattle, goat, horse etc. and in various bat species. Human infections with NiV are rare, which suggests that the shedding of transmissible virus by bats is also a rare spillover event or occurs too infrequently to cause human infection.

Environmental Characteristics

The NiV infection closely follows the spillover of pathogen from fruit bats to intermediate hosts or human beings. In Malaysia, pig farms are proximal to fruit bearing trees, bats consume and contaminate fruits, often urinating on fallen ones, which are subsequently consumed by pigs, leading pathogen spillover. Humans are infected due to proximity to infected pigs. In Philippines, horses get infected by grazing on fruit trees infected by bats. The infection from horses to humans is generally by consumption of infected horse meat or direct contact with infected horses. In Bangladesh and India,

majority of the infections coincide with palm date sap collection times. These palm date sap collection sites are contaminated by fruit bat saliva or urine. These contaminated saps are consumed without any processing, causing NiV infection. In addition, human-to-human transmission of NiV is also documented and there is risk of spread of nosocomial infection in hospital setting.

Transmission and Reservoir

An intermediate animal host was not identified in outbreaks reported in India, suggesting bat-to-human and human-to-human transmissions. Efforts for source identification are important to understand the epidemiology of disease.

However, swine and equine populations have been identified as intermediate host in Malaysia and Philippines, respectively. The fruit bats belonging to the genus Pteropus are natural reservoir host of NiV. NiV transmission is complex, and the virus can be transmitted directly or through an intermediate host.

Direct transmission

a) Bat to Human

- Exposure to bodily fluids of bat such as blood, saliva, or excrement particularly through contaminated food.
- Contaminated date palm tree sap which is traditionally harvested

overnight has been identified as Source of direct NiV infection in Bangladesh.

b) Human to Human

- Through contact with contaminated tissues or body fluids (reported from India, Bangladesh, and Philippines)

Through an intermediate host

- Eating contaminated fruits (swine) or grazing on grass infected with bat droppings.

Transmission of NiV from intermediate host to humans is through direct exposure to contaminated body fluids/tissues. Severity of symptoms is directly related to amount of exposure.

Pathogenesis and Immune response

NiV infection is generally accepted to be caused through oral or nasal route in humans after getting exposed to infected food, body fluids, or tissues. NiV is frequently present in the tracheal and nasopharyngeal secretions and urine of the infected individuals during early phases of illness. This indicates that these mucosal sites are primary sites of NiV replication. The literature, however, is sparse on this.

Secondary sites of NiV infection are generally found as lesions spread throughout the vasculature, lung, and brain. This indicates that NiV infection spread by hematogenous route followed by inflammation of blood

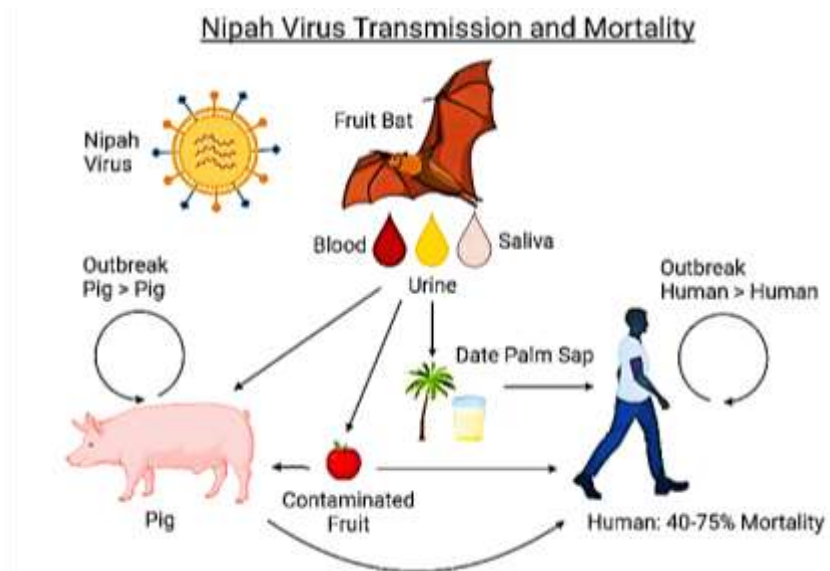


Image Source: Jenner Institute

vessels. Vasculitis is generally observed in small arteries, arterioles, and capillaries and may affect organs like brain, lung, heart, and kidney.

Incubation period: varies from 6-21 days for acute presentation, however, for 90% of the episodes, the incubation period will be less than 2 weeks.

Case Fatality Rate: 40-75% in Laboratory confirmed cases

Case Definitions: (Source IDSP 2019)

Suspect Case

Any person residing in a community of a confirmed Nipah virus (NiV) disease outbreak and has:

- Fever with new onset of altered mental status or seizure AND/OR
- Fever with headache AND/OR
- Fever with Cough or shortness of breath AND/OR
- Direct contact with a confirmed case

Probable Case

Any suspected person:

- who resided in the same village/ward, where suspect/confirmed case of Nipah were living during the outbreak period and who died before complete diagnostic specimens could be collected OR
- who came in direct contact with confirmed patient/(s) in a hospital setting during the outbreak period and/or who died before complete diagnostic specimens could be collected

Confirmed Case

A presumptive case with:

- Nipah virus RNA identified by PCR from respiratory secretions, urine, or cerebrospinal fluid OR
- Isolation of Nipah virus from respiratory secretions, urine or cerebrospinal fluid

Definition of a Contact:

A close contact is defined as a patient or a person who came in contact with a Nipah case (confirmed or probable cases) in at least one of the following ways.

- Was admitted simultaneously in a hospital ward/ shared room with a suspect/confirmed case of Nipah
- Has had direct close physical contact with the suspect/confirmed case of Nipah during the illness including during transportation.
- Has had direct close contact with the (deceased) suspect/confirmed case of Nipah at a funeral or during burial preparation rituals
- Has touched the blood and body fluids (saliva, urine, vomitus, etc) of a suspect/confirmed case of Nipah during their illness
- Has touched the clothes or linens of a suspect/ confirmed case of Nipah

These contacts need to be followed up for appearance of symptoms of NiV for the longest incubation period (21 days).

CLINICAL FEATURES

Clinical Presentation in Animals

The NiV is known to be naturally infecting cats, dogs, horses, humans, and pigs. The broad species tropism is also demonstrated by experimental studies showing NiV infection of hamster, guinea pigs, and ferrets.

NiV infection remains asymptomatic in fruit bats. In intermediate hosts, NiV infection presents as mild to severe disease in intermediate hosts (swine and equine).

In pigs, most of the infections are asymptomatic and vary by the age of the host. The incubation period in experimental studies was observed to be 5-7 days post infection.

The older pigs appear to be affected more than young pigs. The virus shows neural and

respiratory tropism in pigs. The symptoms may include neurological manifestations such as twitching, muscle spasm, and ataxic gait. In horses, NiV infection is presented as a severe respiratory disease with fever and tachycardia leading to a rapid deterioration of health. The incubation period is between 5-16 days. The fatality rate in horses is >75%.

Clinical Presentation in Humans

Acute Clinical Presentation. Most patients present with fever, headache, vomiting, and myalgia. During illness, symptoms progress to acute encephalitis with drowsiness, dizziness, altered sensorium areflexia, hypertension, and tachycardia. Patients with altered sensorium may also show associated symptoms such as segmental myoclonus (in NiV-MY infections), pinpoint pupils, and an abnormal doll's eye reflex. Altered sensorium is a poor prognosis in NiV-BD infection, with patients going into a coma resulting in the death of 70% of infected individuals.

Neurologic sequelae. 20% -30% of the recovered patients may have persistent neurological deficits. Neurological sequelae may include clinical depression, cognitive difficulties, quadriparesis, or nerve palsies.

Relapses or late-onset encephalitis. Relapses in patients recovering from acute encephalitis and late-onset encephalitis in asymptomatic individuals have also been reported. The time lapse between these events and initial infection has been reported between a few months up to four years.

LABORATORY DIAGNOSIS

Sample. For laboratory diagnosis of NiV, following samples may be required to be collected depending upon clinical presentation and day of illness.

1. Swab (Nasal and oropharyngeal)
2. Blood/Serum.
3. Urine sample
4. CSF
5. Tissue sample-brain, kidney, spleen etc

from postmortem cases should be collected with caution as they may have high viral load and may require BSL-4 containment for processing.

All samples must be collected with standard, contact and droplet precautions. Sample transport must be done according to internationally recognized. Samples should be transported to the laboratory only after prior consultation and in conditions explained by the reference testing laboratory.

As NiV is a highly contagious pathogen with no available treatment, only essential samples should be collected which are required for clinical management, and containment of samples should be ensured. Further, if any biochemistry or pathological test is required to be done, it should be done in completely closed automated systems ensuring the proper containment levels and biowaste disposal.

Laboratory Diagnosis Protocols

- In acute phase, NiV infection can be confirmed by detecting NiV specific RNA in the clinical samples using molecular methods (RT-PCR)
- In later phase of illness (10-14 days post the symptom onset), the NiV infection can be detected using serological methods (ELISA)

Selection of level of appropriate containment facility should be done after risk assessment based on type of activity planned.

Nipah Virus Diagnosis in Animals

The local veterinarian or animal husbandry departments should be alerted following suspected Nipah virus activity in humans or animals.

Necropsies should be conducted on recently dead and euthanized acutely diseased pigs and should always be conducted with all biosafety precautions in suitable containment facility.

TREATMENT

Currently there is no known treatment or vaccine available for either people or animals. Treatment is limited to intensive supportive care, including rest, hydration, and treatment of symptoms as they occur. Ribavirin, an antiviral may have a role in reducing mortality among patients with encephalitis caused by Nipah virus disease, but its efficacy is unclear. Immunotherapeutic treatments (monoclonal antibody therapies) are currently under development and evaluation for treatment of NiV infections. One such monoclonal antibody, m102.4, has completed phase 1 clinical trials and has been used on a compassionate use basis. *However, focus should be on preventive measures.*

High risk population:

- Those who are exposed to areas inhabited by fruit bats/ articles contaminated by secretions such as, unused wells, caves, fruit orchards, etc are likely to be at higher risk of infection.
- Persons with direct contact with sick pigs or their contaminated tissues.
- Persons in close contact of a suspect/ confirmed case of Nipah while taking care at home, during transportation, in the hospital or sharing a room.
- Persons in close contact with a Nipah virus affected deceased during burial or cremation rituals.
- Health care workers having direct contact with probable or confirmed cases without using standard precautionary measures.

PREVENTION AND CONTROL MEASURES

Risk assessment in field investigations – General Principles

One should follow/look for following:

Review situation prior to commencement of any examination of live or dead animals. Consider differential diagnoses based on species involved, clinical syndromes, previous diagnostic tests & epidemiological features of disease.

Inquire whether (about):

- ✓ The area has a history of zoonoses
- ✓ Presence of any assistants, farm workers or other people at the investigation site, and their likely proximity to potential sources of infection.
- ✓ Investigation site in relation to any environmental features, which may increase the spread of infection because of the investigation (such as proximity to water sources, dams, public thoroughfares and other farming establishments).
- **IEC:** Communicate clearly any concerns or advise precautions to assistants and other people at the investigation site. Manage the investigation site in accordance with the specified guidelines.
- Avoid contact with secretions, excretions and body fluids of potentially infected animals while conducting clinical examinations or collecting specimens.
- Wear suitable protective clothing, including examination gloves. It should be preferably disposable
- Keep the use of sharps to a minimum and be sure to dispose of scalpel blades and needles in an appropriately designed “sharps” container.
- Vector control measures is to be followed
- During examination and sampling of live animals, ensure adequate restraint to reduce the risk of accidental infection of personnel.
- Wash hands and equipment(s) after examinations or specimen collection. Disinfect protective clothing, refuse and biological waste and dispose it off safely.
- Where Nipah virus infection is suspected as a possible differential diagnosis, appropriate PPE should be worn by caregivers, treating physicians, healthcare professionals, and laboratory personnel while handling the patients or samples suspected of NiV infection.

Active case search for cases with acute febrile illness with respiratory or neurological symptoms and isolation of suspected patients and use of barrier nursing during care of these patients.

Health awareness regarding patient handling and patient care with special reference to possible contagiousness of the disease needs to be disseminated in the affected area immediately on reporting of the outbreak.

Community awareness through IEC regarding possible risk factors for the disease like consumption of raw date palm juice, close personal contact with patients, need to avoid fruit bats and contact with domestic animals especially pigs, dogs, cattle and other animals.

Measures of prevention should be taken in high-risk areas

- Wash hands with soap and water after coming in contact with a sick person or animal and before leaving pig farms.
- Avoid consuming raw date palm sap or toddy
- Consume only washed fruits
- Avoid consuming half eaten fruits from the ground
- Avoid entering abandoned wells
- Handling of dead bodies should be done in accordance with the govt. advisory

Public health educational messages should focus on:

• **Reducing the risk of bat-to-human transmission**

Decreasing bat access to date palm sap and other fresh food products with protective coverings (such as bamboo sap skirts) may be helpful. Freshly collected date palm juice should be boiled, fruits should be thoroughly washed and peeled before consumption.

• **Reducing the risk of animal-to-human transmission**

- Gloves and other protective clothing should be worn while handling sick animals or their tissues, and during slaughtering and culling procedures. In endemic areas, when establishing new pig farms, considerations should be given to presence of fruit bats in the area.

• **Reducing the risk of human-to-human transmission**

- Close unprotected physical contact with Nipah virus-infected people should be avoided.
- Regular hand washing
- Travelers to the areas affected should be aware of the possible risk of infection and follow any local guidance issued to minimize this risk

METHODS OF CONTROL

(A) Control of patients, contacts and the immediate environment

- ✓ Establishment of a dedicated isolation facility for confirmed /suspected cases.
- ✓ Standard contact, droplet, and airborne precautions to be emphasized during patient care and aerosol generating procedures to prevent human to human transmission while managing probable/suspected or confirmed cases of NiVD.
- ✓ Search for missed cases, dynamic contact tracing and quarantine of suspected should be carried out.
- ✓ Report to local health authority: case reporting should be mandatory where ever the disease occurs.
- ✓ Strengthening of existing disease surveillance systems, development & implementation of micro plan for contact surveillance (contact of positive cases), line listing of all the confirmed positive cases and multi-sectoral

coordination-response mechanisms through multidisciplinary teams including veterinary, environment and human health officials.

- ✓ **Concurrent disinfection:** Slaughter of infected pigs, horses or swine with burial or incineration of carcass under the supervision of health authority.
- ✓ **Quarantine:** Restrict movement of pigs and horses from infected farms to other areas.

(B) Other Considerations for Prevention and Control

- ✓ Since the original source of transmission by various species of fruit bats, it may be possible to reduce the transmission of Nipah to pigs by removing the fruit source from a farm, practicing import/export caution, and enhanced biosecurity planning.
- ✓ Enhanced hygiene and updated protocols on pig operations are essential.

Nipah as a biological weapon

Nipah virus is important as a potential biological weapon (targeted to animals, humans, or both) for the following reasons:

- Even a small outbreak in pigs could result in mass culling of affected

herds, thereby causing substantial economic loss to the industry or to the national economy.

- Nipah virus if is a zoonotic spillover it is a rare isolated event. However, when person to person transmission is high, virus has a chance to find right combination of mutations to become more transmissible which could propel it into realm of potential to be used as deadly weapon. Nipah virus can infect humans and the case- fatality rate may be as high as 75%.
- There is no effective treatment or vaccine for the disease in either pigs or humans.
- Little is known about Nipah virus, so an outbreak in animals or humans could cause substantial fear and social disruption.
- CDC identifies it as a Category C bioterrorism agent. Category C agents are emerging pathogens that could be engineered for mass dissemination in the future because of availability; ease of production and dissemination; potential for high morbidity and mortality rates and major health impact.

....about CD Alert

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