

A Brief Overview on Nipah Virus: A Bat Born Disease

Thumuganti Spandana¹, Rahela Lubna², Sravanthi Gandu³

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Abstract

Nipah virus is a newly formed Zoonosis. Which causes significant mortality in human & causes impact on public health. According to WHO for animal health Niv is a notifiable disease important to international trades. Niv belongs to the family **paramyxoviridae** and is related to Hendra virus. Nipah virus is a single- Negative (-ve) standard RNA and its size range is from (40 – 1900nm) the presence of reticular cytoplasmic inclusion near to the endoplasmic reticulum distinguish the virus from paramyxoviruses. Fruit bats are identified as the natural reservoir host. Electron micro graph shows Nipah virus particles (**purple**) & Infected Vero cell shows (**Brown**). It is started from the state of Malaysia, Singapore & later in India, Kerala etc. Niv spreads from direct contact with infected animals like bats, pigs & their body fluids like Blood, urine, saliva & food products contamination by body fluids of animals. Niv common symptoms are fever, cold, headache respiratory problems etc. PCR & ELISA are the methods for diagnosis purpose. There is no specific medication or vaccine for the treatment of Nipah virus. Currently several clinical trials on vaccines are going on including **mRNA – based vaccines**. There is a lack of vaccine & therapeutic to cure this disease. Supportive medication used for the treatment of symptoms are Acetaminophen or ibuprofen, Dimenhydrinate or ondansetron, Dextromethorphan, ipratropium, or salbutamol.

Keywords: Nipah virus, paramyxoviridae, PCR & ELISA, zoonotic virus, Encephalitis

INTRODUCTION

- As per WHO Nipah virus is a newly growing bat borne **zoonotic virus** which causes severe disease between (animals and species). Zoonotic means a transmission disease between species, Animals & Domestic animals (like horse, goat, sheep, cats, & Dogs).

It belongs to the genus **Hendra virus** & also causes outbreak.⁽¹⁾

- False color electron micro graph shows Nipah virus particles (**purple**) & Infected Vero cell shows (**Brown**).⁽²⁾
- Nipah name is raised from **kampung Sungai Nipah** a village in the Malaysian peninsula. There pig's farmer became ill with **Encephalitis**.⁽³⁾

Author's Affiliation: ¹Assistant Professor, ²Student, ³Associate Professor, Department of Pharmaceutical Analysis, Trinity College of Pharmaceutical Sciences (Chaitanya Deemed to be University), Peddapalli, Telangana, Hyderabad, India.

Corresponding Author: Thumuganti Spandhana, Assistant Professor, Department of Pharmaceutical Analysis, Trinity College of Pharmaceutical Sciences (Chaitanya Deemed to be University), Peddapalli, Telangana, Hyderabad, India.

E-mail: Spandhanat00@gmail.com

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- Niv spreads from direct contact with infected animals like bats, pigs & their body fluids like Blood, urine, saliva & food products contamination by body fluids of animals (such as palm sap or fruits.)⁽⁴⁾
- Due to Nipah virus infection spreads to Humans & animals which causes sever diseases to people which leads to death & also makes public health concern.⁽⁵⁾
- Niv causes sever neurological & respiratory illness in human. It is a Bio safety level 4. (B1SL4).⁽⁶⁾
- In some fruit juices or mango fruit Niv can survive for at least 3 days. In artificial date palm it can survive at least 7 days at some temp. In fruit bats urine Niv can survive for 18 hrs.⁽⁷⁾
- Nipah belongs to the family **paramyxoviridae** virus, which is closely related to Hendra virus. This virus is having negative sense single stranded non segmented RNA genome.⁽⁸⁾



Fig. 1: Nipah virus (source: provided by author)

History of Nipah virus.

- Since 1998 & 1999 Nipah virus was 1st discoverd & the disease outbreak was started from the pig's & people in **Malaysia & Singapore** Nearly 300 humans' cases were started and more than 100 people were died due to this outbreak.⁽⁹⁾
- There was a major economic impact on the country so, there were nearly 20 additional out breaks since 1999.⁽¹⁰⁾
- To control the outbreak nearly 1 million pigs were killed to control the outbreak.⁽⁹⁾
- In the year, 2001 these disease outbreak has occurred in the **Bangladesh** at the same year it also been identified in **India & Siliguri** and reported as second epidemic.⁽¹¹⁾
- From 2001- 2005 there were nearly five subsequent out breaks in **Bangladesh**. In this year virus spreads from human t human, bat to human & causes high risk in public health.⁽¹²⁾

- In 2007 Nipah virus outbreak was happened in Nadia district of west Bengal nearly death with a fatality case rate of 100%.⁽¹³⁾
- In 2008 there was 2 out breaks of (NIV) in **Bangladesh** within 2 weeks in Rajbari & Manikongi district.
- This results 10 cases with 9 deaths (90% fatality rate). It was due to raw date palm sap.⁽¹⁴⁾
- In Jan 2010 in faridapur & **Bangladesh**, we identified nearly 16 cases of patients & 14 patients were died due to the encephalitis cluster & 7 people effected with sporadic cases & 6 died including physician.⁽¹⁵⁾
- Outbreak of Nipah virus at Hati bandha, lalmonirhat, **Bangladesh** in 2011, 21 school children died due to (NIV) & these was recorded on 4 Feb 2011.⁽²⁾
- Between 2001 – 2013 there was an outbreak in **Bangladesh**. Due to the fruit bats (by drinking raw palm sap contaminated by bats). In 2013 fatality rate cases are 83%. In 2014 there was an outbreak due to close contact with horse or consumption of horse meat in Philippines.⁽¹⁶⁾
- In 2015 outbreak there were 11 cases & 8 were died due to (NIV) in **Bangladesh**. Later there was an increase in 1 case & 1 death in past 2 weeks.⁽¹⁷⁾
- In the year May 2018 in Kozhikode there were 23 NIV cases with nearly 21 deaths in the same year in **India** 18 cases were confirmed with 17

death's.⁽¹⁸⁾

- There was only one NIV case in 2019 with full recovery in Ernakulam district & Kochi in June. 12-year-old boy died due to Nipah virus on 5 Sep 2021 due large outbreak of NIV in Kozhikode.⁽¹⁹⁾

Recent outbreak of Nipah virus:

- In Kerala, Kozhikode district in Northern Kerala on 24 sep 2023 there were 6 confirmed cases with 2 deaths have been reported.⁽²⁰⁾
- From 12-15 Sep 2023 there were total 6 confirmed cases of (Niv) in laboratory. Including 2 deaths reported. This test conducted at the National Institute of virology in Pune and confirmed that the death of 49 years old man is due to Nipah virus in Kerala on 30 Aug.⁽²¹⁾
- On 27 Sep 2023 total confirmed cases were 1288. These identified patients' cases were under quarantine for 21 days & 4 cases were clinically stable.⁽²²⁾
- Government restricted the social distance & mandatory mask wearing in public places & also restricted public events in Kozhikode till 1 oct 2023. According to National Institute of virology (Pune) the virus in Kerala identified as **Indian Geno type 1**.⁽²³⁾
- In India from 15 Sep no new cases are identified. This is sixth outbreak of Nipah virus in India since 2001 said by WHO (**World Health Organization**).⁽²⁴⁾

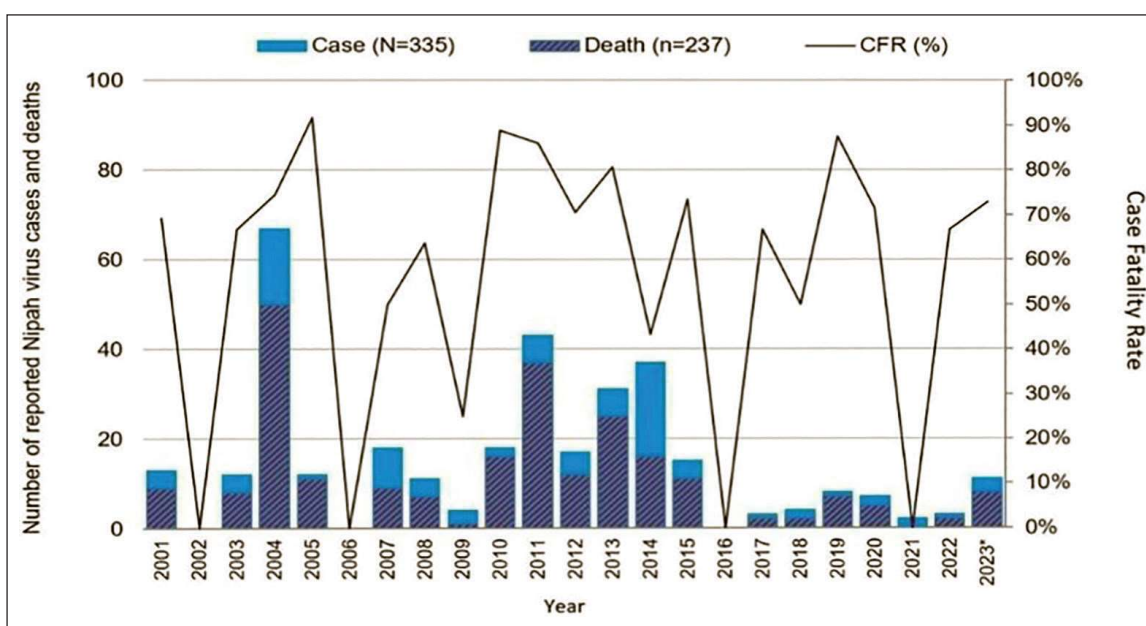


Fig. 2: Number of cases and death of Nipah virus (source: provided by author)



Fig 3: Percentage of Nipah Virus in India, Bangladesh & Malaysia (source: provided by author)

Structure of Nipah virus:

- It is a single - Negative (-ve) standard RNA
- These RNA Protein us made up of long polymerase, phosphoprotein & Nucleocapsid.
- Matrix protein surrounds the Nucleocapsid which is embedded spike like fusion protein.
- Glycoproteins are present on the lipid bilayer & they are in charge of cellular adhesion & helps in host cell entrance.
- Niv size range is from (40 – 1900nm) the presence of reticular cytoplasmic inclusion near to the endoplasmic reticulum distinguish the virus from paramyxoviruses.⁽²⁵⁾

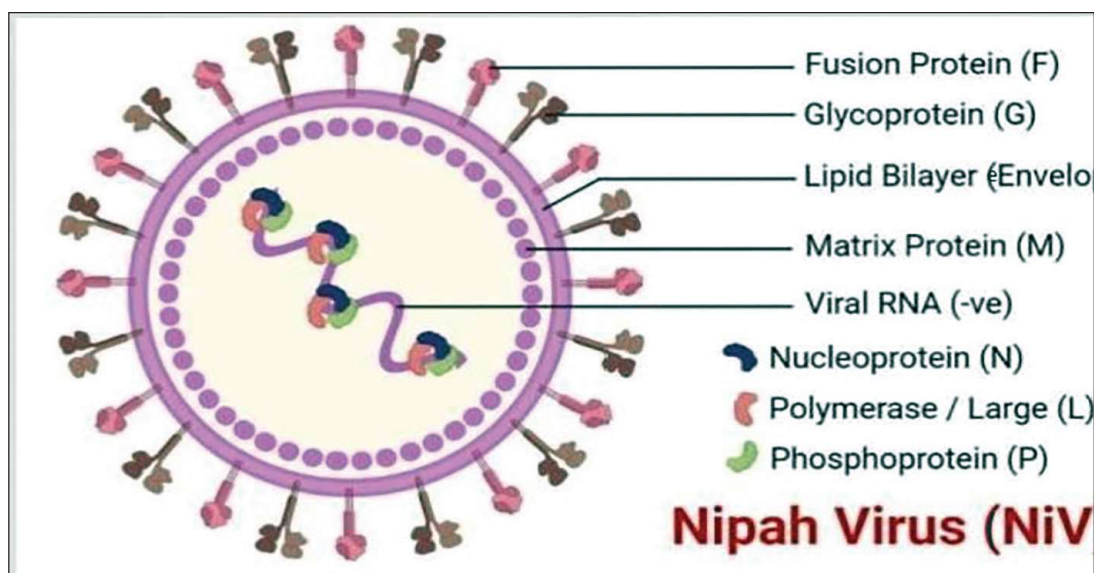


Fig. 4: Structure of NIV (source: provided by author)

Structure of Genome:

- A single standard RNA genome size is around 18.2kbp. It contains 6 structural proteins such as, Nucleoprotein, phosphoprotein, Matrix protein, Fusion protein, Attachment protein & RNA polymerase.
- These are coded as 3' N-P-M-F-G-L 5'
- They p gene also encode 3 non-structural RNA protein by editing (v & w protein) or alternated reading frame (c protein).⁽²⁶⁾

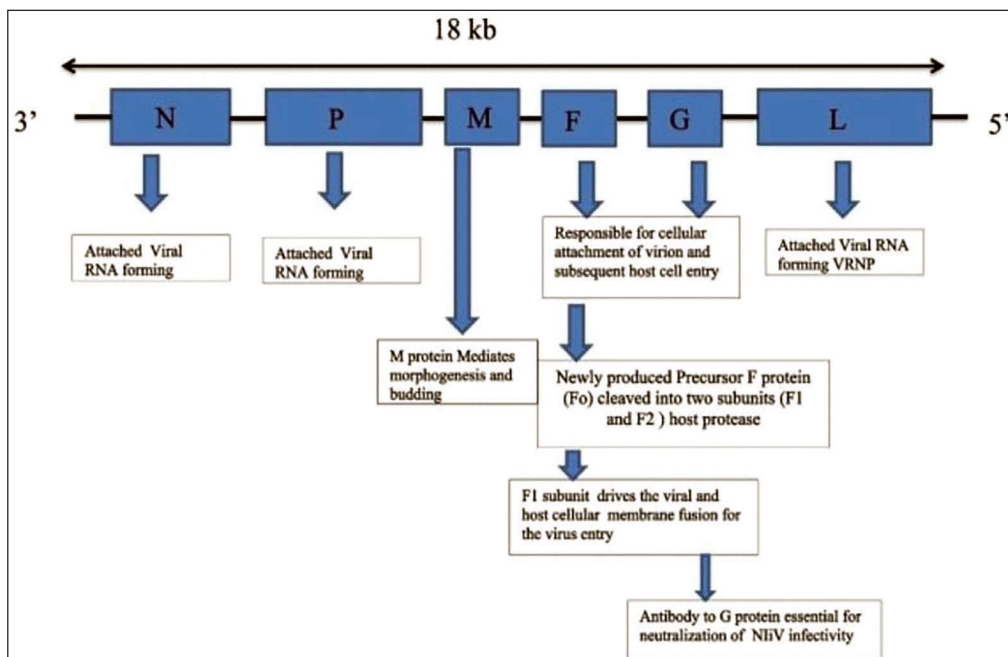


Fig. 5: Genome structure of Nipah virus (source: provided by author)

Pathogenesis

In the first stage Niv infection of virus is observed in the epithelial cells of the bronchioles⁽²⁷⁾. These virus antigens are present in both bronchi & alveoli (type 2 pneumocytes)⁽²⁸⁾. Inflammatory cytokines are induced due to infection in respiratory tract & recruit in cells of immune system & leads in development of disease of ADRS (Adverse drug reactions)⁽²⁶⁾ Infection in the air way epithelium leads to the activation of Inflammatory mediators like interleukin (1L) -1, 1L6, 1L8. Granulocytes colony stimulating factors etc.⁽²⁹⁾ The virus spreads into the endothelial cells of lungs in later stages of

disease & now virus spreads into the blood stream & spreads freely or bounds to the host leukocytes Which finally reaches to blood, spleen & kidney & causes organ failure⁽²⁸⁾. There are 2 distinct pathways to enter CNS 1 flows via. Hematogenous route & other flows via olfactory nerves⁽³⁰⁾. The infection in CNS damages the (BBB) Blood Brain Barrier & IL-1 β along with tumor necrosis (TNF)- α In CNS & starts development of neurological disorders⁽²⁸⁾. Inclusion bodies are present in case of infected CNS in man. Plaque is evident along with necrosis in both gray as well as white matter⁽²⁹⁾.

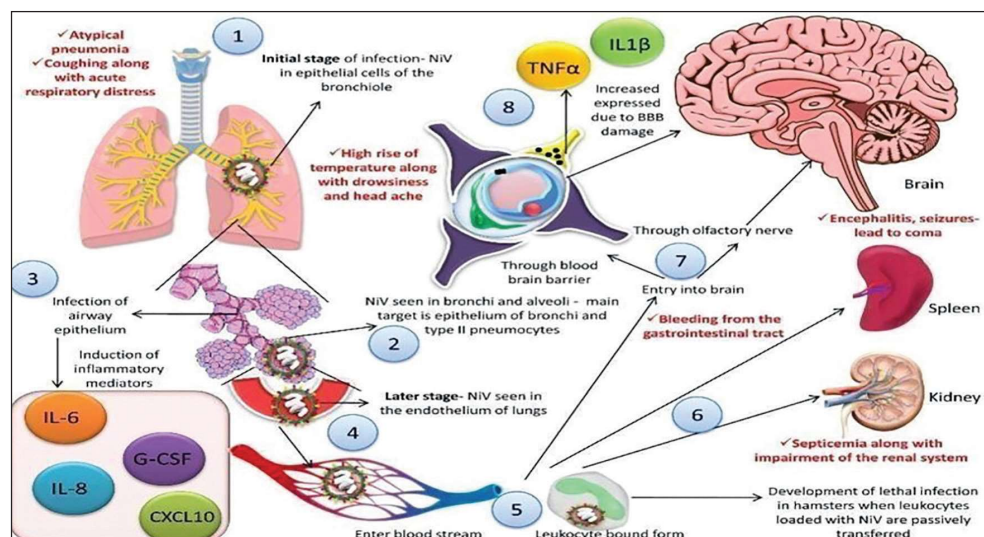


Fig. 6: Pathogenesis of Nipah virus (source: provided by author)

Replication of Nipah virus:

Nipah virus replication occurs in diff organs. It starts from the epithelium of the upper respiratory tract The virus reaches the trachea to lower extent Via the pharynx, lungs and the rest of the respiratory tract, then disseminates systemically, predominantly in the CNS via blood-brain barrier.

It also infects the microvascular endothelial cells of the CNS and results in multifocal encephalitis in human.⁽³¹⁾

Life Cycle of Nipah Virus:

Nipah virus attaches to the Ephrin B2/B3 receptor and enters the cell. The viral genome is released and it replicated and transcribed into viral messenger RNA, which are in turn translated into viral proteins N[nucleocapsid], P [phosphoprotein], M [matrix protein], G [glycoprotein G], F [glycoprotein F/ fusion protein], and L[polymerase]The new viral genome and proteins are assembled, encapsulated, and released from the cell. The colored labels highlight the molecular targets for the vaccines and anti-viral.⁽³²⁾

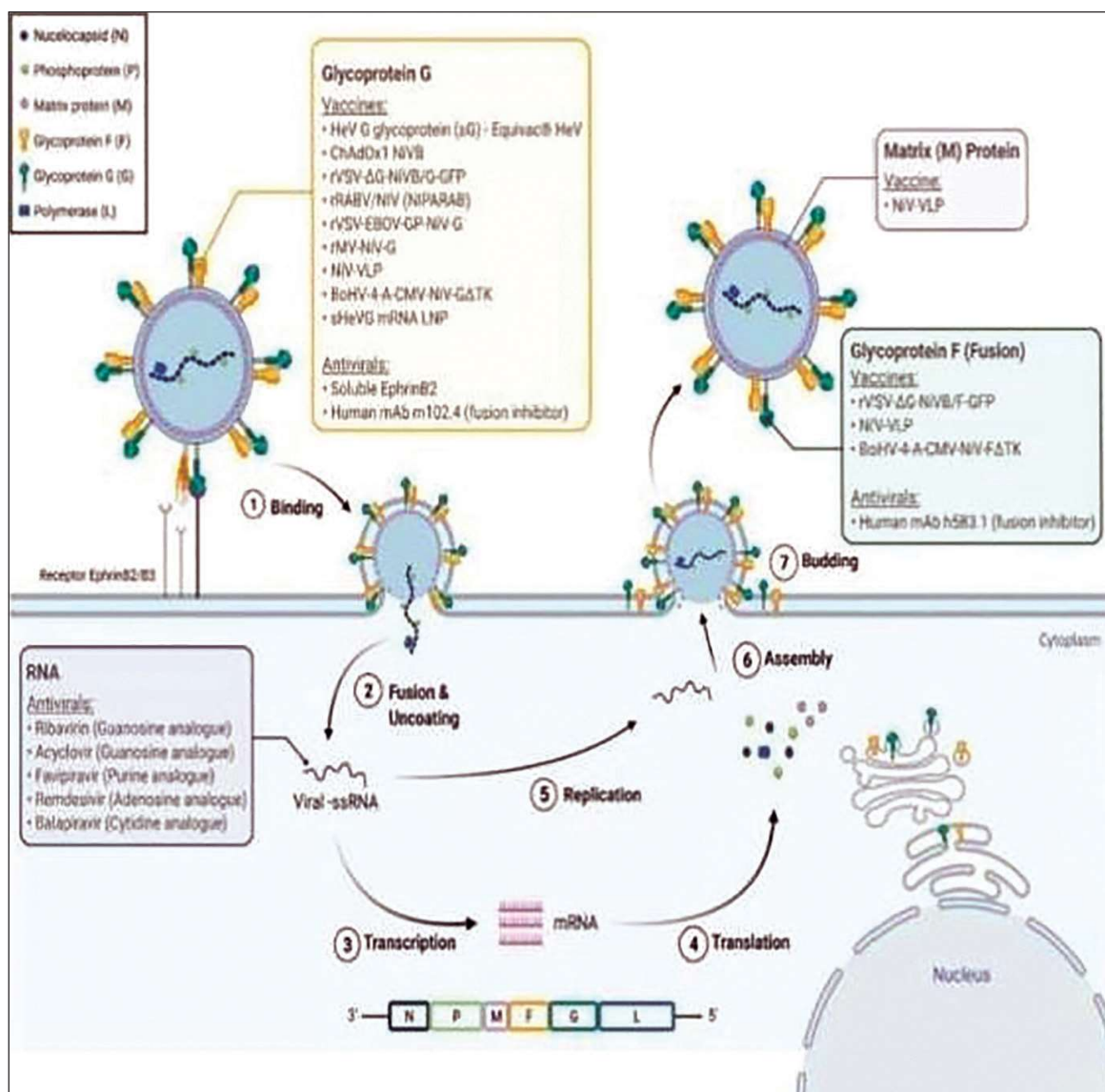


Fig. 7: Life Cycle of Nipah Virus (source: provided by author)

Transmission:

- The mode of transmission of Nipah virus is from the consumption of contaminated fruits

by infected animals & direct contact with infected animals like bats / pigs.

- Consuming the fruits / date palm sap contaminated with saliva or urine from infected fruit bats & it is the one of the most likely sources of spreading the infection.
- NIV spreads directly from human to human through close contact with infected people & there is secretion, exception such as (nasal, respiratory droplets, urine, blood etc.).⁽³³⁾
- Niv transmission occurs by contaminated food and contact with human body fluid. Risk factors are proximity viz; touching, feeding etc. Recently experimental studies with aerosolized Niv in Syrian hamster revealed that Niv droplets (aerosol exposure) might play a role in transmitting Niv during close contact.⁽³⁴⁾

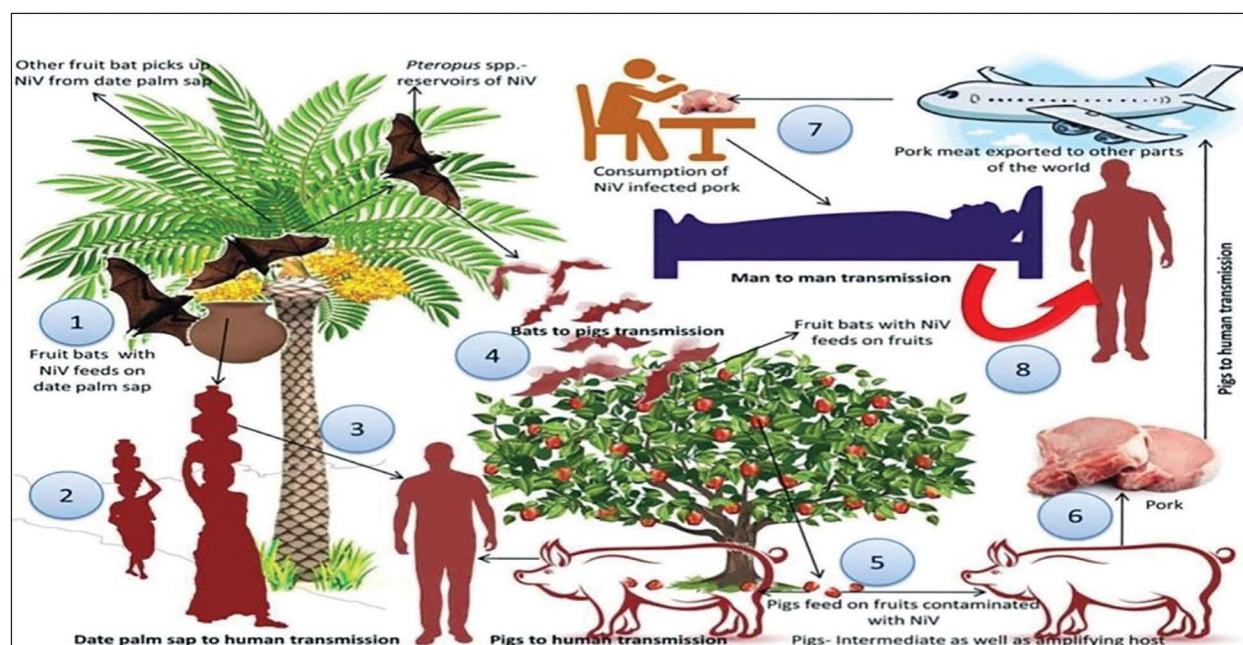


Fig. 8: Transmission of Nipah virus

From the above information.

Human to Human transmission

- Fruit bat with Niv feeds on the date palm sap.
- These date palms are collected & consumed
- by human which causes human to human transmission.
- It also spread from close contact with Niv infected people at home & also transmit from dead body of Nipah patients in hospital.

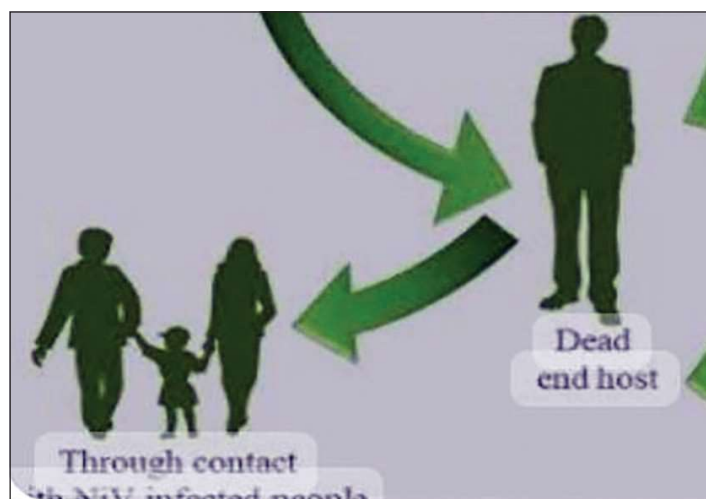


Fig. 9: Human to Human transmission (source: provided by author)

Animal to Animal transmission

- Fruit bats with Niv feeds on the fruit & if they are consumed by animals (like pig's) they get infected.
- It also spread from animal to animal from fluids.

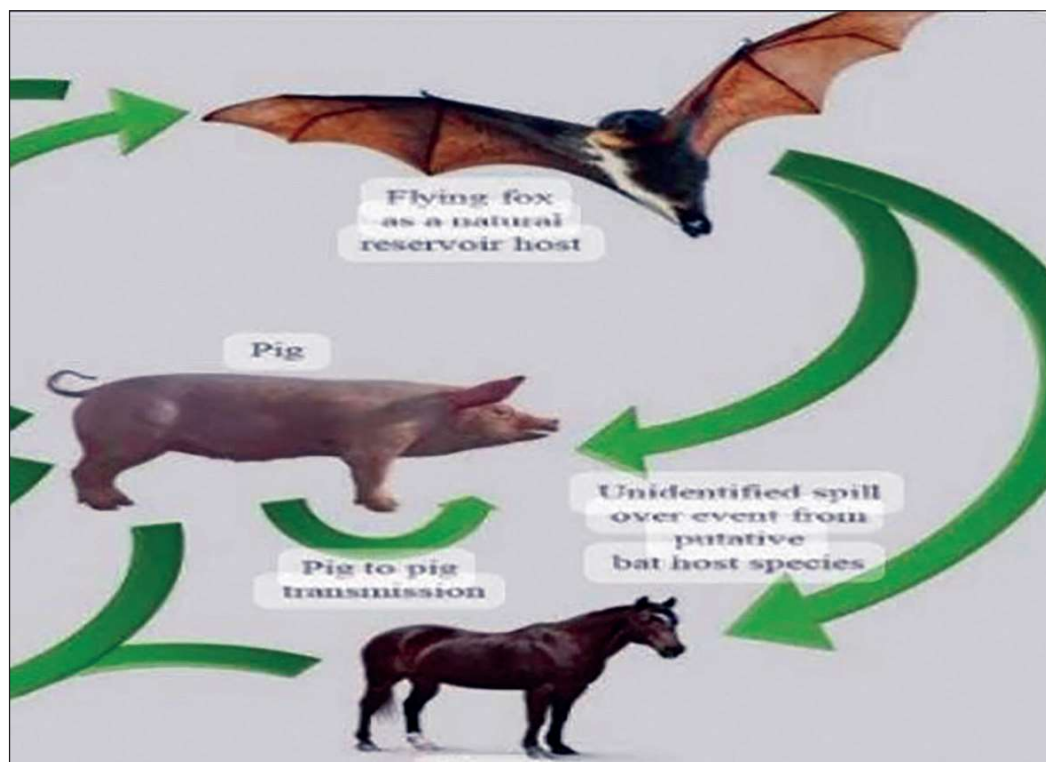


Fig. 10: Animal to Animal transmission (source: provided by author)

Animal to Human transmission

- Direct contact with infected pigs will infect the human health.
- When the infected meet is transported to other parts of world which is consumed by human and gets infected.⁽³⁵⁾

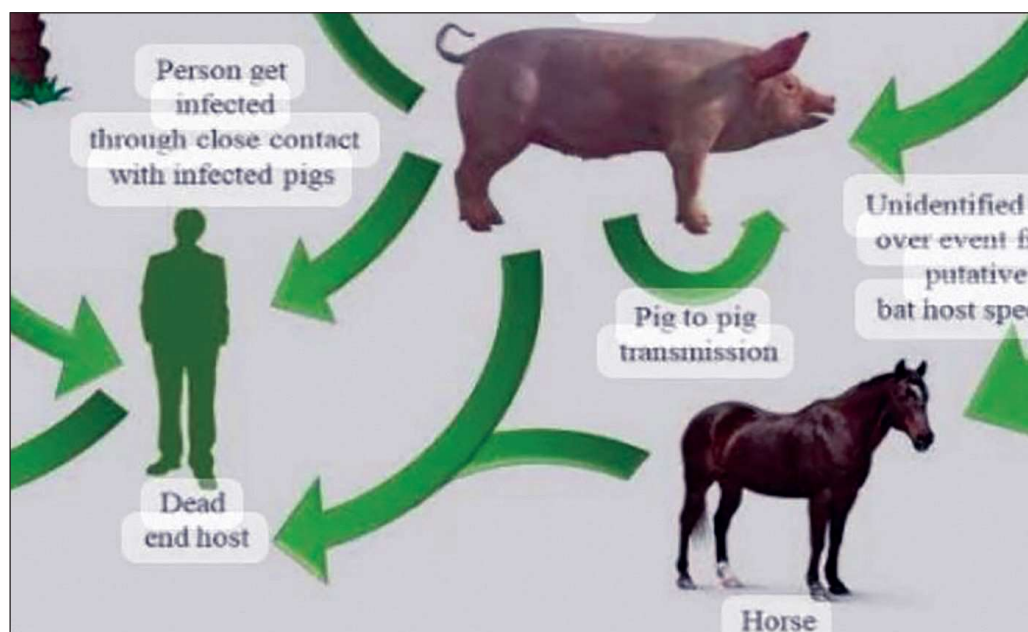


Fig. 11: Animal to Human transmission (source: provided by author)

Sign's & Symptoms:

Niv infections are in both animals & humans, but respiratory symptoms are more in pig's compared to humans.

In human

- Virus causes severe illness in human with the respiratory system as well as CNs.⁽³⁶⁾
- Symptoms appears within 4-14 days after exposure to virus & become infected.
- These infected person shows signs like high fever with headache & drowsiness and also

include signs like respiratory illness such as sore throat, cough etc.

- With in 24- 48 hrs. There may be development of **encephalitis** along with **seizure** & also leads to **coma** in severe cases.⁽³⁷⁾
- Due to **drowsiness** & headache there may be **mental confusion** as well as **disorientation** & also progress towards **coma** within 1- 2days. In the initial phase, respiratory problems become evident & develops a typical pneumonia.⁽³⁶⁾

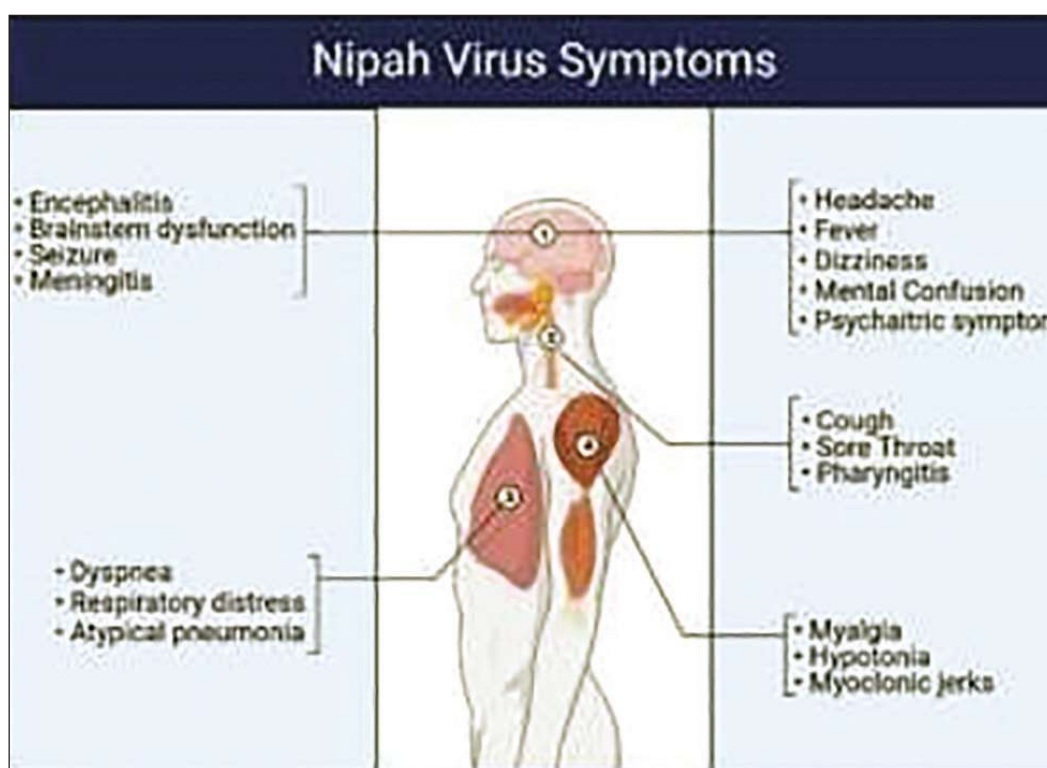


Fig. 12: Signs And Symptoms in Humans (source: provided by author)

In animals:

- **Horses** infected with Niv develop acute, fatal, neurological sign's or suddenly dies without any signs.
- **Dogs** and **cats** are infected in farms shows clinical signs like fever, respiratory distress, mucopurulent nasal etc.
- **Cats** with Niv develop fever, depression increase respiratory rate.
- **Goat** with Niv shows signs like illness, neurological syndrome, and other diseases.
- No symptoms are appeared in the fruit bats.

- **pig's** acute illness has been appeared & nonproductive cough etc.⁽⁴⁰⁾

Mild Symptoms	Sever Symptoms
Fever	Psychiatric
Headache	Disorientation
Vomiting	Drowsiness
Muscle pain	Encephalities
Twitching of facial muscle	Pneumonia
Difficulty in breathing	Convulsions
Sore throat	Meningitis

Causes:

- Close contact with infected animals or it's body fluids.
- Consumption of contaminated food.
- Respiratory droplets.
- Contaminated objects such as cloths, towels etc.
- Mother to fetus via placenta after childbirth.
- Contact with infected skin or lesions.
- Consumption of contaminated date palm sap.
- Human can also be infected by consuming meat of infected animals.
- Consuming the contaminated fruits without washing.

Prevention:

1. **Reducing the risk of animal to human transmission:** Protective personal equipment such as mask or gloves should be used while handling the sick animals or while performing the experiment. Try to avoid close contact with infected pig's as much as possible. sample taken from the animal which is suspected with Niv infection should be handled carefully by trained staff to the laboratories.
2. **Reducing the bat to human transmission:** The fruit should be discarded if there is an any signs

or bite of bat. Fruit should be washed and peel before eating. Freshly collected date Palm juice should be boiled before drinking. Bamboo SAP skirts are used as protective covering which decreases attack of bat on the date palm SAP. We should manage fresh food product area in such a way that it should be away from the attack of bats.

3. **Reducing the risk of human-to-human transmission:** Wear gloves and mask while going near to the infected. Avoid unprotected close contact with Nipah virus infected people. After visiting virus infected people hands should be washed. The things such as clothes, utensils, soaps etc. which are used by virus infected people should not be used by others. maintain distance from virus infected people while they are sneezing coughing to avoid their Air or water droplets.⁽⁴¹⁾

Diagnosis:

- Nipah virus infection can be diagnosed during the phase like acute and convalescent diseases. The main test used is **polymerase chain reaction (PCR)** from body fluid. Other included test for PCR is virus isolation by cell culture.
- It can be diagnosed by **urine, blood, throat or nasal and cerebrospinal fluids**. To identify the presence of Niv RNA



Fig. 13: PCR Diagnosis kit

Serology test:

- When Nipah virus infected patients are diagnosed by serology test IgM antibodies are detected during first 5 days of illness in 65% of patients. IgM and IgG are universally positive (+ ve) in patients who survived by two weeks ⁽⁴⁵⁾.
 - Latest stages IgM and IgG are detected
- by using serological test such as **ELISA. (Enzyme linked Immunosorbent Assay)**
 - IgM antibodies are detectable during the first 5 days of symptomatic illness in approximately 66% of people ⁽⁴⁶⁾
 - It is a most typical test for finding Nipah virus to identify the presence of antibody titers.



Fig. 14: ELISA Diagnosis kit (*source:* provided by author)

Virus isolation test

- Before PCR, Virus isolation is used to confirm the diagnosis of Niv infection because it could characterize the strain precisely Vero E6 cell line is preferred for the viral isolation from the samples such as (urine, CSF, nasal swab sample and brain and lungs tissue). This should be carried out in a BSL4 facility.⁽⁴⁷⁾

Immunohistochemistry test:

- Wide range of Formalin fixed tissue are used to examine to detect the Nipah virus by immunohistochemistry.
- Detection of virus antibody interaction by immunoelectron microscopy provides valuable information on virus structure and antigen reactivity even during primary isolation of virus.⁽⁴⁸⁾



Fig. 15: Immunohistochemistry Test (*source:* provided by author)

Treatment:

- There is no specific medication or vaccine for the treatment of Nipah virus. Currently several clinical trials on vaccines are going on including **mRNA – based vaccines**. From these ones is based on protein which is closely related to the **Hendra virus** and another that uses a harmless Vesicular stomatitis virus to deliver a Nipah virus protein.
- In **Bangladesh International Centre for diarrheal disease research** is studying around 50 Nipah survivor to better understand the virus response on body & vaccine support development.⁽⁴⁹⁾

Primary treatment is self-supportive care for Niv:

- Avoiding contact from Bats and avoiding visiting the place where Bats live.
- Quarantine yourself for few days after infected.
- Maintain hygienic environment.
- Wash hands regularly.
- While visiting infected people wear Gloves & Mask.
- Avoid eating raw fruits and vegetables.⁽⁵⁰⁾

Treatment of symptoms as they occur. Supportive medications are:

- **Acetaminophen** or **ibuprofen** are used to relieve pain & fever.
- **Dimenhydrinate** or **ondansetron** to control nausea and vomiting.
- **Dextromethorphan**, **ipratropium**, or **salbutamol** are used to improve respiratory symptoms by Inhalers or Nebulizers.
- **Benzodiazepine**, **Levetiracetam** or **phenytoin** are used as Anti-seizures.
- **Encephalitis** is used to maintain control on neurological symptoms.
- Immunotherapeutic treatment known as Monoclonal antibody therapies are currently under the development for the treatment of Niv virus. Monoclonal antibodies m102.4 is undergoing clinical trials & also been used on a case-by-case. After Niv exposure Antiviral therapies, such as remdesivir, have been shown to be effective in studies on Human primates.
- **Ribavirin** was also used to treat a small number of patients in the initial Niv outbreak; However, the efficacy of this drug in human is unclear.⁽⁵¹⁾

CONCLUSION

Nipah Virus Is a Zoonotic disease that can spread from bat to humans & from humans to humans. It can cause encephalitis and has a high mortality rate. There is no approved Vaccine or treatment for Nipah virus. Surveillance and Preventative measures are Key to Controlling Outbreaks. Due to the worldwide distribution of bats outbreaks in new areas are likely to occur. Nipah virus is a threat to global health Security. It is difficult to diagnose because of its high Case fatality rate and acute Cause of disease. Early detection & Surveillance are Key to Controlling outbreaks. International collaborates & information sharing are essential for unified global response.

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