WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 3, 238-259. Review Article ISSN 2277– 7105

A REVIEW ON NIPAH VIRUS

[1*]Mr. Kishor Devidas Gayakwad, [2]Mr. L. R. Bagwan and [3]L. D. Hingane (Phd Scholar)

[1,2]At. Post Kharus Bk. Tq. Umarkhed Dist: Yavatmal Umarkhed Maharastra India 445206.

[3]Principal At Aditya Pharmacy College Beed.

Article Received on
22 Dec. 2020,

Revised on 12 Jan. 2021,
Accepted on 02 Feb. 2021

DOI: 10.20959/wjpr20213-19810

***Corresponding Author**
Mr. Kishor Devidas Gayakwad
At. Post Kharus Bk. Tq. Umarkhed Dist: Yavatmal Umarkhed Maharastra India 445206.

ABSTRACT

Nipah virus, a paramyxovirus related to Hendra virus, first emerged in Malaysia in 1998. Clinical presentation ranges from asymptomatic infection to fatal encephalitis. Malaysia has had no more cases since 1999, but outbreaks continue to occur in Bangladesh and India. In the Malaysia-Singapore outbreak, transmission occurred primarily through contact with pigs, whereas in Bangladesh and India, it is associated with ingestion of contaminated date palm sap and human-to-human transmission. Bats are the main reservoir for this virus, which can cause disease in humans and animals. There are currently no effective therapeutics, and supportive care and prevention are the mainstays of management**.**

INTRODUCTION

Hendra virus (HeV) and Nipah virus (NiV) are two members of the genus Henipa virus (HNV; family Paramyxoviridae) that cause acute and severe respiratory illness and encephalitis in humans. HeV was identified in 1994 as the causative agent of an acute respiratory disease and febrile illness in horses and humans, respectively. To date there have been only seven human infections with HeV, of which four were fatal (57%).

Several outbreaks of NiV have been identified in Malaysia, Singapore, Bangladesh and India since 1998. The outbreaks in Malaysia and Singapore have primarily been associated with the development of severe febrile encephalitis with a case fatality rate of 38%, while the more recent outbreaks in Bangladesh and India are associated with a higher prevalence of respiratory disease as well as a higher case fatality rate ranging from 43% to 100% in sporadic cases.

While the exact route of transmission in humans is not known, experimental infection in different animal species suggests that infection can be efficiently initiated after inhalation of virus particles. Endothelial cells have been identified

As an important target of infection; however, it is unknown how the virus spreads to the central nervous system (CNS). Here we review the current knowledge on henipa viruses pathogenesis.

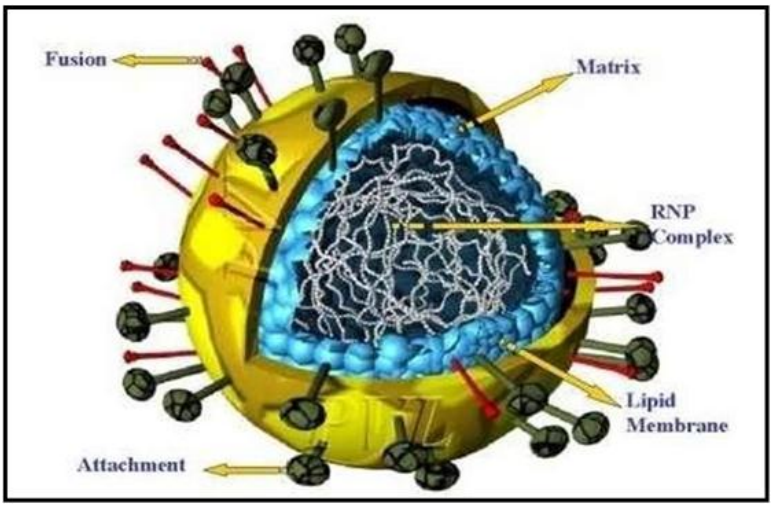

Figure 1: Nipah virus (NiV).

Respiratory infection

The respiratory epithelium is an important first line of defence and actively involved in inflammation and host defence against infectious diseases. In human cases of NiV infection, NiV can be detected in bronchiolar epithelial cells and is shed mainly by nasopharyngeal and tracheal secretions in the early phase of the illness. Patients with symptomatic respiratory tract infections were significantly more likely to transmit NiV. Histological changes in the lungs of NiV cases include necrotizing alveolitis with haemorrhage, pulmonary edema, and aspiration pneumonia.

Multinucleated giant cells are occasionally noted in alveolar septum and alveolar spaces adjacent to necrotic areas. Intra-alveolar inflammatory cells are common. The first fatal human case of HeV infection resulted in severe respiratory disease in which the lungs had gross lesions of congestion haemorrhage and edema associated with histological chronic alveolitis.

Overall, histopathological changes of tracheal/bronchial epithelium were uncommon. In

experimental animal models, viral antigen is initially detectable in the bronchi and alveoli, primarily targeting the bronchial epithelium and type II pneumocytes (Figure 1A).We recently showed that HNV can efficiently infect epithelial cells from the lower human respiratory tract and replicate to high titers. While human-to-human transmission has been observed only in outbreaks with NiV-B, these data suggest that both NiV and HeV have the potential for human-to-human transmission through aerosols.

HNV infection of the respiratory epithelium results in the induction of inflammatory cytokines which result in the recruitment of immune cells and can progress to an Acute Respiratory Distress Syndrome (ARDS)-like disease. Infection of the lower respiratory tract epithelium results in a differential inflammatory response depending on the sites of infection. HNV infection of the small airway epithelium resulted in induction of key inflammatory mediators such as IL-6, 8, IL-1α, MCP-1, G-CSF, GM- CSF and CXCL10. Interestingly, inflammatory cytokine expression was significantly lower in trachea/bronchial epithelium. This observation is in agreement with previous reports that no inflammation is observed in the bronchial epithelium of NiV cases.

Many of these key cytokines in HNV infection play a role in ARDS and are also highly expressed during infection with other virulent respiratory viruses, such as H5N1 and SARS-CoV.

Viremia

During the late stages of disease, virus replication spreads from the respiratory epithelium to the endothelium in the lungs (Figure 1B). The infection can sometimes trigger a prominent vasculitis in small vessels and capillaries as characterized by endothelial syncytium and mural necrosi.

Large vessels are usually not affected. HNV can then enter the bloodstream and disseminate throughout the host in either free form or by binding host leukocytes.

In addition to the lungs, important target organs are the brain, spleen and kidneys, and viremia following respiratory infection can lead to multi-organ failure. Interestingly, HNV has been shown to bind to CD3+ leukocytes without entry or replication of the virus. In hamsters, passive transfer of NiV loaded leukocytes to naïve animals results in lethal infection.[21] In contrast in pigs, HNV can productively infect monocytes, CD6+CD8+ T

lymphocytes and NK cells.

CD6 is a ligand for the activated leukocyte cell adhesion molecule ALCAM (CD166), which is highly expressed on the microvascular endothelial cells of the blood- air and the blood-brain barrier. HNV infection of T cells expressing CD6 may explain the preferential tropism of NiV for small blood vessels of the lung and brain. It is currently unknown whether binding of HNV or infection of human leukocytes will affect the phenotype of the cells, such as increase CD6 expression, there by preferentially homing to the CNS. Entry into the CNS is thought to occur through two distinct pathways anterogradely via the olfactory nerve and via the haematogenous route through the choroid plexus and cerebral blood vessels.

Infection of the CNS in humans is characterized by vasculitis, thrombosis, parenchymal necrosis, and presence of viral inclusion bodies. Plaques with necrosis are found in both the gray and white matter and vasculitis, thrombosis, and parenchymal edema and inflammation are found in the vicinity of these plaques.

Inflammatory cells found in the CNS primarily consist of neutrophils, macrophages, lymphocytes, and reactive microglia.

HNV antigen can typically be detected in neurons and neuronal. Processes and endothelial cells (Figure 1C). Occasionally, viral antigen is also detected in ependymal cells and rare glial cells in the white matter

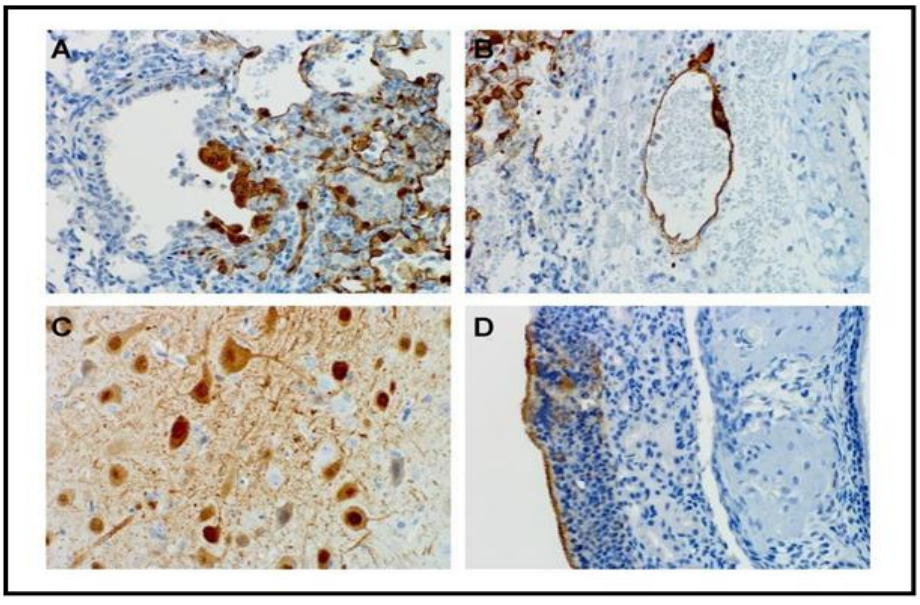

Fig. 2 A-D. Cell tropism of Nipah virus in lungs and brain of infected ferrets Nipah

virus nucleoprotein is detected in bronchial epithelium (A) and endothelium (B) in the lungs, neurons in the brain (C) and olfactory epithelium (D) in the nasal turbinate of ferrets intranasal infected with the Malaysia strain of Nipah virus. 40X magnification.

Entry in the CNS

HNV infection of the CNS and the development of neurological signs are associated with the disruption of the blood-brain barrier (BBB) and expression of TNFα and IL-1β.

These pro-inflammatory cytokines have been shown to play a role in increasing the permeability of the blood-brain barrier as well as the induction of neuronal injury and death. While the source of TNF-α and IL-1β expression in the brain is currently unknown, they can be released by microglia, which are also infected by HNV.

Experimental studies in various animal models have shown direct entry of the CNS by HNV, through the olfactory nerve. In these models, NiV infects the olfactory epithelium in the nasal turbinate (Figure 1D). NiV subsequently infects neurons extending through the cribriform plate into the olfactory bulb, providing a direct route entry into the CNS. NiV then disseminates to the olfactory tubercle and throughout the ventral cortex. It is currently unknown whether this route is also biologically relevant in human infections, since the olfactory epithelial surface is relatively large in these species compaired to man.

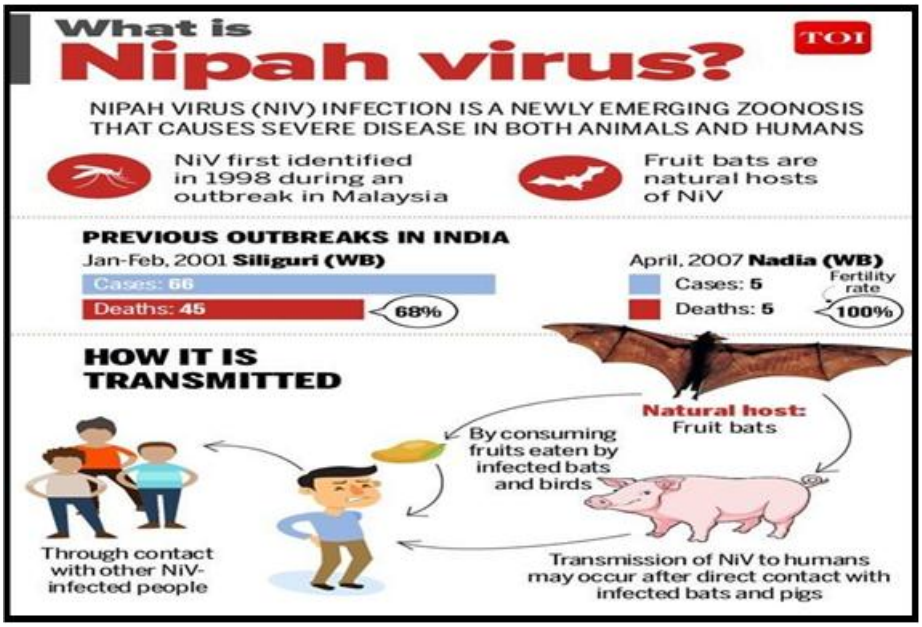

Fig. 3: Showing the transmission of nipah virus.

Review of literature

- **Olivier escaffre E-tal:-** Has done work on Nipah virus

Hendra virus (HeV) and Nipah virus (NiV) are emerging zoonotic viruses that cause severe and often lethal respiratory illness and encephalitis in humans. Henipa viruses can infect a wide range of species and human-to-human transmission has been observed for NiV. While the exact route of transmission in humans is not known, experimental infection in different animal species suggests that infection can be efficiently initiated after respiratory challenge. The limited data on histopathological changes in fatal human cases of HeV and NiV suggest that endothelial cells are an important target during the terminal stage of infection however, it is unknown where these viruses initially establish infection and how the virus disseminates from the respiratory tract to the central nervous system and other organs. Here we review the current concepts in henipavirus pathogenesis in humans.

- **Fatema wahed E-tal:-** has done work on Nipah virus

Nipah virus, a member of the genus Henipavirus, a new class of virus in the Paramyxoviridae family, has drawn attention as an emerging zoonotic virus in south east and south Asian region. Case fatality rate of Nipah virus infection ranges from 40-70% although it has been as high as 100% in some outbreaks. Many of the outbreaks were attributed to pigs consuming fruits partially eaten by fruit bats, and transmission of infection to humans. In Bangladesh, 7 outbreaks of Nipah virus infection were identified during the period 2001–2007.

In Bangladesh, Nipah virus infection was associated with contact with a sick cow, consumption of fresh date palm sap (potentially contaminated with pteropid bat saliva), and person-to-person transmission. In the most recent epidemic at least 15 people died due to Nipah virus infection in Hatibandha, Lalmonirhat district in a remote northern Bangladesh town in 2011.

Human infections range from asymptomatic infection to fatal encephalitis. Infected people initially develop influenza like symptoms of fever, headaches, myalgia, vomiting and sore throat. This can be followed by dizziness, drowsiness, altered consciousness, and neurological signs that indicate acute encephalitis. Some people can also experience atypical pneumonia and severe respiratory problems. The virus is detected by ELISA, PCR, immune fluorescent assay and isolation by cell culture.

Treatment is mostly symptomatic and supportive as the effect of antiviral drugs is not

satisfactory, and an effective vaccine is yet to be developed. So the very high case fatality addresses the need for adequate and strict control and preventive measures.

- **Dhumal Kuldip E-tal:-** has done work on Nipah virus

Nipah virus infection is a newly emerging zoonosis that causes severe disease in both animals and human. Nipah virus it is infectious disease which first appeared in domestic pigs in Malaysia and Singapore in 1998 and 1999. Nipah virus is a previously unknown virus of the family Paramyxoviridae genus Henipavirus that has been identified in the northern peninsula of Malaysia. The virus has caused illness and death in humans and pigs. It is related to Hendra virus that infects horses. The apparent source of infection for humans is direct contact with pigs. Transmission of virus is thought to be from body fluids of infected pigs. Human-to-human transmission has not been documented. A recent outbreak of neurological disease in horses and humans in the Philippines also appears to have been caused by this virus. In this article some points are highlight such as sign and symptoms, transmission, how to control Nipah virus, treatment along with diagnosis.

- **Sayali C. Dudhal E-tal:-** has done work on Nipah virus

Nipah virus infection in humans causes a range of clinical presentations, from asymptomatic infection (subclinical) to acute respiratory infection and fatal encephalitis. The case fatality rate is estimated at 40% to 75%. This rate can vary by outbreak depending on local capabilities for epidemiological surveillance and clinical management.

Nipah virus can be transmitted to humans from animals (such as bats or pigs), or contaminated foods and can also be transmitted directly from human-to-human. Fruit bats of the *"Pteropodidae"* family are the natural host of Nipah virus. There is no treatment or vaccine available for either people or animals. The virus was also able to spread from farm to farm through transportation of unidentified infected pigs. Most likely the workers whom were infected can in direct contact with saliva or other respiratory secretions from an infected pig.

Historical background

Nipah virus was first identified and confirmed in Malaysia in 1999 when the virus crossed the species barrier from bats to pigs and then infected humans, inducing encephalitis with upto 40% mortality. The survivors were inflicted with residual neurological problems3. The virus itself was named after a town in Malaysia. The outbreak was attributed to pigs consuming fruits partially eaten by fruit bats, and transmission of infection to humans. Similar outbreaks

in China and Singaporefollowed. Case fatality rate of the 2001outbreak which took place in Siliguri, India, near the northern border of Bangladesh was 68%. The patients affected by this outbreak presented with both encephalitis and respiratory symptoms.

In Bangladesh, 4outbreaks of Nipah virus infection was identified during the period 2001–2004. Outbreaks were different in Bangladesh due to lack of identifiable intermediate animal hosts (i.e. pig). 2004 outbreak included a number of victims under19 years of age who collected and ate fruits partly eaten.

Table 1: Morbidity and Mortality due to Nipah or Nipah-like virus, Asia-Pacific Region, 1998-2008.

Year/Month	Location	No. of cases	No.of Death	Case fatality
Sep 1998-Apr 99	Malaysia	265	105	40%
March 1999	Singapore	11	1	9%
Feb 2001	Siliguri (India)	66	45	68%
Apr-May 2002	Meherpur, Bangladesh	13	9	69%
Jan 2003	Naogaon, Bangladesh	12	8	67%
Jan 2004	Goalondo, Bangladesh	29	22	76%
Apr 2004	Faridpur, Bangladesh	36	27	75%
Jan –Mar 2005	Tangail, Bangladesh	12	11	92%
Jan –Feb 2007	Thakurgaon, Bangladesh	7	3	43%
Mar-Apr 2007	Kuushtia, Bangladesh	8	5	63%
April 2007	Nadia, India	5	5	100%
Feb 2008	Manikganj, Bangladesh	11	6	55%
Apr2008	Shatkira , Bangladesh	2	1	50%
Total		477	248	52%

Who report on nipah virus

- Nipah virus is an emergent paramyxo virus which causes disease both in human and animals. The outbreak of Nipah virus in human was first recognized in Asia in Malaysia in 1999. In the SEA Region, Nipah virus outbreaks have been confirmed in Bangladesh in 2001, 2003 and 2007, and in India in 2001 and 2007.
- Nipah virus manifests primarily as encephalitis. It is highly pathogenic to humans, with high case fatality rate, ranging from 40 to 75%.
- In Malaysia outbreak, transmission occurred primarily through contact with infected swine. In Bangladesh, the infection seems to have occurred directly from fruit bats (believed to be the reservoir) without involvement of intermediate host (swine). The spread can also occur possibly by droplet infection.
- Clinical presentation can range from asymptomatic infection to fatal encephalitis. Those

infected initially have a sudden onset of flu-like symptoms such as fever, headaches, pain in the muscles, vomiting and sore throat, followed by dizziness, drowsiness, altered consciousness (partial or complete loss of consciousness) and focal neurological signs indicating acute encephalitis. Encephalitis and seizures occur in severe cases. This progresses to coma within 24-48 hours.

- The incubation period varies from four to 18 days, although an incubation period of as long as 45 days has been reported.
- Involvement of the central nervous system is especially severe in the brain but direct neuronal infection may also play a role. Abundant viral antigens have been seen in neurons. Other organs such as lungs (as described above), heart and kidneys can also be affected.
- There are currently no effective therapeutics and vaccines available to treat Nipah virus infection. Intensive supportive care is the mainstay of case management.
- Interestingly, the epidemiology of Nipah has evolved, with our understanding, from a disease which spread from occupation contact (with pigs) to possibly person to person, and also as a food-borne disease.
- CDC lists it as a critical potential biological weapon because of its availability, ease of production and dissemination, and high virulence in terms of high mortality and health impact.

Nipah virus recent outbreak in kerala may-2018, india

- Kerala's Kozhikode is on high alert as a deadly virus called 'Nipah' (NiV) claimed six lives in the state. The fast-spreading virus Nipah reported has a high mortality rate of 70%.

Kerala records 10 deaths due to suspected nipah virus infection

- **Kozhikode:-"**The death toll due to contagious fever has risen to ten, including three confirmed Nipah cases and seven suspected deaths following symptoms of the contagious viral disease". The death of three members of a family in Changaroth panchayat during the last fortnight was confirmed as due to Nipah virus in the tests conducted at National Virology Institute, Pune, on Sunday The latest victim suspected to have died due to Nipah infection is Lini, 31, a nurse of the Perambra Taluk Hospital. Lina, hailing from Peruvannamuzhi, had tended to one of the patients, who was later confirmed to have had Nipah infection. The second incident recorded in Nadia district at West Bengal in 2007,

India.

- According to WHO the virus claimed over 300 lives across Malaysia, Singapore, Bangladesh and India between 1998 and 2008.

Description of nipah virus

"Nipah virus infection is an emerging zoonosis that causes severe disease in humans and animals. Zoonosis means diseases which transmit to humans from animals. The natural host of the virus is fruit bats of the Pteropodidae Family, Pteropus genus (fruit-eating species), according to WHO".

Nipah virus infection (NiV) is a viral infection caused by the Nipah virus. Symptoms from infection vary from none to fever, cough, headache, shortness of breath, and confusion. This may worsen into a coma over a day or two.

Complications can include inflammation of the brain and seizures following recovery. The Nipah virus is a type of RNA virus in the genus Henipavirus. It can both spread between people and from other animals to people. Spread typically requires direct contact with an infected source. The virus normally circulates among specific types of fruit bats. Diagnosis is based on symptoms and confirmed by laboratory testing.

Management involves supportive care. As of 2018 there is no vaccine or specific treatment. Prevention is by avoiding exposure to bats and sick pigs and not drinking raw date palm sap. As of 2013 a total of 582 human cases of Nipah virus are estimated and 50 to 75 percent of those who were infected died. In 2018, an outbreak of the disease resulted in at least 16 deaths in the Indian state of Kerala.

The disease was first identified in 1998 during an outbreak in Malaysia while the virus was isolated in 1999. It is named after a village in Malaysia, Sungai Nipah. Pigs may also be infected and millions were killed in 1999 to stop the spread of disease.

Reservoir of virus

Fruit bats of the genus Pteropus have been identified as natural reservoirs of NiV. A seroepidemiologic study in Malaysia implicated four fruit bat species, Pteropus hypomelanus, P.vampyrus, Cynopterus brachyotis, Eonycteris spelaea, and an insectivorous bat, Scotophilus kuhlii. Nipah virus has been isolated from the brain and spinal fluid of victims in

Malaysia. Infective virus has also been isolated from environmental samples of bat urine and partially-eaten fruit in Malaysia.

Given the distribution of the locally abundant fruit bats in South Asia, NiV outbreaks are likely to continue to occur in affected countries. The bats are migratory.this has generated intensive surveillance for evidence of Nipah virus infection in bats in these countries. Evidence of NiV could be demonstrated in P. giganteus in Bangladesh.

Nipah virus has been isolated from Lyle's flying fox (Pteropus lylei) in Cambodia and viral RNA found in urine and saliva from P. lylei and Horsfield's roundleaf bat (Hipposideros larvatus) in Thailand.[19] Antibodies to a Nipah-like virus have been found in sera from fruit bats collected in India, Indonesia and Timor-Leste.

The status of NiV infection in other countries of the South-East Asia Region is not known. Antibodies to henipaviruses have also been found in fruit bats in Madagascar (Pteropus Rufus, Eidolon dupreanum) and Ghana (Eidolon helvum) indicating a wide geographic distribution of the viruses. No infection of humans or other species has been observed in Cambodia, Thailand or Africa.

Countries where Nipah virus infection in bats was demonstrated by antibody detection method and where Nipah virus infection in bats was confirmed by isolation, countries where Nipah virus infection in bats was confirmed by RNA detection.

Future aspects of niv

Several steps have been taken in the right direction towards eradicating this extremely harmful disease. After the initial outbreak of Nipah virus in 1998, the Malaysian and Singaporean governments developed a two phase plan in hope to control any future outbreak. Phase one was set to eliminate a majority of the pigs present within the country. Phase two introduced an antibody testing protocol to regulate and observe farms which may be of high risk for an outbreak.[35] Both countries also banned the transportation of pigs within the respective countries as well as initiated an educational program to aid the farms in proper handling and the virus itself. As previously stated some initial ground work has also been laid in identifying a possible vaccine which inhibits the activity of F and G proteins on the viral cell.

Despite these positive steps, Nipah virus should be at the top of the list of major concerns for the human race for several reasons.

1) **Increased human to human transmission in recent outbreaks**

Transmission of NiV has now become a concern in many hospitals in Southeast Asia. There have been several cases of doctors becoming infected from treating patients as well as infections resulting from contact with corpses.

The more recent outbreaks in Bangladesh and India are suggested to have an estimated 75% or more of the known infections resulting from humans to human transmission. The main mode of transmission from human to human is hypothesized to be through respiratory secretions and close contact.

This mutated strain of NiV has the potential to be extremely detrimental in densely populated cities.

2) **Rising fatality rate in humans:** The most recent outbreak in Bangladesh in February of 2013 resulted in increasing the overall fatality rate of Nipah virus infection in Bangladesh

Knowledge of molecular mechanisms of infection: The molecular mechanisms of how the virus is passed from species to species are still fairly.

3) **Lack of** species as well as the risk of more outbreaks.

4) **Shared habitats:** With a rapidly growing human population in the world, particularly in Southeast Asia, there is an increase of overlapping of habitats between humans, Pteropus fruit bats, and pigs. This only increases the chance of transmission of NiV upto.[77]

5) **Pteropus fruit bat migration and pig dependence:** Pteropus fruit bats are migratory animals which can survive in a wide range of environment, while much of rural Southeast Asia is dependent on their pig farms as a source.

The combination of these two aspects opens up many pathways to many new countries and new populations of humans with no previous exposure to NiV.

6) **NiV is an RNA virus and a zoonotic virus:** RNA viruses have a high mutation rate which enables them to keep a leg up on both vaccines and host immune systems. Zoonotic viruses also have a high mutation rate. Because NiV is both of these, it is

hypothesized it has an extremely high rate of mutation.

Genome and protein of nipah virus

Single stranded negative sense RNA, 18246 bop (Malaysia isolate) and 18252 bop (Bangladesh isolate) Genome has six transcriptional unit that six structural proteins. They are nucleo capsid (N), Phospho protein (P), matrix protein (M), fusion protein (F), glycoprotein (G), polymerase (L). Protein associated with genome: Large (L) protein, phosphor protein (P). Viral Proteins: fusion protein (F) and attachment glycoprotein protein (G). Phospho protein (P): it role as a polymerase cofactor, enhancing polymerase processivity and allowing the encapsulation of the newly synthesized viral genomes

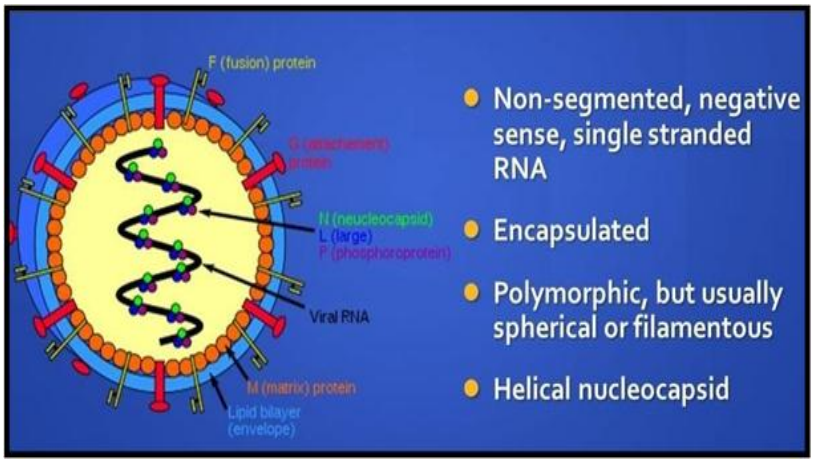

Fig. 4: Structure and genome of Nipah Virus. (Nipah Virus is a RNA virus belongs to family *Paramyxoviradae* and Genus *Henipavirus*. Size: 40-600 nm, Shape*: Pleuromorphic*, Envelop: Present.)

The mode of transmission

- Infected bats shed virus in their excretion and secretion such as saliva, urine, semen and excreta but they are symptomless carriers.
- Nipah virus is a zoonotic virus. Flying fox (family Pterodidae and particularly species of genus Pteropus) are the natural host for Nipah virus.
- Direct contact: Human get infection by direct contact with infected animals (pigs and fruit bats) or human Droplet infection: respiratory droplets, nasal or throat secretion of infected animals.
- Eating contaminated fruits and juices with body secretion of infected animals Human to human transmission with direct contact with infected person.

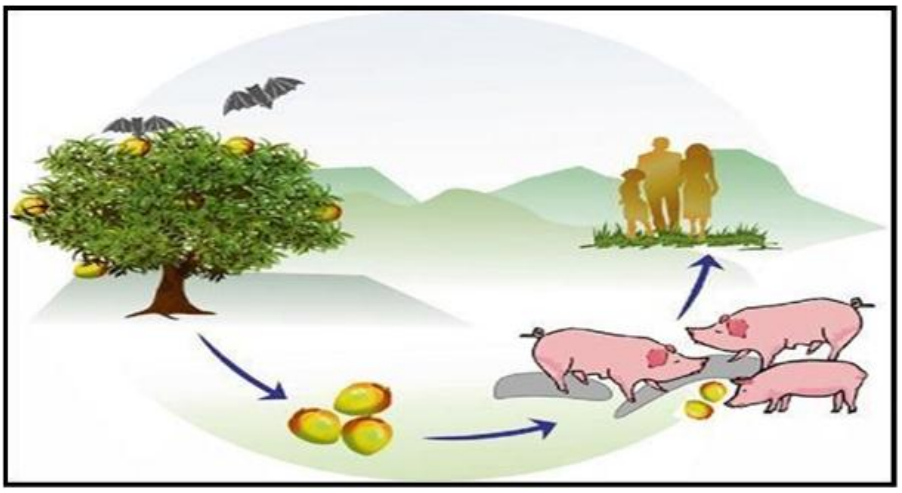

Figure 5: Nipah virus transmission cycle.

Transmission Studies involving in contact pigs revealed that infection occurs quickly, possibly at first contact. [1] In Pteropus bats Nipah virus has been found repeatedly in urine and viral RNA has been detected rarely in oropharyngeal swabs and rectal swabs from naturally or experimentally infected bats. Transmission of the virus is through direct contact with body fluids. Another theory is that humans may become infected via aerosol transmission from respiratory or urinary secretions.

Transmission is thought to have occurred via unprotected exposure to secretions from the pigs or unprotected contact with the tissue of a sick animal. [14,12] Nipah virus infection is made using reverse transcriptase polymerase chain reaction (RT-PCR) from throat swabs, cerebrospinal fluid, urine and blood analysis during acute and convalescent stages of the disease. IgG and IgM antibody detection can be done after recovery to confirm Nipah virus infection. Immuno histochemistry on tissues collected during autopsy also confirms the disease. Viral RNA can be isolated from the saliva of infected persons. NiV can survive for days on sugar rich solutions such as fruit pulp.

Bats transmit this virus to domesticated animals is uncertain but ingestion of contaminated fruit, water or aborted bat foetuses or birth products (e.g. pigs) is suspected.

The infection in pigs which was then followed by a rapid spread through intensively reared pigs. Furthermore transmission between farms may be due to fomites or carrying the virus on clothing, equipment, boots, and vehicles.

This virus is reported to have a half- life of 18 hours in the urine of fruit bats.The NiV is

highly contagious among pigs, spread by coughing. [24] Direct contact with infected pigs was identified as the predominant mode of transmission in humans when it was first recognized in a large outbreak in Malaysia in 1999. Ninety percent of the infected people in the 1998- 1999 outbreaks were pig farmers or had contact with pigs.

Signs and Symptoms

According to Centres for Disease Control and Prevention

A. Infection with Nipah virus is associated with encephalitis.
B. An infected client explore the symptoms of fever and headache within three-14 days of exposure an Incubation period of five to 14 days.
C. Important signs are fever, headache, dizziness and vomiting, followed by drowsiness, disorientation and mental confusion.
D. More than 50% of the clients faced a reduced level of consciousness and brain dysfunction.
E. Some clients may have a respiratoryillness.
F. Almost half of the patients showing severe neurological signs.

The symptoms start to appear within 3–14 days after exposure. Initial symptoms are fever, headache, drowsiness followed by disorientation and mental confusion. These symptoms can progress into coma as fast as in 24–48 hours. Encephalitis, inflammation of the brain, is a potentially fatal complication of Nipah virus infection. Respiratory llness can also be present during the early part of the illness.

Nipah-case patients who had breathing difficulty are more likely than those without respiratory illness to transmit the virus. The disease is suspected in symptomatic individuals in the context of an epidemic Outbreak.

Initially patients develop Influenza like symptoms such as: Fever, Sore throat, Headaches, Vomiting and Myalgia or Muscle pain. Acute Respiratory infection difficulty in breathing. Some patients develop atypical pneumonia. Neurological illness results in encephalitis and seizures. Case fatality rate ranges from 43% to 100% in sporadic cases. Patients surviving acute encephalitis have been reported to show long term neurological conditions such as personality change and seizures. Encephalitis and seizures occur in severe cases, progressing to coma within 24 to 48 hours.

Table 2: of Frequency of clinical Symptoms and Signs in 32 Fatal Cases of Nipah Virus Infection.

Symptoms	%
Fever	100
Drowsiness	88
Headache	82
Disorientation/confusion	76
Giddiness	61
Myalgia	54
Cough/Respiratory symptoms	40
Convulsion	28
Vomiting	19

Signs	%
Reduced consciousness	89
Segmental myoclonus	50
Hyperreflexia/areflexia	50
Seizure	40
Cranial nerve palsy	29
Pyramidal signs	21
Nystagmus/cerebellar signs	17
Meningism	10
Dysphasia	5

Pathophysiology

Pathological features

The macroscopic features were nonspecific. In the CNS, lesions were generally difficult to identify; however, in a few cases, small, discrete, occasionally hemorrhagic, necrotic lesions were found. Only 2 of 10 brains examined showed unequivocal herniation. Case 29 had cerebella tonsil hernia ion, and case 31 had uncial herniation and showed a large intracerebral clot in the frontal lobe with intraventricular extension and Duet haemorrhages in the midbrain and pons. Histopathological changes were seen in the blood vessels and parenchyma of multiple organs and are presented accordingly.

Blood vessels

The distribution of histopathological lesions and immune staining is shown in Table 3. Extensive involvement of blood vessels in the CNS, lung, heart, and kidney was observed in Nipah virus infection. However, blood vessels in the CNS were the most severely involved.

Vasculitis was not found in medium-sized vessels (e.g., renal artery and vein, anterior and middle cerebral arteries) or large arteries (e.g., aorta and pulmonary trunk). No vasculitis was

found in there lapse encephalitis case 32 ;(Table 3).Vasculitis was characterized by various degrees of segmental endothelial destruction, mural necrosis, and karyorrhexis (Figure 6; A to D). Mural necrosis often appeared fibrinous. Inflammatory cell infiltration of vascular walls by neutro phils and mononuclear cells was usually focal and either partial or transmutable (Figure 6 A and B).Thrombosis

Table 3: Fatal nipah virus infection: frequency of necrosis, Vasculitis, and Immunostaining of viral antigens in major organs.

Pathologic Findings	Brain no. (%)	Lung no. (%)	Heart no. (%)	Kidney no. (%)	Spleen no. (%)
Necrosis*	28/30(93)	17/29 (59)	1/29 (3)	10/29 (34)	10/24 (42)
Vasculitis	24/30 (80)	18/29 (62)	9/29 (31)	7/29 (24)	0/24 (0)
Viral antigens	27/32(84)	7/29(24)	4/24 (17)	6/25 (24)	1/21 (5)

Syncyticum or multinucleated giant endothelial cells were seen in blood vessels of various organs (Figure 6; B, E, F and G). In the CNS, they were found in 27% of the cases (Table 4), mostly in patients whose duration of illness ranged from 6 to 15 days. The syncytial typically consisted of several overlapping or sharply melded nuclei with moderate to abundant cytoplasm (Figure 6F).

CNS

In the CNS, the main pathological findings were vasculitis, thrombosis, parenchymal necrosis, and presence of viral inclusions (Table 4 and Figures 6). Vascular involvement of gray and white matter was seen throughout the CNS. The spinal cord was examined in eight cases and showed similar pathological lesions in three cases as observed elsewhere in CNS. Pathological lesions similar to those seen elsewhere in CNS were seen in spinal cords of three of eight cases examined.

The olfactory bulb was examined in nine cases and did not show any significant histopathology. Common histopathological lesions and their relative frequency in the CNS are summarized in Table 3. Plaques with various degrees of necrosis was found in both the grey and white matter. These necrotic plaques were round or oval with diameters that ranged from 0.2 mm to 5 mm. Vasculitis, thrombosis, and various degrees of parenchymal edema and inflammation were frequently found in the vicinity of the plaques. The inflammatory cellular infiltrate consisted of neutrophils, macrophages, lymphocytes, and reactive microglia. Areas of microcytic degeneration were seen, most commonly, in the vicinity of necrotic

plaque.

Microcytic change with non adjacent plaques was also occasionally seen. In white matter, damaged axons occasionally formed axonal spheroids similar to those seen in diffuse axonal injury No large geographic infarctions of the type associated with occlusion of medium-sized or larger arteries were seen.

where in the parenchyma, focal neuronophagia, microgial nodule formation and perivascular cuffing were seen.

Overall, parenchymal inflammation was present in 67% of cases (Table 4).

Table 4: Microscopic features in the central nervous system in 30 fatal cases of nipah virus infection*.

Histopathologic lesion	Frequency, %
Necrotic plaque	93
Perivascular cuffing	90
Thrombosis	87
Vasculitis	80
Parenchymal inflammation	67
Viral inclusions	63
Meningitis	57
Syncytia	27

Prevention and Control

Controlling nipah virus in domestic animals

There is no vaccine against Nipah virus. Routine cleaning and disinfection of pig farms (with sodium hypochlorite or other detergents) is expected to be effective in preventing infection. If an outbreak is suspected, the animal premises should be quarantined immediately. Culling of infected animals with close supervision of burial or incineration of carcasses may be necessary to reduce the risk of transmission to people. Restricting or banning the movement of animals from infected farms to other areas can reduce the spread of the disease. As Nipah virus outbreaks in domestic animals have preceded human cases.

Reducing the risk of infection in people

In the absence of a vaccine, the only way to reduce infection in people is by raising awareness of the risk factors and educating people about the measures they can take to reduce exposure to the virus. Public health educational messages should focus on the following.

- Reducing the risk of bat-to-human transmission. Efforts to prevent transmission should first focus on decreasing bat access to date palm sap. Freshly collected date palm juice should also be boiled and fruits should be thoroughly washed and peeled before consumption.
- Reducing the risk of human-to-human transmission. Close physical contact with Nipah virus-infected people should be avoided. Gloves and protective equipment should be worn when taking care of ill people. Regular hand washing should be carried out after caring for or visiting sick people.
- Reducing the risk of animal-to-human transmission. Gloves and other protective clothing should be worn while handling sick slaughtering and culling procedures.

Controlling infection in health-care settings

Health-care workers caring for patients with suspected or confirmed Nipah virus infection, or handling specimens from them, should implement standard infection control precautions. Samples taken from people and animals with suspected Nipah virus infection should be handled by trained staff working in suitably equipped laboratories.

Efforts in development of an effective vaccine

A vaccine is being developed. A recombinant subunit vaccine formulation protects against lethal Nipah virus challenge in cats. ALVAC Canary pox vectored. Nipah F and G vaccine appears to be a promising vaccine for swine and has potential as a vaccine for humans.

Addition of a cholesterol group to HRC peptides active against Nipah virus targets these peptides to the membrane where fusion occurs, dramatically increasing their antiviral effect because of increased ability to penetrate CNS.

Diagnosis

Initial signs and symptoms of Nipah virus infection are nonspecific, and the diagnosis is often not suspected at the time of presentation. This can hinder accurate diagnosis and creates challenges in outbreak detection, effective and timely infection control measures, and outbreak response activities. In addition, the quality, quantity, type, timing of clinical sample collection and the time needed to transfer samples to the laboratory can affect the accuracy of laboratory results.

Nipah virus infection can be diagnosed with clinical history during the acute and

convalescent phase of the disease. The main tests used are real time polymerase chain reaction (RT-PCR) from bodily fluids and antibody detection via enzyme-linked immune sorbent assay (ELISA). Other tests used include polymerase chain reaction (PCR) assay, and virus isolation by cell culture.

Treatment

Currently there is no effective treatment for Nipah virus infection. The treatment is limited to supportive care. It is important to practice standard infection control practices and proper barrier nursing techniques to avoid the transmission of the infection from person to person. All suspected cases of Nipah virus infection should be isolated and given intensive supportive care.

Creating a vaccine is currently extremely difficult because the mutation rate of RNA viruses is extremely high as is most zoonotic diseases, of which Nipah virus is both. however several studies have been conducted in targeting the F and G proteins which would inhibit binding of the NiV cells to any host cell.

Ribavirin has been shown effective invitro tests, but has not yet been proven effective in humans.

Passive immunization using a human monoclonal antibody that targets the Nipah G glycoprotein has been evaluated in the ferret model as post-exposure prophylaxis. The anti-malarial drug chloroquine was shown to block the critical functions needed for maturation of Nipah virus, although no clinical benefit has been observed.

CONCLUSION

Nipah virus is a recently discovered zoonotic disease causing in South Asia were sporadic outbreaks have been reported in Malaysia, Singapore, India and Bangladesh. The case-fatality varies from 40% to 70% depending on the severity of the clinical manifestations such as encephalitis as well as the availability of adequate healthcare facilities.

The results of this study emphasize the importance of perceived health status. The upcoming years is likely to see the advancement of this indulgent and significantly practical applications as a vaccines for Nipah virus to get into human clinical trials, prevention of infection through modifying risk factors for the development of therapeutics and techniques capable for treating infected patients to diminish morbidity and mortality.

Research over the last 20 years has provided in sight for mechanisms of pathological process and transmission of Nipah virus.

REFERENCES

1. "Signs and Symptoms Nipah Virus (NiV)". CDC, 2.
2. "WHO Nipah Virus (NiV) Infection". www.who.int, 2018.
3. "Transmission Nipah Virus (NiV)". CDC, 2018.
4. "Diagnosis Nipah Virus (NiV)". CDC, 2018.
5. "Prevention Nipah Virus (NiV)". CDC, 2018.
6. "Nipah virus outbreaks in the WHO South-East Asia Region". South-East Asia Regional Office. WHO, 2018.
7. Broder, Christopher C.; Xu, Kai; Nikolov, Dimitra B.; Zhu, Zhongyu; Dimitra, Dimiter S.; Middleton, Deborah; Pallister, Jackie; Geisbert, Thomas W.; Bossart, Katharine N.; Wang, Lin-Fa (October 2013). "A treatment for and vaccine against the deadly Hendra and Nipah viruses". Antiviral Research, 2018; 100(1): 8–13.
8. CNN, Manveena Suri,"10 confirmed dead from Nipah virus outbreak in India". CNN, 2018.
9. "Nipah virus outbreak: Death toll rises to 14 in Kerala, two more cases identified". Hindustan Times, 2018.
10. "Nipah Virus (NiV) CDC". Www.cdc.gov. CDC, 2018.
11. Lucy, Stephen P.; Hossain, M. Jahangir; Gurley, Emily S.; Ahmed, Be-Nazir; Banu, Shakila; Khan, Salah Uddin; Homaira, Nusrat; Rota, Paul A.; Rollin, Pierre E.; Comer, James A.; Kenah, Eben; Ksiazek, Thomas G.; Rahman, Mahmudur. "Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007". Emerging Infectious Diseases, 2018; 15(8): 1229–1235.
12. Field H, Rashid AM, Morrissey C, van der Heide B, Rota P, et al. Nipah virus infection in bats (order Chiroptera) in peninsular Malaysia. Emerg
13. Chua KB, Bellini WJ, Rota PA, Harcourt BH, et al. Nipah virus: a recently emergent deadly paramyxovirus. Science, 2000; 288: 1432-1435.
14. Chua KB, Koh CL, Hooi PS, Isolation of Nipah virus from Malaysian Island flying-foxes. Microbes Infect, 2002; 4(2): 145–51.
15. Eaton BT, Broder CC, Middleton D, Wang LF, 2006. Hendra and Nipah viruses: different and dangerous. Nat. Rev. Microbial, 2006; 4: 23–35.
16. Hsu, VP, Hossain, MJ, Parashar UD et al. Nipah virus encephalitis re-emergence,

Bangladesh. Emerg. Infect. Dis, 2004; 10: 2082-2087.

17. Reynes JM, Counor D, Ong S, Faure C, Seng V, Molia S, et al. Nipah virus in Lyle's flying foxes, Cambodia. Emerg Infect Dis, 2005; 7.
18. Wacharapluesadee S, Lumlertdacha B, Boongird K, Wanghongsa S, Chanhome L, Rollin P, et al. Bat Nipah virus, Thailand. Emerg Infect Dis, 2005; 11: 1949-51
19. Heymann DL. Henipavirus: Hendra and Nipah viral diseases. Control of Communicable Diseases Manual, American Public Health Association, 2008; 19: 275-278.
20. Lehlé C, Razafitrimo G, Razainirina J, et al. "Henipavirus and Tioman virus antibodies in pteropodid bats, Madagascar". Emerging Infect. Dis, 2007; 13(1): 159–61.
21. Hayman D, Suu-Ire R, Breed a, "Evidence of henipavirus infection in West African fruit bats". Plops ONE, 2008; 3(7): 2739.
22. Goh KJ, Tan CT, Chew NK, Tan PSK, Kamarulzaman A, Sari SA, Wong KT, Abdullah BJJ, Chua KB, Lam SK. Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. N. Engl. J. Med, 2000; 342: 1229–1235.