ejpmr, 2018,5(6), 703-712

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

GLOBAL THREAT OF NIPAH VIRUS AND TREATMENT

Jalpa Soni, Avani Patel, Khushbu Patel, Dhiren Chaudhary, Tejas Chaudhari and Prof. Dr. Dhrubo Jyoti Sen*

Department of Pharmacology and Pharmaceutical Chemistry, Shri Sarvajanik Pharmacy College, Gujarat Technological University, Arvind Baug, Mehsana-384001, Gujarat, India.

***Corresponding Author: Prof. Dr. Dhrubo Jyoti Sen**
Department of Pharmacology and Pharmaceutical Chemistry, Shri Sarvajanik Pharmacy College, Gujarat Technological University, Arvind Baug, Mehsana-384001, Gujarat, India.

Article Received on 19/04/2018 **Article Revised on 09/05/2018** **Article Accepted on 29/05/2018**

ABSTRACT

Nipah virus (NiV) is a highly pathogenic, recently emerged paramyxovirus that has been responsible for sporadic outbreaks of respiratory and encephalitic disease in Southeast Asia. High case fatality rates have also been associated with recent outbreaks in Malaysia and Bangladesh. Although over two billion people currently live in regions in which NiV is endemic or in which the Pteropus fruit bat reservoir is commonly found, there is no approved vaccine to protect against NiV disease.

KEYWORDS: Fruit Bats, Domestic Pigs, Hendra Virus, Nipah Virus, PRES, BPS, ELISA.

Disease & Pathogen: Nipah Virus (NiV) is an emerging infectious disease which first appeared in domestic pigs in Malaysia and Singapore in 1998 and 1999. There is evidence of Nipah infection among several species of domestic animals including dogs, cats, goats and horses. Sheep may also be affected. However, since the initial outbreak it has primarily affected humans in different parts of the world. The disease causes respiratory and occasionally nervous signs in pigs. It has devastating zoonotic potential. The organism which causes Nipah Virus encephalitis is an RNA virus of the family *Paramyxoviridae*, genus Henipavirus and is closely related to Hendra virus. Hendra virus, formerly known as equine morbillivirus pneumonia or acute equine respiratory syndrome, is an acute, viral respiratory infection of horses and humans that has been reported in Australia. Nipah Virus infection, also known as Nipah Virus encephalitis, was first isolated and described in 1999. The name, Nipah, is derived from the village in Malaysia where the person from whom the virus was first isolated succumbed to the disease. Nipah Virus is a disease listed in the World Organization for Animal Health (OIE: Office International des Epizooties) Terrestrial Animal Health Code and must be reported to the OIE (OIE Terrestrial Animal Health Code). Hendra virus is not yet an OIE listed reportable disease.

Other Names: Porcine Respiratory and Encephalitis Syndrome, Porcine Respiratory and Neurologic Syndrome, Barking Pig Syndrome.[1-3]

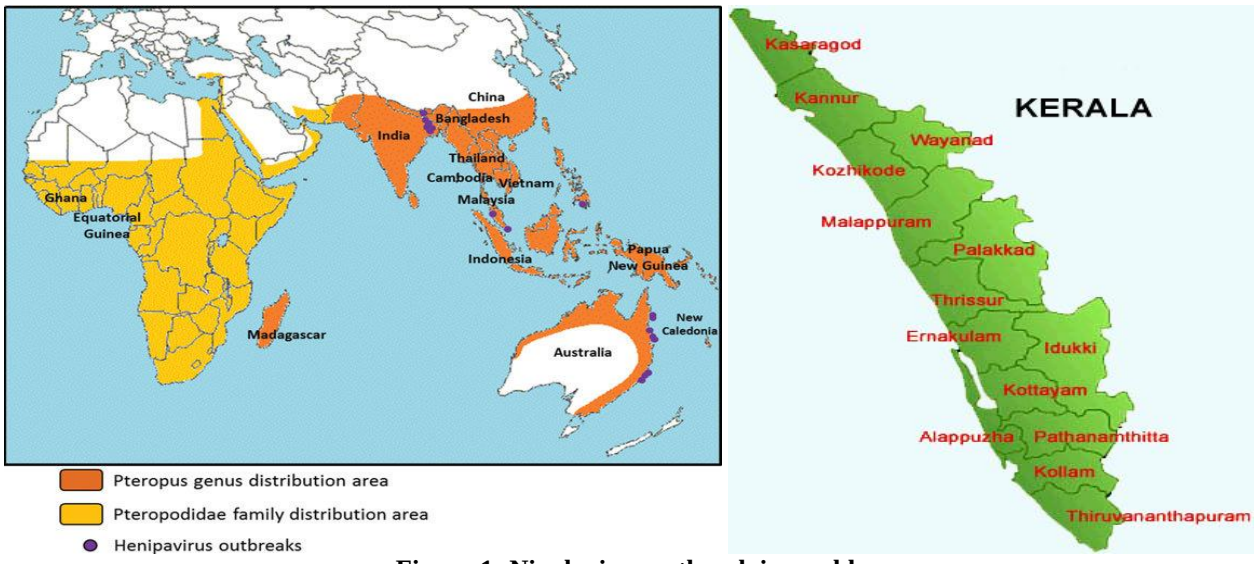

Figure-1: Nipah virus outbreak in world.

Nipah virus infection is a viral disease carried by fruit bats. It affects humans, pigs and occasionally other domesticated animals.

Outbreak of disease: There have been Nipah Virus infection outbreaks in pigs Malaysia and Singapore and human disease in Malaysia, Singapore, India and Bangladesh. Evidence of the virus without clinical disease has also been found in fruit bats in Cambodia, Thailand and Madagascar.

Transmission and spreading of Nipah virus: Fruit bats, also known as 'flying foxes' of the genus Pteropus are natural reservoir hosts of the Nipah and Hendra viruses. The virus is present in bat urine and potentially, bat feces, saliva and birthing fluids. Perhaps as a result of deforestation programmes, the Malaysian pig farms where the disease first originated had fruit trees which attracted the bats from the tropical forest, thus exposing domestic pigs to bat urine and feces. It is thought that these excretions and secretions initiated 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, vehicles, etc.

Figure-2: Fruit bats (the host) and Nipah virion.

Public Health Risk: Nipah Virus is a zoonotic disease. Transmission to humans in Malaysia and Singapore has almost always been from direct, contact with the excretions or secretions of infected pigs. Reports from outbreaks in Bangladesh suggest transmission from bats without an intermediate host by drinking raw palm sap contaminated with bat excrement, or climbing trees coated in bat excrement. In Bangladesh and India, there have been reports of possible human-to-human transmission of the disease so precautions are necessary for hospital workers caring for infected patients. Precautions should also be taken when submitting and handling laboratory samples, as well as in slaughterhouses. Typically the human infection presents as an encephalitic syndrome marked by fever, headache, drowsiness, disorientation, mental confusion, coma and potentially death. During the outbreak in Malaysia, up to 50% of clinically apparent human cases died. There is no specific treatment for Nipah Virus. Supportive care is the general treatment for this disease.

Clinical Signs: Nipah Virus in pigs affects the respiratory and nervous systems. It is known as porcine respiratory and neurologic syndrome, Porcine Respiratory and Encephalitic Syndrome (PRES) and Barking Pig Syndrome (BPS). It is a highly contagious disease in pigs; however the clinical signs vary depending on the age and the individual animal's response to the virus. In general, mortality (death due to the disease) is low except in piglets. However, morbidity (illness from the disease) is high in all age groups. Most pigs develop a febrile respiratory disease with a severe cough and difficulty breathing. While the respiratory signs predominate, encephalitis has been described, particularly in sows and boars, with nervous signs including twitching, trembling, muscle fasciculation, spasms, muscle weakness, convulsions and death. Some animals, however, remain asymptomatic. Natural infection of dogs with NiV causes distemper like syndrome with a high mortality (death) rate.

Diagnosis: The disease is difficult to diagnose based on clinical signs alone, however confirmation can be made through prescribed laboratory tests (OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals).

Prevention & Control: Prevention and control measures focus on immediate eradication by mass culling of infected and in-contact pigs and on antibody surveillance of high risk farms to prevent future outbreaks. After culling, the burial sites are disinfected with chlorinated lime. It is also recommended to use sodium hypochlorite (bleach) to disinfect the contaminated areas and equipment. Other important control measures have been

a ban on transporting pigs within the countries affected, a temporary ban on pig production in the regions affected, as well as improvement of biosecurity practices. Education and use of personal protective equipment (PPE) by persons exposed to potentially infected pigs is highly recommended. Also, improved hygiene at pig operations is suggested. One of the most important biosecurity measures for affected areas is to decrease the likelihood of the bat reservoir coming into contact with pig production facilities. Research into development of vaccines has been ongoing in Australia and France.[4-6]

Nipah Virus (NiV) Infection: Nipah virus (NiV) infection is a newly emerging zoonosis that causes severe disease in both animals and humans. The natural host of the virus is fruit bats of the *Pteropodidae* Family, Pteropus genus. NiV was first identified during an outbreak of disease that took place in Kampung Sungai Nipah, Malaysia in 1998. On this occasion, pigs were the intermediate hosts. However, in subsequent NiV outbreaks, there were no intermediate hosts. In Bangladesh in 2004, humans became infected with NiV as a result of consuming date palm sap that had been contaminated by infected fruit bats. Human-to-human transmission has also been documented, including in a hospital setting in India. NiV infection in humans has a range of clinical presentations, from asymptomatic infection to acute respiratory syndrome and fatal encephalitis. NiV is also capable of causing disease in pigs and other domestic animals. There is no vaccine for either humans or animals. The primary treatment for human cases is intensive supportive care.

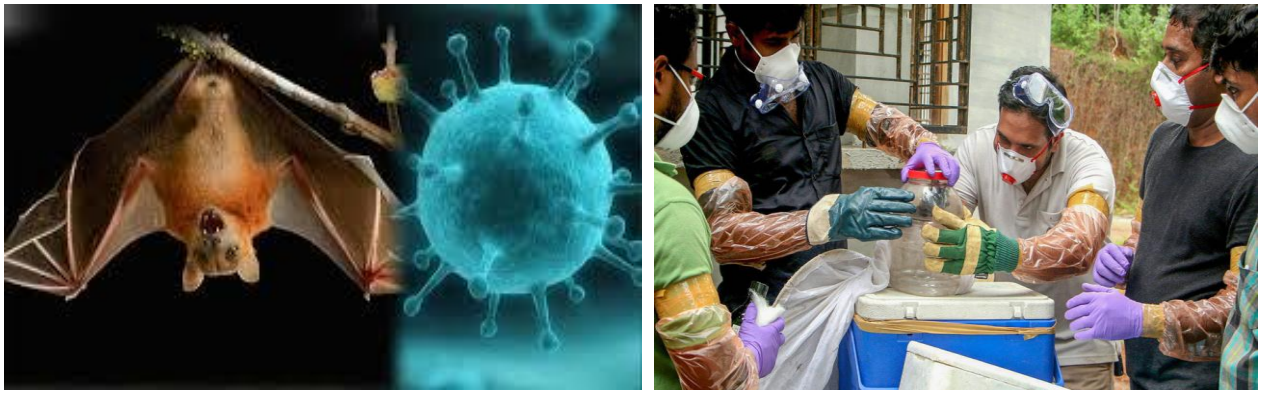

Figure-3: Virus with host & medication.

Henipavirus is a genus of RNA viruses in the family Paramyxoviridae, order Mononegavirales containing five established species. Henipaviruses are naturally harbored by pteropid fruit bats (flying foxes) and microbats of several species. Henipaviruses are characterized by long genomes and a wide host range. Their recent emergence as zoonotic pathogens capable of causing illness and death in domestic animals and humans is a cause of concern. In 2009, RNA sequences of three novel viruses in phylogenetic relationship to known henipaviruses were detected in African straw-colored fruit bats (*Eidolon helvum*) in Ghana. The finding of these novel henipaviruses outside Australia and Asia indicates that the region of potential endemicity of henipaviruses may be worldwide. These African henipaviruses are slowly being characterized.[7-9]

Group: Group V ((−)ssRNA), Order: Mononegavirales, Family: Paramyxoviridae, Genus: Henipavirus

Type species: *Hendra henipavirus.*

Species: *Cedar henipavirus*, *Ghanaian bat henipavirus*, *Hendra henipavirus*, *Mojiang henipavirus*, *Nipah henipavirus.*

Genus Henipavirus: species and their viruses.

Table 1: Henipavirus genus and species.

Genus	Species	Virus (Abbreviation)
Henipavirus	*Cedar henipavirus*	Cedar virus (CedV)
	Ghanaian bat henipavirus	Kumasi virus (KV)
	Hendra henipavirus	Hendra virus (HeV)
	Mojiang henipavirus	Mòjiāng virus (MojV)
	Nipah henipavirus	Nipah virus (NiV)

Virus structure: Henipavirions are pleomorphic (variably shaped), ranging in size from 40 to 600 nm in diameter. They possess a lipid membrane overlying a shell of viral matrix protein. At the core is a single helical strand of genomic RNA tightly bound to N (nucleocapsid) protein and associated with the L (large) and P (phosphoprotein) proteins, which provide RNA polymerase activity during replication. Embedded within the lipid membrane are spikes of F (fusion) protein trimers and G (attachment) protein tetramers. The

function of the G protein is to attach the virus to the surface of a host cell via EFNB2, a highly conserved protein present in many mammals. The structure of the attachment glycoprotein has been determined by X-ray crystallography. The F protein fuses the viral membrane with the host cell membrane, releasing the virion contents into the cell. It also causes infected cells to fuse with neighboring cells to form large, multinucleated syncytia.

Genome structure: As all mononegaviral genomes, Hendra virus and Nipah virus genomes are non-segmented, single-stranded negative-sense RNA. Both genomes are 18.2 kb in length and contain six genes corresponding to six structural proteins. In common with other members of the Paramyxoviridae family, the number of nucleotides in the henipavirus genome is a multiple of six, consistent with what is known as the 'rule of six'. Deviation from the rule of six, through mutation or incomplete genome synthesis, leads to inefficient viral replication, probably due to structural constraints imposed by the binding between the RNA and the N protein. Henipaviruses employ an unusual process called RNA editing to generate multiple proteins from a single gene. The specific process in henipaviruses involves the insertion of extra guanosine residues into the P gene mRNA prior to translation. The number of residues added determines whether the P, V or W proteins are synthesized. The functions of the V and W proteins are unknown, but they may be involved in disrupting host antiviral mechanisms.[10-12]

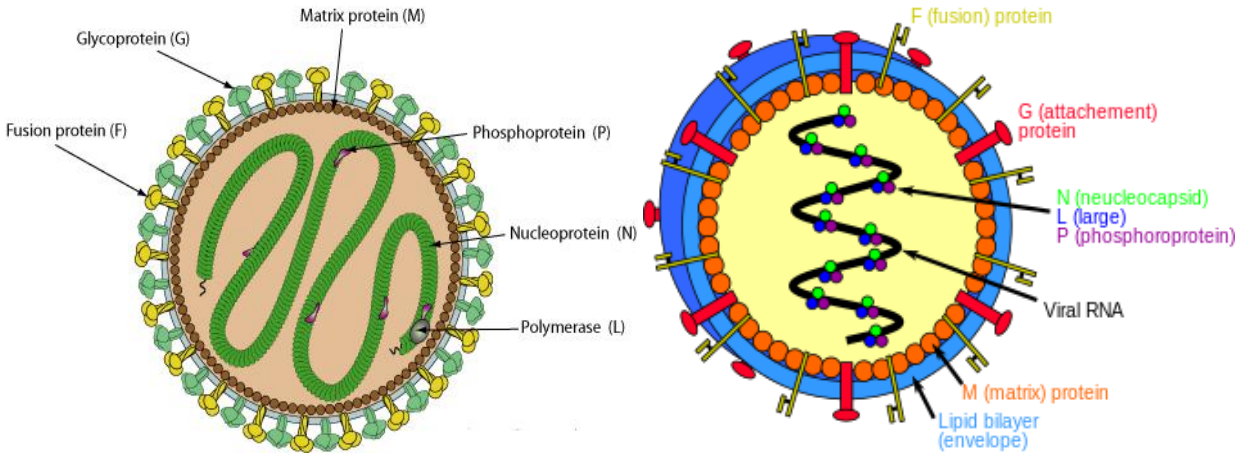

Figure-4: Hendra Virus and Nipah Virus genome.

History: Nipah virus was identified in April 1999, when it caused an outbreak of neurological and respiratory disease on pig farms in peninsular Malaysia, resulting in 257 human cases, including 105 human deaths and the culling of one million pigs. In Singapore, 11 cases, including one death, occurred in abattoir workers exposed to pigs imported from the affected Malaysian farms. The Nipah virus has been classified by the Centers for Disease Control and Prevention as a Category C agent. The name "Nipah" refers to the place, Kampung Baru Sungai Nipah in Port Dickson, Negeri Sembilan, the source of the human case from which Nipah virus was first isolated. Nipah virus is one of several viruses identified by WHO as a likely cause of a future epidemic in a new plan developed after the Ebola epidemic for urgent research and development before and during an epidemic toward new diagnostic tests, vaccines and medicines. The outbreak was originally mistaken for Japanese encephalitis (JE), however, physicians in the area noted that persons who had been vaccinated against JE were not protected, and the number of cases among adults was unusual. Despite the fact that these observations were recorded in the first month of the outbreak, the Ministry of Health failed to react accordingly, and instead launched a nationwide campaign to educate people on the dangers of JE and its vector, Culex mosquitoes.

Figure-5: Reservoir Host & Spillover Host of Nipah Virus.

Symptoms of infection from the Malaysian outbreak were primarily encephalitic in humans and respiratory in pigs. Later outbreaks have caused respiratory illness in humans, increasing the likelihood of human-to-human transmission and indicating the existence of more dangerous strains of the virus. Symptoms also include breathing trouble, inflammation of the brain, fever, headache, drowsiness, disorientation and delirium. Based on seroprevalence data and virus isolations, the primary reservoir for Nipah virus was identified as Pteropid fruit bats, including *Pteropus vampyrus* (Large Flying Fox) and *Pteropus hypomelanus* (Small flying fox), both of which occur in Malaysia. The transmission of Nipah virus from flying foxes to pigs is thought to be due to an increasing overlap between bat habitats and piggeries in peninsular Malaysia. At the index farm, fruit orchards were in close proximity to the piggery, allowing the spillage of urine, faeces and partially eaten fruit onto the pigs. Retrospective studies demonstrate that viral spillover into pigs may have been occurring in Malaysia since 1996 without detection. During 1998, viral spread was aided by the transfer of infected pigs to other farms, where new outbreaks occurred.[13-15]

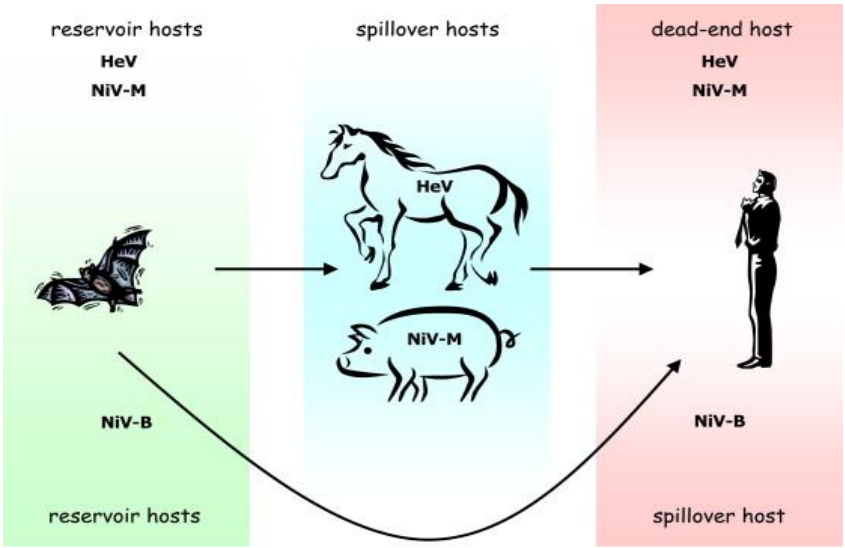

Figure-6: Cycle of Nipah Virus (NiV) & Hendra Virus (HeV).

Evolution: The most likely origin of this virus was in 1947 (95% credible interval: 1888–1988). There are two clades of this virus—one with its origin in 1995 (95% credible interval: 1985–2002) and a second with its origin in 1985 (95% credible interval: 1971–1996). The mutation rate was estimated to be 6.5×10^{-4} substitution/site/year (95% credible interval: 2.3×10^{-4} – 1.18×10^{-3}), similar to other RNA viruses.

Outbreaks: Locations of henipavirus outbreaks (red stars–*Hendra virus*; blue stars–*Nipah virus*) and distribution of henipavirus flying fox reservoirs (red shading–*Hendra virus*; blue shading–*Nipah virus*).

Eight more outbreaks of Nipah virus have occurred since 1998, all within Bangladesh and neighboring parts of India. The outbreak sites lay within the range of Pteropus species (*Pteropus giganteus*). As with Hendra virus, the timing of the outbreaks indicates a seasonal effect. Cases occurring in Bangladesh during the winters of 2001, 2003, and 2004, were determined to have been caused by the Nipah virus.

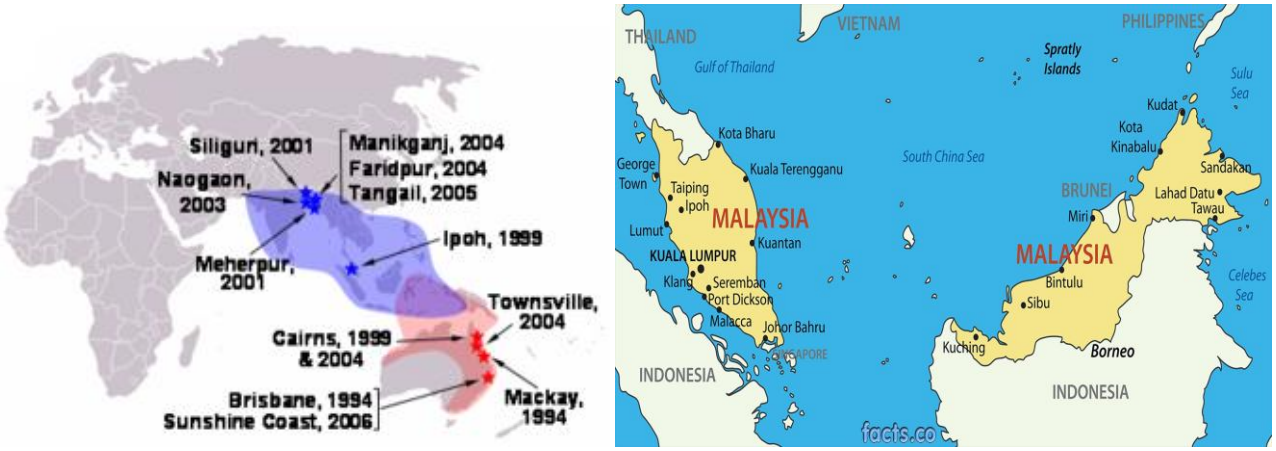

Figure-7: Zonal epidemic of Nipah Virus.

In February 2011, a Nipah outbreak began at Hatibandha Upazila in the Lalmonirhat District of northern Bangladesh. To date (7 February 2011), there have been 24 cases and 17 deaths in this outbreak. 2001 January 31–23 February, Siliguri, India: 66 cases with a 74% mortality rate. 75% of patients were either hospital staff or had visited one of the other patients in hospital, indicating person-to-person transmission. 2001 April – May, Meherpur District, Bangladesh: 13 cases with nine fatalities (69% mortality). 2003 January, Naogaon District, Bangladesh: 12 cases with eight fatalities (67% mortality). 2004 January – February, Manikganj and Rajbari districts, Bangladesh: 42 cases with 14 fatalities (33% mortality). 2004 19 February – 16 April, Faridpur District, Bangladesh: 36 cases with 27 fatalities (75% mortality). 92% of cases involved close contact with at least one other person infected with Nipah virus. Two cases involved a single short exposure to an ill patient, including a rickshaw driver who transported a patient to hospital. In addition, at least six cases involved acute respiratory distress syndrome, which has not been reported previously for Nipah virus illness in humans. This symptom is likely to have assisted human-to-human transmission through large droplet dispersal. 2005 January, Tangail District, Bangladesh: 12 cases with 11 fatalities (92% mortality). The virus was probably contracted from drinking date palm juice contaminated by fruit bat droppings or saliva. 2007 February – May, Nadia District, India: up to 50 suspected cases with 3–5 fatalities. The outbreak site borders the Bangladesh district of Kushtia where eight cases of Nipah virus encephalitis with five fatalities occurred during March and April 2007. This was preceded by an outbreak in Thakurgaon during January and February affecting seven people with three deaths. All three outbreaks showed evidence of person-to-person transmission. 2008 February – March, Manikganj and Rajbari districts, Bangladesh: Nine cases with eight fatalities. 2010 January, Bhanga subdistrict, Faridpur, Bangladesh: Eight cases with seven fatalities. During March, one physician of Faridpur Medical College Hospital caring for confirmed Nipah cases died. 2011 February: An outbreak of Nipah Virus has occurred at Hatibandha, Lalmonirhat, Bangladesh. The deaths of 21 schoolchildren due to Nipah virus infection were recorded on 4 February 2011. IEDCR has confirmed the infection is due to this virus. Local schools were closed for one week to prevent the spread of the virus. People were also requested to avoid consumption of uncooked fruits and fruit products. Such foods, contaminated with urine or saliva from infected fruit bats, were the most likely source of this outbreak. 2018 May: Deaths of 6 people in Perambra near Calicut, Kerala, India have been confirmed as a result of the virus.

Nipah virus has been isolated from Lyle's flying fox (*Pteropus lylei*) in Cambodia and viral RNA found in urine and saliva from *Pteropus lylei* and Horsfield's roundleaf bat (*Hipposideros larvatus*) in Thailand. Infective virus has also been isolated from environmental samples of bat urine and partially eaten fruit in Malaysia. 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 have been observed in Cambodia, Thailand or Africa thus far.[16-18]

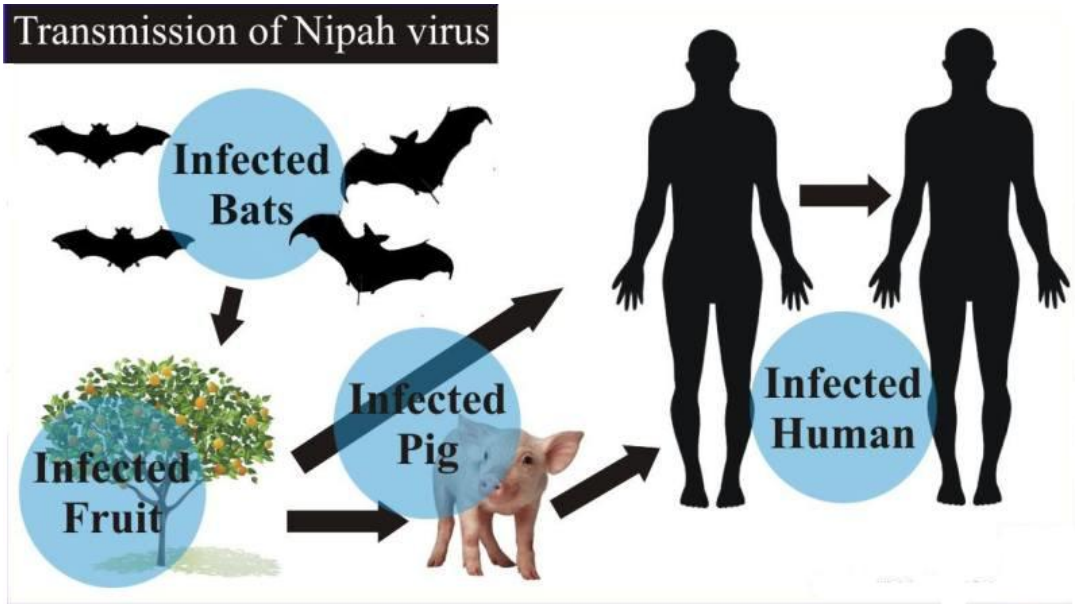

Figure-8: Nipah Virus Transmission.

Pathology: In humans, the infection presents as fever, headache and drowsiness. Cough, abdominal pain, nausea, vomiting, weakness, problems with swallowing and blurred vision are relatively common. About a quarter of the patients have seizures and about 60% become comatose and might need mechanical ventilation. In patients with severe disease, their conscious state may deteriorate and they may develop severe hypertension, fast heart rate and very high temperature. Nipah virus is also known to cause relapse encephalitis. In the initial Malaysian outbreak, a patient presented with relapse encephalitis some 53 months after his initial infection. There is no definitive treatment for Nipah encephalitis, apart from supportive measures, such as mechanical ventilation and prevention of secondary infection. Ribavirin, an antiviral drug, was tested in the Malaysian outbreak and the results were encouraging, though further studies are still needed. While no vaccine currently exists, a recent (2012) study of a trial vaccine developed using the outer proteins of *Hendra* virus was shown to induce protection against *Nipah* in African Green Monkeys. In animals, especially in pigs, the virus causes a porcine respiratory and neurologic syndrome, locally known as "barking pig syndrome" or "one mile cough." Ephrin B2 has been identified as the main receptor for the henipaviruses. Treatment is limited to supportive care. Because Nipah virus encephalitis can be transmitted person-to-person, standard infection control practices and proper barrier nursing techniques are important in preventing hospital-acquired infections (nosocomial transmission). The drug ribavirin has been shown to be effective against the viruses *in-vitro*, but human investigations to date have been inconclusive and the clinical usefulness of ribavirin remains uncertain. Passive immunization using a human monoclonal antibody targeting the Nipah G glycoprotein has been evaluated in the post-exposure therapy in the ferret model and found to be of benefit. Initial signs and symptoms of NiV infection are non-specific and the diagnosis is often not suspected at the time of presentation. This can hinder accurate diagnosis and creates challenges in outbreak detection and institution of effective and timely infection control measures and outbreak response activities. In addition, clinical sample quality, quantity, type, timing of collection and the time necessary to transfer samples from patients to the laboratory can affect the accuracy of laboratory results. NiV infection can be diagnosed together with clinical history during the acute and convalescent phase of the disease. Main tests including real time polymerase chain reaction (RT-PCR) from bodily fluids as well as antibody detection via ELISA. Different tests include: enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR) assay, virus isolation by cell culture. There are currently no drugs or vaccines specific for NiV infection although this is a priority disease on the WHO R&D Blueprint. Intensive supportive care is recommended to treat severe respiratory and neurologic complications.[19,20]

Conclusion: Nipah virus (NiV) is a member of the family Paramyxoviridae, genus Henipavirus. NiV was initially isolated and identified in 1999 during an outbreak of encephalitis and respiratory illness among pig farmers and people with close contact with pigs in Malaysia and Singapore. Its name originated from Sungai Nipah, a village in the Malaysian Peninsula where pig farmers became ill with encephalitis. Given the relatedness of NiV to Hendra virus, bat species were quickly singled out for investigation and flying foxes of the genus Pteropus were subsequently identified as the reservoir for NiV (Distribution Map). In the 1999 outbreak, Nipah virus caused a relatively mild disease in pigs, but nearly 300 human cases with over 100 deaths were reported. In order to stop the outbreak, more than a million pigs were euthanized, causing tremendous trade loss for Malaysia. Since this outbreak, no subsequent cases (in neither swine nor human) have been reported in

either Malaysia or Singapore. In 2001, NiV was again identified as the causative agent in an outbreak of human disease occurring in Bangladesh. Genetic sequencing confirmed this virus as Nipah virus, but a strain different from the one identified in 1999. In the same year, another outbreak was identified retrospectively in Siliguri, India with reports of person-to-person transmission in hospital settings (nosocomial transmission). Unlike the Malaysian NiV outbreak, outbreaks occur almost annually in Bangladesh and have been reported several times in India.

Figure-9: Transmission of Nipah Virus.

Transmission: Transmission of Nipah virus to humans may occur after direct contact with infected bats, infected pigs, or from other NiV infected people. In Malaysia and Singapore, humans were apparently infected with Nipah virus only through close contact with infected pigs. The NiV strain identified in this outbreak appeared to have been transmitted initially from bats to pigs, with subsequent spread within pig populations. Incidental human infections resulted after exposure to infected pigs. No occurrence of person-to-person transmission was reported in this outbreak. Conversely, person-to-person transmission of Nipah virus in Bangladesh and India is regularly reported. This is most commonly seen in the family and caregivers of Nipah virus-infected patients. Transmission also occurs from direct exposure to infected bats. A common example is consumption of raw date palm sap contaminated with infectious bat excretions.

Signs and Symptoms: Infection with Nipah virus is associated with encephalitis (inflammation of the brain). After exposure and an incubation period of 5 to 14 days, illness presents with 3-14 days of fever and headache, followed by drowsiness, disorientation and mental confusion. These signs and symptoms can progress to coma within 24-48 hours. Some patients have a respiratory illness during the early part of their infections, and half of the patients showing severe neurological signs showed also pulmonary signs. During the Nipah virus disease outbreak in 1998-99, 265 patients were infected with the virus. About 40% of those patients who entered hospitals with serious nervous disease died from the illness. Long-term sequelae following Nipah virus infection have been noted, including persistent convulsions and personality changes. Latent infections with subsequent reactivation of Nipah virus and death have also been reported months and even years after exposure.

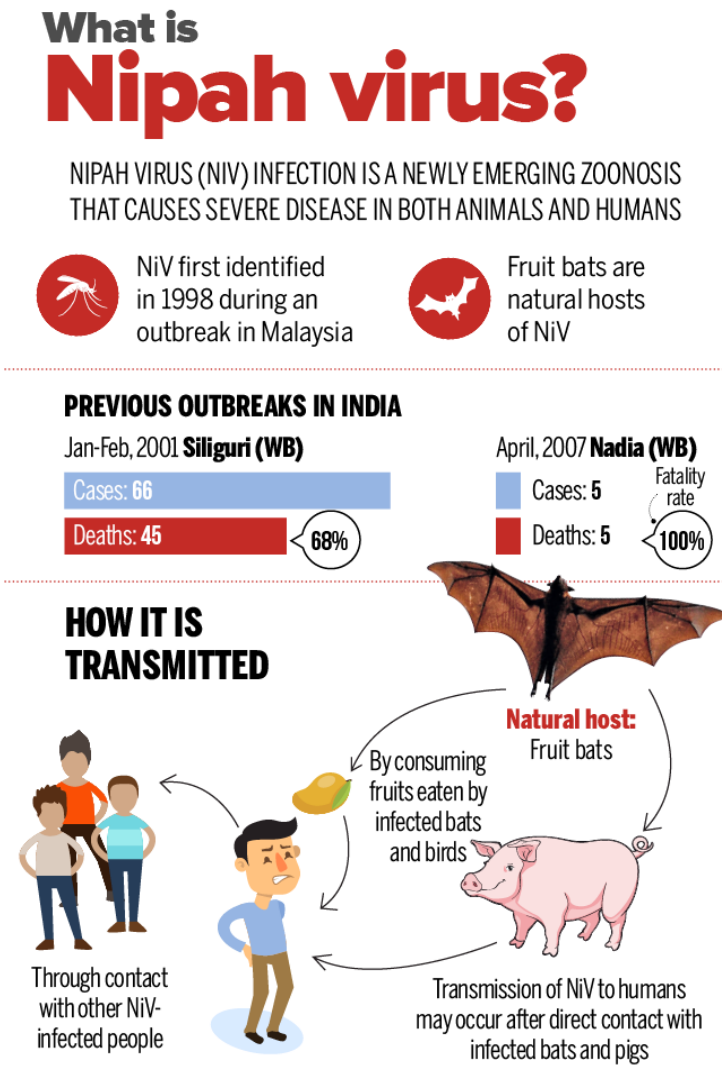

Figure-10: Nipah Virus zoonosis.

Risk of Exposure: In the Malaysia and Singapore outbreak, Nipah virus infection was associated with close contact with Nipah virus-infected pigs. In Bangladesh and India, where Nipah virus infection is more frequent, exposure has been linked to consumption of raw date palm sap and contact with bats. Importantly, human-to-human transmission has been documented and exposure to other Nipah virus infected individuals is also a risk factor.

Diagnosis: Laboratory diagnosis of a patient with a clinical history of NiV can be made during the acute and convalescent phases of the disease by using a combination of tests. Virus isolation attempts and real time polymerase chain reaction (RT-PCR) from throat and nasal swabs, cerebrospinal fluid, urine, and blood should be performed in the early stages of disease. Antibody detection by ELISA (IgG and IgM) can be used later on. In fatal cases, immune-histochemistry on tissues collected during autopsy may be the only way to confirm a diagnosis.

Treatment: Treatment is limited to supportive care. Because Nipah virus encephalitis can be transmitted person-to-person, standard infection control practices and proper barrier nursing techniques are important in preventing hospital-acquired infections (nosocomial transmission). The drug ribavirin has been shown to be effective against the viruses *in-vitro*, but human investigations to date have been inconclusive and the clinical usefulness of ribavirin remains uncertain. Passive immunization using a human monoclonal antibody targeting the Nipah G glycoprotein has been evaluated in the post-exposure therapy in the ferret model and found to be of benefit.

Prevention: Nipah virus infection can be prevented by avoiding exposure to sick pigs and bats in endemic areas and not drinking raw date palm sap. Additional efforts focused on surveillance and awareness will help prevent future outbreaks. Research is needed to better understand the ecology of bats and Nipah virus, investigating questions such as the seasonality of disease within reproductive cycles of bats. Surveillance tools should

include reliable laboratory assays for early detection of disease in communities and livestock, and raising awareness of transmission and symptoms is important in reinforcing standard infection control practices to avoid human-to-human infections in hospital settings (nosocomial). A subunit vaccine, using the Hendra G protein, produces cross-protective antibodies against HENV and NIPV has been recently used in Australia to protect horses against Hendra virus. This vaccine offers great potential for henipavirus protection in humans as well.

Herbal Medicine for Nipah Virus: *Nyctanthes arbor-tristis* (pavala malli leaves) [Parijatha Leaves]: Take 6 leaves, put it in 200ml water and Boil it and make into 100ml decoction. At the end put pepper powder and 3 drops of lemon. Drink the Kashaya 3-4 times a day. Gelsemium 200, Homeopathy medicine for Nipah Virus, Weekly 3 doses for 3 weeks. Ignatia-30 3 Drops a day.

REFERENCES

1. Broder CC. Henipavirus outbreaks to antivirals: the current status of potential therapeutics. Current Opinion Virology, 2012; 2(2): 176-87.
2. Chadha MS, Comer JA, Lowe L, et al. Nipah virus-associated encephalitis outbreak, Siliguri, India. Emerging Infectious Disease, 2006; 12(2): 235-40.
3. Chua KB, Goh KJ, Wong KT, et al. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. Lancet, 1999; 354(9186): 1257-9.
4. Daniels P, Ksiazek T, Eaton BT. Laboratory diagnosis of Nipah and Hendra virus infections. Microbes and Infection, 2001; 3(4): 289-95.
5. Field HE, Mackenzie JS, Daszak P. Henipaviruses: emerging paramyxoviruses associated with fruit bats. Current Topics Microbiology and Immunology, 2007; 315: 133-59.
6. Gurley ES, Montgomery JM, Hossain MJ, et al. Person-to-person transmission of Nipah virus in a Bangladeshi community. Emerging Infectious Disease, 2007; 13(7): 1031-7.
7. Hossain MJ, Gurley ES, Montgomery JM, et al. Clinical presentation of Nipah virus infection in Bangladesh. Clinical Infectious Diseases, 2008; 46(7): 977-84.
8. Lim CCT, Lee KE, Lee WL, et al. Nipah virus encephalitis: Serial MR study of an emerging disease. Radiology, 2002; 222(1): 219-26.
9. Luby SP, Gurley ES, Hossain MJ. Transmission of human infection with Nipah virus. Clinical Infectious Disease, 2009; 49(11): 1743-8.
10. Mounts AW, Kaur H, Parashar UD, et al. A cohort study of health care workers to assess nosocomial transmissibility of Nipah virus, Malaysia, 1999. Journal of Infectious Disease, 2001; 183(5): 810-3.
11. Murray K, Selleck P, Hooper P, et al. A morbillivirus that caused fatal disease in horses and humans. Science, 1995; 268: 94-7.
12. Paton NI, Leo YS, Zaki SR, et al. Outbreak of Nipah-virus infection among abattoir workers in Singapore. Lancet, 1999; 354(9186): 1253-6.
13. Rahman MA, Hossain MJ, Sultana S, et al. Date Palm Sap Linked to Nipah Virus Outbreak in Bangladesh, 2008. VectorBorne and Zoonotic Disease, 2012; 12(1): 65-73.
14. Reynes J-M, Counor D, Ong S, et al. Nipah virus in Lyle's Flying Foxes, Cambodia. Emerging Infectious Disease, 2005; 11(7): 1042-7.
15. Rollin PE, Rota P, Zaki S, Ksiazek TG. Hendra and Nipah viruses. in: Versalovic J, Carroll KC, Funke G, Jorgensen JH, Landry ML, Warnock DW, editors. Manual of Clinical Microbiology. 10th ed. Washington, DC: ASM Press, 2011; 1479-87.
16. Sim BF, Jusoh MR, Chang CC, Khalid R. Nipah Encephalitis: A report of 18 patients from Kuala Lumpur Hospital. Neurology Journal Southeast Asia, 2002; 7: 13-8.
17. Tan CT, Goh KJ, Wong KT, et al. Relapsed and Late-Onset Nipah Encephalitis. Ann. Neurology, 2002; 51(6): 703-8.
18. Wacharapluesadee S, Boongird K, Wanghongsa S, et al. A Longitudinal Study of the Prevalence of Nipah Virus in Pteropus lylei Bats in Thailand: Evidence for Seasonal Preference in Disease Transmission. Vector-Borne and Zoonotic Disease, 2010; 10(2): 183-90.
19. Williamson M, Torres-Velez FJ. Henipavirus: a review of laboratory animal pathology. Veterinary Pathology, 2010; 47(5): 871-80.
20. Wong KT, Shieh WJ, Kumar S, et al. Nipah virus infection. Pathology and pathogenesis of an emerging paramyxoviral zoonosis. American Journal of Pathology, 2002; 161(6): 2153-67.