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Research Article

Study The Epidemiology, Pathology And Prior Epidemis Of The Zoonotic Nipah Virus

Abhishek Katwal¹, Arshit Thakur^{*2}, Palvi Sharma³

^{1,2}Student, Abhilashi College of Pharmacy, Nerchowk ,Mandi, H.P.175008 ³Assistant Professor, Abhilashi College of Pharmacy, Nerchowk ,Mandi, H.P.175008

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ABSTRACT

The Nipah virus (NiV) is a zoonotic infection that is very dangerous to animal and human populations alike. This abstract explores the pathology, epidemiology, and historical context of NiV, providing insight into its intricate nature. According to epidemiology, fruit bats belonging to the Pteropus genus serve as the natural reservoir hosts for NiV. Direct contact with sick bats or their excrement, as well as ingestion of contaminated fruits or date palm sap, are common routes of human transmission. Furthermore, human-to-human transmission has been reported, especially in hospital environments, where it has resulted in outbreaks of various sizes. Pathologically, NiV infection can show up as a wide range of clinical presentations, from mild feverish illness or no symptoms at all to serious neurological and respiratory problems, including encephalitis. The virus causes vascular leakage and multi-organ dysfunction syndrome (MODS) because it has a preference for endothelial cells. Those who suffer from neurological sequelae often die at high rates, making them especially deadly. In the past, epidemics of NiV have been linked to South and Southeast Asia, specifically to Bangladesh, India, Malaysia, and Singapore. When the virus first appeared in Malaysia in 1998, pig breeders had an outbreak, which led to human infection. In Bangladesh, outbreaks in the past have been connected to eating raw date palm sap tainted with bat excrement. For successful prevention, detection, and control methods, it is essential to comprehend the epidemiology, pathophysiology, and historical background of NiV. It is imperative to maintain vigilant monitoring of bat populations, adopt appropriate hygiene measures, and promptly address outbreaks in order to effectively reduce the danger associated with this fatal zoonotic virus.

INTRODUCTION

The nipah virus is a newly discovered zoonotic pathogen that kills 40–75% of human cases by

causing severe febrile encephalitis. The high death rate of the Nipah virus and the lack of effective vaccinations or therapeutics make it a disease with

*Corresponding Author: Arshit Thakur

Address: Student, Abhilashi College of Pharmacy, Nerchowk , Mandi, H.P.175008

Email : arshitthakur921@gmail.

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a biosafety level-4 and a select agent with high risk for public health and security. Pteropus fruit bats are the natural reservoir for the Nipah virus and related Henipavirus species. When people came into touch with live, infected pigs, the nipah virus, which causes neurologic and respiratory diseases in pigs, first appeared in Malaysia in 1998. The examined research in this paper indicates that the root causes of the observed phenomena were anthropogenic forces, such as agricultural intensification and expansion.Between 2001 and 2005, Bangladesh had five further epidemics brought on by the Nipah virus. In this case, it seems to have spread straight from bats to people, and person-to-person transmission is visible, indicating a higher risk to the public's health (1).

What is Nipahvirus

The Nipah virus (NiV) is a paramyxovirus belonging to the Henipavirus genus, Paramyxovirinae subfamily, Paramyxoviridae family, order Mononegavirales. It is a newly discovered virus that can cause fatal encephalitis and severe respiratory illnesses in people. It is an enclosed, single-stranded, nonsegmented RNA virus with negative sense and helical symmetry. Six genes, namely nucleocapsid (N). phosphoprotein (P), matrix fusion (M), glycoprotein (F), attachment glycoprotein (G), and long polymerase (L), are arranged consecutively in the RNA genome from $3\sim-5\sim$. The virus ribonucleoprotein (vRNP) was formed when the N, P, and L bonded to the viral RNA. According to Ternhag and Penttinen, the F and G proteins are in charge of the virion's cellular attachment and subsequent host cell penetration.(2).

Diagnosis

Virus detection specimens can be obtained from symptomatic individuals or during post-mortem examinations. Samples for serological analysis ought to be gathered 10–14 days after the start of the infection, late in the course of it. For diagnosis, the NCDC in India suggests using throat swabs (in viral transport medium), blood, urine, and/or CSF. Samples need to be gathered securely and delivered in triplicate containers at between 2 and 8 °C. It is advised to store at -20°C after 48 hours of collection. The clinical sample processing needs to be done in a BSL 4 facility. Nonetheless, sample irradiation may be a useful method for virus inactivation, rendering the samples safe for use in a BSL-2 laboratory (3). The monoclonal antibodybased antigen capture ELISA, which is used for NiV detection and discrimination from HeV, is one type of enzyme-linked immunosorbent assay (ELISA) that is frequently used for antibody detection. Recombinant full-length N protein and shortened G protein have recently been used in ELISA experiments to identify virus-specific antibodies, especially in serum samples from pigs. For the purpose of screening porcine serum samples, the High Security Animal Disease Laboratory (HSADL) in Bhopal has also created an ELISA based on recombinant N protein. Furthermore, in pig and ruminant sera, including those from goats and cattle, antibodies against NiV glycoprotein sG have been found using a microsphere assay based on luminex technology (7). Real-time polymerase chain reaction (RT-PCR) from biological fluids and enzyme-linked immunosorbent assay (ELISA) for antibody detection are the two primary assays used. The polymerase chain reaction (PCR) assay and virus isolation by cell culture are two other techniques employed. enzyme-linked that are An immunosorbent assay (ELISA) is used to test for antibodies later in the course of the illness and after recovery(14).

Factors affecting for outbreaks

Epidemics can be caused by a variety of factors, including anthropogenic, environmental, and biological factors that upset environments and ecosystems. The onset of zoonotic outbreaks can be greatly influenced by these disturbances, which include deforestation, depletion of resources,



changes in natural landscapes, increasing farming and industrial activity, and climate change. In order to handle current and future outbreaks, it is essential to comprehend the epidemiological background of previous epidemics, such as the Nipah virus (NiV) outbreak, including its mode of transmission, preventive, and control strategies. By examining these elements, possible causes can be found and strategies for managing and preventing outbreaks can be informed(13).

NiV Transfer from Bats to Humans

Three routes of NiV transmission from bats to humans have been discovered by epidemiological studies conducted in Bangladesh. Ingestion of fresh date palm sap is the pathway most often implicated. Sap from date palms is collected in December and March, especially in west central Bangladesh. A sap hole is carved into the trunk of the tree, and over night, sap slowly seeps into an exposed clay pot. Studies using infrared cameras verify that P. giganteus bats often visit date palm sap plants and sip the sap when gathering it. Domestic animals are a second way that NiV might spread from bats to humans in Bangladesh. Partial-eaten fruit coated with saliva is frequently dropped by fruit bats. In Bangladesh, domestic animals hunt for these kinds of foods. On occasion, domestic animals are fed date palm sap that has been polluted with bat feces and is therefore unsafe for human consumption. NiV infection is possible in domestic animals, and they can spread the virus to people and other animals. In Meherpur, Bangladesh, in 2001, coming into contact with a sick cow was highly linked to contracting Nipah.

Third, direct contact with bat fluids contaminated with NiV may occur for certain individuals. Climbers had a higher risk of contracting NiV infection during the 2004 Goalando outbreak compared to control patients(4)

Sign and symptom

NiV was detected in the patients of the Malaysian outbreak, and it was discovered that in addition to

saliva and throat swabs, urine samples also contained traces of the virus. Thus, use caution if you are using the restroom with an infected individual (5). Both people and pigs can get symptoms from infections caused by the highly pathogenic Nipah virus (NiV). Notably, compared to humans, respiratory symptoms are typically more severe in pigs. Humans exposed to NiV have a severe and quickly spreading sickness that mainly affects the central nervous system (CNS) and respiratory system. (10). Typically, signs and symptoms appear 3-14 days following NiV exposure. Patients may first notice a sudden increase in body temperature, along with headaches and lethargy. Mental disorientation and confusion may then follow, quickly leading to a coma within one to two days.One of the most serious side effects of NiV infection is encephalitis, which frequently appears in the early stages and can include atypical pneumonia. Acute respiratory discomfort and coughing may be present in certain people (11). The symptoms indicate an incubation period of 5-14 days, an exposure period, and a fever and headache for 3-14 days, followed by the opposite symptoms.

The first signs and symptoms include body aches, headaches, fever, and tiredness, which are followed by confusion and disorientation. Coma may set in when these symptoms worsen in as little as 24 to 48 hours. The most terrifying side effect of a NiV infection is encephalitis. Moreover, respiratory impairment may exist in the early stages of the infection. Muscle aches, vomiting, and sore throat are possible further symptoms. Patients may experience gastrointestinal bleeding, renal failure, and septicemia in extreme circumstances. Within 24 to 48 hours, encephalitis can cause seizures that lead to a coma (12). Patients suffering from nipah cases who have respiratory problems are more likely to spread the virus than those who do not. People who exhibit



symptoms may have the sickness in the midst of an epidemic outbreak (5).

Signs and symptoms	Description		
Fever	Typically, high fever, often accompanied by headache		
Headache	Severe headache, often persistent		
Muscle pain	Muscle aches and pain ,sometimes severe		
Cough	Dry cough or respiratory symptoms		
Respiratory distress	Difficulty breathing, shortness of breath		
Encephalitiszures	In severe case, Nipha virus can cause inflammation of the brain		
	(encephalitis), leading to symptoms such as confusion,		
	disorientation, and seizures		
Coma	Some patients may are common		
Nausea and vomiting	Gastrointestinal symptoms are common		
Seizures	Seizures may occur in severe cases		
Altered consciousness	Confusion, delirium, or altered mental status		
Death	In severe cases, Nipha virus infection can be fatal		

Table of Sign and Symptoms

Epidemiology and diseases outbreak

NiV sickness was initially identified in Malaysia in 1998 in individuals who had come into contact with swine. When 11 male abattoir workers (average age: 44) in Singapore were exposed to an acute Nipah virus outbreak in March 1999 due to the importation of pig meat from Malaysia, one of them died. Patients had increased Nipah virus transmission. 1. Nipah viruses naturally occur in fruit bats. NiV fruit bats consume date palm sap as food. Fruit pulp solutions, which are high in sugar, are conducive to the survival of viruses. The origin and impact of the Nipah virus (NiV) on populations human are highlighted by epidemiological studies that show the chronology and spread of NiV outbreaks. NiV was first discovered in 1998 during an outbreak in Sungai Nipah, Malaysia, where pigs served as intermediate hosts for human transmission (8).

Then, in March 1999, 11 male workers in Singapore's abattoirs became acutely infected with NiV after consuming imported pig meat. Cases in Malaysia were initially misidentified as Japanese encephalitis or Hendra-like viral encephalitis; however, in 2000, the identity of the virus was established by NiV genome sequencing conducted at the CDC in the United States. In response, the Malaysian Ministry of Health declared 101 human fatalities and killed almost 900,000 pigs (7) In Kerala, India's Kozhikode area, there was a noteworthy outbreak in 2018. There, the index case is said to have acquired NiV from fruit-eating bats. The outbreak has a high fatality rate of 91% despite the lack of clinical or statistical proof (Arunkumar et al 2019). (7) Zoonotic virus outbreaks are caused by a number of variables, such as interactions between humans and animals in the context of changing environmental conditions and human-to-human contact(9). Comprehending these processes is crucial for devising efficacious preventative and control tactics.

Medication for NIV

Griffithsin/GRFT, a protein derived from red algae and its synthetic trimerictandemer (3mG), has demonstrated antiviral efficacy against NiV by obstructing viral entry and fusion (particularly syncytia formation) . Strong antiviral activities against NiV at low micromolar range have been demonstrated using R1479, a cytidine analogue with broad-spectrum antiviral Antiviral medications that target particular stages of the NiV



life cycle are undergoing testing. When NiV patients were treated with ribavirin, a broadspectrum nucleoside analog, during early outbreaks, there were some positive effects . A trial conducted during the first outbreak in Malaysia in 1998–1999 discovered a correlation between ribavirin medication and a 36% reduction in mortality as well as a decline in neurological impairments in survivors. Its efficacy during the 2018 outbreak in Kerala, India, was questionable, albeit Remdesivir demonstrated 100% survival in a deadly NiV challenge trial using the African green monkey (AGM) model when challenged against NiVinfection . When given immediately after infection for 14 days, favipiravir—a synthetic prodrug that suppresses the function of RdRpshowed total protection against the fatal NiVM infection in the Syrian golden hamster model.

At low doses (nanomoles), Griffithsinaction against flaviviruses . When tested against NiV infection, the broad-spectrum prodrug GS-5734 demonstrated anti-RNA production activity. A low (micromolar) concentration of 0.89-3.08 µM of ALS-8112, nucleoside another analogue, demonstrated strong antiviral activity against NiV in vitro tests. In order to stop the fusion of the viral envelope with the host plasma membrane, peptide fusion inhibitors were also created . In vitro NiV suppressed by chloroquine infection was treatment. NiV F protein activity is blocked by it. However, more investigation is needed to evaluate these medications' antiviral efficacy in their natural hosts. Subunit vaccines, which employ pieces of a pathogen's protein or glycoprotein to elicit a defense response in the immune system, are one potential strategy. For example, when given subcutaneously to cats, soluble G glycoprotein alone can stimulate the formation of serumneutralizing antibodies. For up to two months, vaccinated cats had noticeably greater antibody levels (titre ~20,000)(6). Clinical diagnosis and immunizationsSince there is no effective treatment

for NiV infection, prevention of the virus is essential.

- Intensive supportive care with a 70% morbidity rate is the main course of treatment.
- Nonetheless, reports of the death ratio range from 75% to 100%. The medication is recommended to supplement care.
- To stop the virus from spreading between people, it's critical to use appropriate barrier nursing techniques and conventional infection management procedures.
- Every suspected NiV infection case needs to be kept apart and get very close monitoring.
- Although ribavirin has demonstrated efficacy in in vitro experiments, human efficacy has not been established.
- In the ferret model, passive immunization with a human monoclonal antibody that targets the Nipah G glycoprotein has been studied as a post-exposure prophylactic measure (5).

Complication of nipah

The Nipah virus is a zoonotic virus, which means that people can contract it from animals. Since its initial discovery in Malaysia in 1998, outbreaks have taken place in a number of Southeast Asian nations. Infection with the Nipah virus can lead to the following complications:

1. Encephalitis:

Encephalitis is one of the most dangerous consequences of a Nipah virus infection. It is an inflammation of the brain. Frequent symptoms of encephalitis include headaches, fever, lightheadedness, drowsiness, and convulsions. In severe situations, a coma may cause death.

2. Respiratory issues:

Breathing problems, coughing, pneumonia, and other respiratory symptoms can also be brought on by the Nipah virus. Severe respiratory issues can lead to respiratory failure and death.

3. Long-term neurological effects:



Long-term neurological effects of a Nipah virus infection include changed personalities, chronic seizures, and cognitive deficits in survivors. These problems could significantly affect the impacted people's quality of life.

4. Relapse:

Some patients who survive a Nipah virus infection may experience relapses of the illness following an initial period of recovery. More problems could arise from severe relapses.

5. Spread to others:

Communities may experience outbreaks of the Nipah virus as a result of people living in close proximity to one another. Stopping the virus from spreading can be challenging, particularly in hospital settings where there is a chance of worker-patient transmission.

6. Death:

In prior outbreaks, the death rate from Nipah virus infection ranged from 40% to 75%. The virulence of the viral strain and the accessibility of medical care are two examples of variables that may affect mortality rates.

7. Economic impact:

Nipah virus epidemics can have a major negative impact on the economy because of increased medical expenses, lost productivity, trade restrictions, and harm to sectors including tourism and agriculture.

Medication and treatment

An individual with NiV infection may exhibit a range of clinical manifestations, including preclinical, asymptomatic infection, acute respiratory infection, and severe encephalitis that culminates in death. As suggested by the likely case diagnosis, a fever may be consistently present, accompanied by altered mental status, headache, extreme weakness, cough, dyspnea, diarrhea, myalgia, and vertigo.

• Twenty percent or more of individuals have neurological aftereffects, such as altered personality, mental illnesses, and seizures.

- According to WHO data, the recovered patients experienced delayed onset encephalitis.
- According to a 2009 study, the average number of people that one infected person can infect with NiV in rural Bangladesh is known as the R0 value, and it was found to be 0.48.
- NiV protein targets that can be explored for CADD and discovery to fight NiV. Although there is no approved medication available for NiV,

we have tried to summarize major medications used over the years to treat or alleviate the symptoms and severity of the disease, along with their suggested dose and administered routes. Followed by the present status of computational drug research and future directions for NiV drug discovery is discussed in detail to offer researchers a complete current state of the art of Nipah research.(15). The paramyxoviruses known as Nipah viruses are carried by bats and are the archetypal members of the Henipavirus genus. The henipaviruses first appeared in the 1990s, when they spread from their natural bat hosts to humans and cattle, resulting in severe illness outbreaks. Since the Hendra virus first appeared in Australia in 1994, seven human infections have occurred, resulting in four case fatalities. After the Nipah virus first surfaced in Malaysia, Bangladesh and India have also seen epidemics.

- There are few antiviral strategies against the henipaviruses that have been explored in animal models, and no recognized or licensed medicines exist for treating henipavirus infection or disease in humans
- One well-known first line of treatment for presumed viral infections with no established etiology is ribavirin. Antiviral activity of ribavirin is demonstrated against a broad range of RNA and certain DNA viruses(16).



• Initial immunization strategies using the henipavirus G or F viral glycoproteins were first evaluated using recombinant vaccinia viruses providing evidence that complete protection from disease was achievable by eliciting an immune response to the Nipah virus envelope glycoproteins. Other studies using recombinant canarypox-based vaccine candidates for potential use in pigs. (16).

Risk factors

Henipaviruses are enveloped RNA viruses that cause respiratory illnesses in horses and pigs as well as encephalitis in humans.They belong to the family Paromyxoviridae and genus Henipavirus. Human sickness can advance quickly from a minor illness (fever, headache, myalgia) to a coma and death within 10 days after an incubation period of 4 to 18 days; the case-fatality ratio is 40%–76%. In 1994.

- A respiratory ailment in horses was linked to sickness in two humans in Australia, marking the first known case of Henipavirus infection in humans (11). Subsequently, the Hendra virus
- the causative agent—was isolated from asymptomatic flying foxes, which are Pteropodidae fruit bats. According to Field et al.horses may have contracted the disease indirectly through contact with diseased fruit bats, as they were identified as the intermediary hosts connected to human (17).

Risk factor used in Singapore

In which IGM antibodies were detected in serum specimens using an IgM-capture antibody enzyme immunoassay (EIA), and IgG antibodies were detected using an indirect EIA. Since antibodies directed against the Nipah virus cross-react with Hendra antigens, Hendra virus antigens were utilized in all serologic testing. Brain tissue from the fatal case, serum, cerebrospinal fluid (CSF), and blood were all added to Vero E-6 cells. Samples of blood, CSF, and tissue were examined using reverse transcription.

- A case was initially defined as an abattoir worker with onset of febrile encephalitis or pneumonia during 9–20 March 1999 who tested positive for anti-Nipah IgM antibodies. A control was defined as an abattoir A worker who tested negative for IgM antibodies. We attempted to recruit ~4 times as many control subjects as case patients.
- Interviews were done between April 10 and 22, 1999, with case patients (or the family members and coworkers of the dead patient) and control individuals.

From February 22 to March 19, 1999, information was kept on illnesses, jobs done at the abattoir, use of personal protective equipment and clothing, and contact with swine body fluids. Trained interviewers performed in-person or telephone interviews using a standardized questionnaire and each participant's preferred language. (18).

Frequency and Transmission

In the context of human disease outbreaks, modeling NiV transmission in experimental animal systems has proven to be challenging. NiV transmission to naïve cage mates in experimentally infected hamsters happened through direct touch; however, no transmission occurred when possibilities for transmission were restricted to aerosol exposure (recapitulated in Ref. [55•]). Contrary to the results of hamsters exposed directly in experiments, transmission of NiV infection did not cause sickness in naïve animals, and so the

- The Nipah virus can spread both human-tohuman and zoonotic.
- Two ways that NiV infection spreads from flying foxes to humans are through bat-tohuman transmission, which has happened in Bangladesh and India, and transmission via an intermediate animal host, which caused the outbreak in Malaysia. Both food-borne and

transmission through an intermediate animal host of a suspected.

- NiV were observed in the Philippines; specifics of this outbreak are covered in more depth below.
- Human-to-human transmission of NiV has been documented during the first known epidemic of NiV in the Philippines and has played a crucial role in the development of this extremely deadly infection in Bangladesh. It has also been observed in India.

Close contact with clinically ill patients is the primary source of human-to-human transmission. Therefore, variables like patient care and fundamental infection control measures will be crucial in reducing the risk of NiV infection spreading to other people in the future. (19).

Most likely as a result of virus spillover from Malaysian flying foxes, NiV-Malaysia first appeared in 1998 during an outbreak of infectious respiratory and neurologic illness in commercially produced pigs. Farm and abattoir workers contracted the disease from pigs.

• which led to a global outbreak of severe fever encephalitic disease in humans (3–5); over 250 cases were documented in Malaysia and Singapore, with a case-fatality rate close to 40%. During the outbreak, no human-to-human transmission cases were recorded (7,8). Nonetheless, asymptomatic seroconversion against NiV-Malaysia in a healthcare worker, identified post-epidemic, and a newly reported case of late-onset NiV encephalitis linked to transmission from an infected family member have raised the possibility of uncommon human-to-human transmission.(20)

The quantity and location of the population at risk are determined by the geographic expanse of case occurrence. Furthermore, the introduction of pathogens into previously unexplored ecological regions or populations (due to factors like increased population density or mobility) might change the dynamics of transmission and potentially accelerate the pathogen's spread and impact.

- It is also possible to track indicators of modifications in spillover mechanisms using the NiV monitoring data. Depending on the source of the spillover, the number of people infected from the reservoir during each spillover incident may differ.
- For instance, there may be substantial differences between clusters linked to drinking palm sap and those linked to pig exposure.
- the latter being the primary pathway for the spread of the NiV outbreak in Malaysia. (21).

Year	Country	No of cases	Deaths
2023	Bangladesh	11	8
2022	Bangladesh	3	2
2021	India	1	1
2021	Bangladesh	2	0
2020	Bangladesh	7	5
2019	India	1	0

Death rate in 2023,2022,2021,2020,2019

Pteropodidae bat species were later found to be the virus's natural reservoir hosts, and fruit droppings into pigsties was hypothesized to be the virus's route of transmission in piggery units. Periodic NiV outbreaks have also been documented in Bangladesh and India since 2001; by 2014, the virus has spread to additional



South Asian nations. Following the reporting of 17 symptomatic cases in the Philippines.

- There has been evidence connecting deforestation to climate change with a higher likelihood of human–animal conflicts and the possibility for NiV to spread to other tropical regions of the world.
- Inactivated pathogens or their proteins are frequently used as antigens in conventional vaccinations; however, researchers prefer different kinds of antigens to minimize the risk of biohazard.
- It was thought that the virus was spread by infected horses, resulting in acute encepPteropodidae bat species were later found to be the virus's natural reservoir hosts, and fruit droppings into pigsties was hypothesized to be the virus's route of transmission in piggery units.
- Periodic NiV outbreaks have also been documented in Bangladesh and India since 2001; by 2014, the virus has spread to additional South Asian nations (22).

RESULT AND DISCUSSION:

Nipah virus is a zoonotic pathogen primarily transmitted from fruit bats to humans. It causes severe respiratory and neurological symptoms, with high mortality rates. Prevention involves avoiding contact with infected animals and implementing strict infection control measures. Research efforts focus on understanding the virus and developing vaccines and treatments Research into Nipah virus continues to be important for better understanding its biology, transmission dynamics, and pathogenesis. This knowledge can inform the development of vaccines, antiviral drugs, and improved surveillance and control strategies to mitigate the threat posed by Nipah virus to human health.

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