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THE SILENT MENACE: AN IN-DEPTH ANALYSIS OF NIPAH VIRUS

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ABSTRACT:

This article delves into the shadowy threat of one of the world's most deadly emerging viruses. This elusive pathogen, transmitted from bats to humans, has incited fear with its high fatality rates and mysterious outbreaks. Our exploration uncovers the intricate web of transmission, from initial animal hosts to devastating human-to-human spread. We dissect current gaps in diagnosis and treatment, painting a vivid picture of a virus that defies easy containment. Highlighting cutting-edge research and future prospects, this analysis calls for urgent global action to pre-empt the next outbreak. By weaving together epidemiology, socio-economic impact, and preventive strategies, this study offers a critical wake-up call to the lurking danger of Nipah virus, urging a united front to stave off a potential global health crisis.

KEYWORDS: Nipah virus, zoonotic threat, high mortality, transmission dynamics, global health, outbreak containment, innovative research, preventive strategies.

1. INTRODUCTION

In the shadows of tropical fruit trees and the nocturnal flights of bats lies a daunting threat to public health: the Nipah virus (NiV). Nipah virus has caused only a few known outbreaks in Asia, but it infects a range of animals and causes severe disease and death in people, so there is a public health concern. A 2018 annual review of the WHO R&D Blueprint list of priority

diseases concluded that a comprehensive approach involving countermeasures against Nipah virus was urgently needed ^[1].

As we embark on this journey of exploration, it's essential to recognize that Nipah virus is more than just a pathogen; it's a complex ecosystem of interactions between hosts, environments, and human societies. Its ability to traverse species barriers and cause severe respiratory and neurological manifestations in humans underscores the urgent need for a multifaceted understanding of this enigmatic virus.

By integrating current knowledge and pinpointing areas that need further investigation, this review aims to stimulate additional research efforts to elucidate the complexities of Nipah virus biology and epidemiology. By fostering collaboration across disciplines and boundaries, we aspire to enhance our ability as a group to mitigate the negative impacts of the Nipah virus while safeguarding the security of global health.

Nipah virus

The Nipah virus (NiV) is an RNA virus in the Paramyxoviridae family. It belongs to the genus Henipavirus, which also contains the Hendra virus (HeV) and the recently identified Cedar virus. Bats naturally harbor henipaviruses.^[2] In 1998, the Malaysian town of Kampung Sungai Nipah became the first to report the illness. Transmission from person to person also happens. There have also been reports of outbreaks in other South and Southeast Asian nations ^[3]. A variety of nations in South and Southeast Asia such as Bangladesh, Cambodia, East Timor, Indonesia, the immense Democratic Republic of India, Malaysia, Papua New Guinea, Vietnam, and Thailand have experienced outbreaks of the lethal Nipah virus that scientists have linked to flying foxes including *Pteropus vampyrus*, *P. hypomelanus*, *P. lylei*, and the massive *P. gigantea* ^[4]. Considering its high incidence of human mortality, the World Health Organization (WHO) has designated the NiV virus as an international health emergency and lined it to the list of epidemic dangers that are given priority in research and development efforts, zoonotic nature, potential for human-to-human transmission, and lack of a vaccine. In turn, NiV was categorized as category C in the grouping of diseases that constitute a threat by the Centers for Disease Control and Prevention (CDC) and the National Institute of Allergy and Infectious Diseases (NIAID) (Ochani et al., 2019). September 2023 marked the reporting of the latest Nipah virus infections in India. Six cases with confirmed laboratory results were found in Kerala between September 12 and September 15, 2023, indicating that the outbreak had place there. Two cases were fatal out of these. As of September 17, 2023 (NETEC) (India Today), there had been no more detections from these cases ^[5]. While reports of individuals afflicted with this malady have been infrequent and diagnosing it is difficult, restricting probes into its nature. A microbe so risky it warrants a Biosafety Level 4 rating, NiV's study has been hampered owing to constrained access to such fortified facilities in many lands. With eagerness, inquiries into its epidemiology, how it spreads, and feasible ways to foil transmission are desperately required. The study's objectives included characterizing the NiV virus in light of its epidemic possibility and assessing the success of earlier avertive and intrusion strategies. In the event of an epidemic spreading beyond a local level, conclusions and observations drawn from this study may serve as recommendations for the creation of a plan of action.

Nipah virus characteristics

The term "NiV" is derived from the locality of Sungai Nipah, commonly known as Nipah River Village, located in the state of Negeri Sembilan, Malaysia. This is where the initial confirmation of NiV presence, marked by the presence of NiV-specific IgM antibodies in cerebrospinal fluid (CSF) reacting against Hendra viral antigens, was established. These findings were identified in serum samples from patients displaying encephalitis symptoms in 1999. NiV exhibits pleomorphism, appearing either spherical or thread-like, and is enclosed within a membrane with dimensions ranging from 40 to 1900 nm. It features a single layer of

surface protrusions, each with an average length of approximately 17 nm. This virus displays numerous similarities to other paramyxoviruses [6].

Negatively polarized single-stranded RNA is present in the Nipah virus. Despite being the main causal agents for 25–44% of lately emanating infectious diseases, RNA viruses have a greater potential to infect new host species due to their remarkably rapid replication and production rates. The NiV genome comprises six genes and can be either 18,246 or 18,252 base pairs in length depending on the strain. These genes correspond to six transcription units: the RNA polymerase protein (L), the large protein or phosphoprotein (P), the matrix protein (M), the fusion protein (F), the attachment glycoprotein (G), and the nucleocapsid (N). The P gene, alongside encoding the phosphoprotein, is also responsible for encoding the NiV proteins C, V, and W, which play a crucial role in determining the virus's pathogenicity [6]. The physical linkage of the G and F proteins is necessary for the early phases of the viral life cycle, which involve attaching to and fusing with the host cell. After attachment to the EphrinB2/B3 receptor, the NiV genome is released and replicated within the cell. Subsequently, through transcription, which is facilitated by the L and P proteins, the viral messenger RNA is translated into the primary structural proteins [7].

Epidemiology

The Nipah virus, dubbed NiV after Sungai Nipah village in Malaysia where it emerged, made a dreadful leap between species in 1999. Bats passed the virus to pigs through partially consumed fruit, and the pigs then infected humans with a horrific encephalitis. Up to forty percent of the afflicted perished from the brain inflammation. Additionally, survivors faced prolonged neurological hardships. Initially, the outbreak showed in pigs that consumed fruit touched by fruit bats, thereby communicating the sickness to humans. The transmission across barriers sparked havoc, as victims succumbed rapidly or endured life-changing deficits. An acute NiV infection outbreak among 11 male slaughterhouse workers, ages 44 on average, was documented in Singapore in March 1999. The outbreak may have been caused by the importation of pork from Malaysia and resulted in one fatality. A total of 246 cases of NiV-caused febrile encephalitis were documented between 1998 and 1999 in Malaysia and Singapore, including diseased pigs that showed neurological and respiratory symptoms. The first NiV outbreak in Bangladesh was officially confirmed in 2004 as a result of serum samples carrying anti-NiV antibodies. Since then, genome analysis has allowed researchers to determine the viral nucleic acid of NiV. Nine outbreaks were reported in Bangladesh between 2004 and 2010. A similar NiV outbreak occurred in 2011 and claimed the lives of fifteen people in Hatibandha, a remote town in the northern Bangladeshi district of Lalmonirhat. The ingestion of raw date palm fruits contaminated with NiV was found to be the primary source of transmission in Bangladesh.

A febrile sickness and disturbed sensorium were the hallmarks of this pandemic. A few NiV isolates from the Siliguri outbreak showed striking genetic similarities to those from the Bangladeshi outbreak. In 2007, there was confirmation of another epidemic in Nadia, West Bengal. A NiV infection outbreak was detected in Kozhikode, northern Kerala, India in 2018, and fruit bats were found to be the source of the disease. Most of the 2018 outbreak's deaths were among infected patients and the healthcare workers who provided care for them. A total of 60 NiV-infected people perished in the districts of Malappuram and Kozhikode, according to a real-time polymerase chain reaction (RT-PCR) laboratory diagnostic. The BD strain of MY and the genomes of the confirmed NiV isolates showed a great deal of similarity, according to DNA sequencing. The Kerala State Health Department in Kozhikode, Kerala, India, most recently notified the discovery of a fifth NiV epidemic on September 4, 2021. On August 29, 2021, a 12-year-old kid started exhibiting symptoms. Sadly, he passed away on September 5, 2021. RT-PCR verified NiV to be present in each boy's serum, cerebrospinal fluid, and plasma;

IgM antibodies were found in the plasma. Since then, the NiV infection has killed at least 20 people and continues to propagate quickly in Kerala, a state in southern India.

With open borders to India to the south, east, and west, Nepal, a country in South Asia along the foothills of the Himalayas, faces the possibility of a major Nipah virus (NiV) outbreak brought on by human transmission. Furthermore, it's thought that some fruit bat colonies in the foothills of Nepal engage in seasonal migrations that feature cross-border travel, which increases the possibility of zoonotic virus transmission. The swift spread of infectious diseases is a result of the expanding human population in South and Southeast Asian nations. The risk of zoonotic disease transmission can be elevated by the proximity of pig and poultry breeding and cattle rearing to fruit bat colonies. Although bats prefer warmer conditions, certain species of bats can withstand colder temperatures by hibernating or going into torpor. As a result, some bats in Nepal's mountainous regions roost in man-made structures in order to stay warm. The latent risk underscores the significance of research, preparation, and an empirical understanding of the disease, even in the absence of conclusive proof of a bat-borne virus outbreak in Nepal. South Asian authorities need to be on surveillance for any possible NiV outbreaks. Numerous investigations have verified that *Pteropus* and other fruit bat species act as NiV's natural hosts. This virus seems to spread from its animal reservoir to people, which is alarming for potential outbreaks in the future. Fruit bats can spread the NiV virus to people and domestic animals through contaminated food or direct human-to-human contact, as confirmed by sequencing research. As a result, it is crucial to routinely check for NiV infection in household animals like pigs. Farms should use proper cleaning and disinfection practices to stop outbreaks. To stop the spread of disease, quarantine, zoonotic disease testing of domestic animals, and limiting the movement of animals from contaminated farms should all be implemented at border checkpoints in South Asian countries. It is imperative that the One Health strategy be implemented with rigor, including surveillance and quarantine of household animals to function as a system of early warning for veterinary and human public health officials.

Transmission of nipah virus

As reservoir hosts for a number of high-risk infections, such as the Marburg virus, rabies, and Nipah virus, bats are essential. It's interesting to note that the bat population itself is not seriously harmed by these viruses. Comprehensive research is necessary to comprehend the processes of the Nipah virus circulation between fruit bats, pigs, and humans, as well as the transmission of the virus from pigs to humans, date palm sap to humans, and bats to pigs. Nipah viruses are naturally retained by fruit bats, specifically those of the *Pteropus* species. These bats have been connected in various ways to the spread of the virus and related diseases in a number of confirmed outbreaks that have occurred in diverse geographic locations. Through spillover transmission, the virus has spread from bats to a number of other species, including humans. There is, however, little further transfer from person to person. People are usually infected with the Nipah virus in locations where humans, pigs, and bats coexist. Pigs are raised commercially, and farms usually have fruit trees placed close by to provide shade. These fruits attract fruit bats of the *Pteropus* species, known as NiV reservoirs, which causes NiV to spread to pigs, other animals, and people. Cross-continental movement of contaminated pig meat aids in the spread of the virus from infected animals to humans in other parts of the world. This combination of factors, which includes the close proximity of fruiting trees, fruits such as date palms, fruit bats, pigs, and humans, creates the conditions for the formation and dissemination of novel and fatal zoonotic virus illnesses like Nipah. Transmission of the Nipah virus (NiV) can happen in a number of ways, including eating food tainted with the virus and coming into touch with infected people or animals. Close contact with infected people, such as touching, feeding, or caring for someone who has the virus, can enable contact and cause droplet-based NiV transmission, among other factors that raise the risk of infection. NiV droplets (aerosol

exposure) may also contribute to the transmission of NiV during close contact, according to recent experimental research using aerosolized NiV in Syrian hamsters. In Bangladesh, the Nipah virus can spread through three different channels. The most common method of viral transmission is eating fresh date palm sap; however, drinking tari (fermented date palm juice), may also be a viable method. Preventing bats from getting date palm sap can help avoid the NiV infection that comes with eating tari. According to research using infrared cameras, bats like *Pteropus giganteus* frequently visit date palm trees. While collecting sap, the bats may come into touch with the trees and lick them. In sugar-rich environments, such fruit pulp, the virus can persist for several days. Raw date palm sap eating was connected to a Nipah virus outbreak in the Tangail area of Bangladesh. Notably, patients in Bangladesh usually have symptoms between December and March, when date palm sap is collected. Furthermore, findings revealed that anti-Nipah viral antibodies were significantly seroprevalence in *Pteropus* bats, suggesting that the virus has sufficiently developed to permit transmission across these bat species.

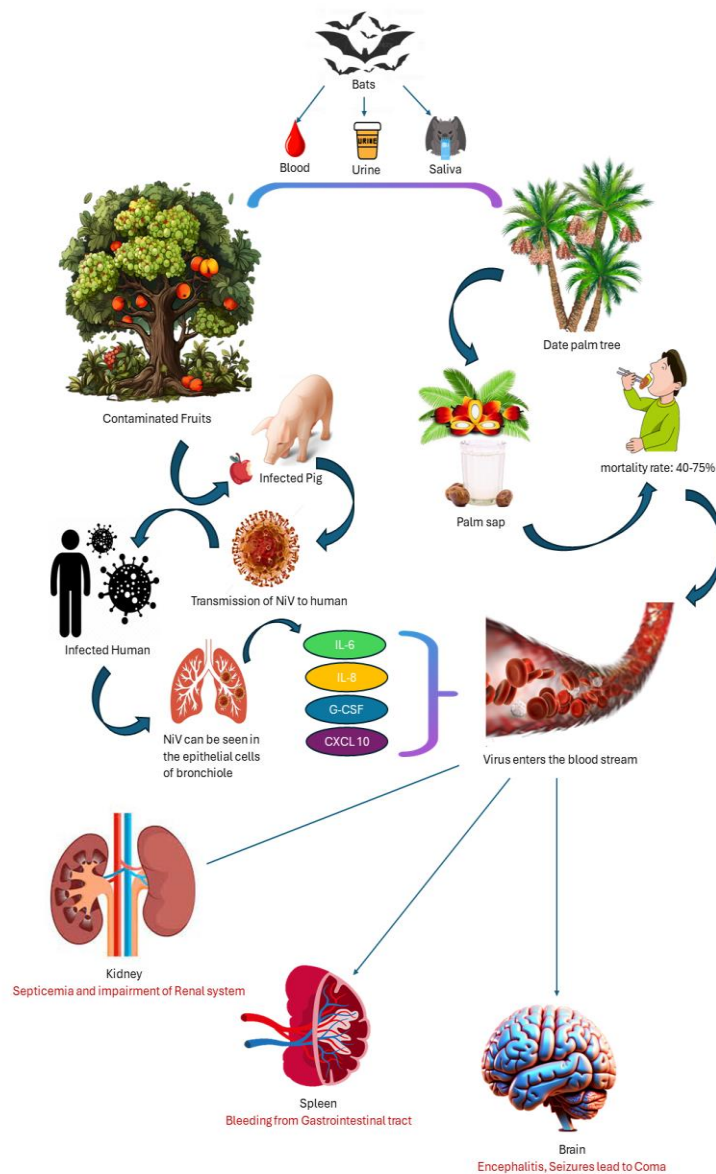


FIG 1. NIPAH VIRUS INFECTION PATHWAY

Fig 1 shows the Nipah virus (NiV) infection route, emphasizing how it spreads and what impacts it has on the human body.

The virus is primarily transmitted from bats, which shed the virus through their blood, urine, and saliva. Bats can contaminate fruits or palm sap, which when consumed, can infect humans. Another transmission route involves pigs, which can become infected by consuming contaminated fruit and then transmit the virus to humans. Once in the human body, the Nipah virus enters the bloodstream and will be found in the epithelial cells of the bronchioles. The infection triggers an immune response, with elevated levels of cytokines such as IL-6, IL-8, G-CSF, and CXCL10, indicating an intense inflammatory reaction. Serious side effects from this systemic infection might include septicemia, renal impairment, gastrointestinal bleeding, and brain encephalitis. The resulting brain inflammation can cause seizures and potentially lead to a coma, contributing to a high mortality rate of 40-75%.

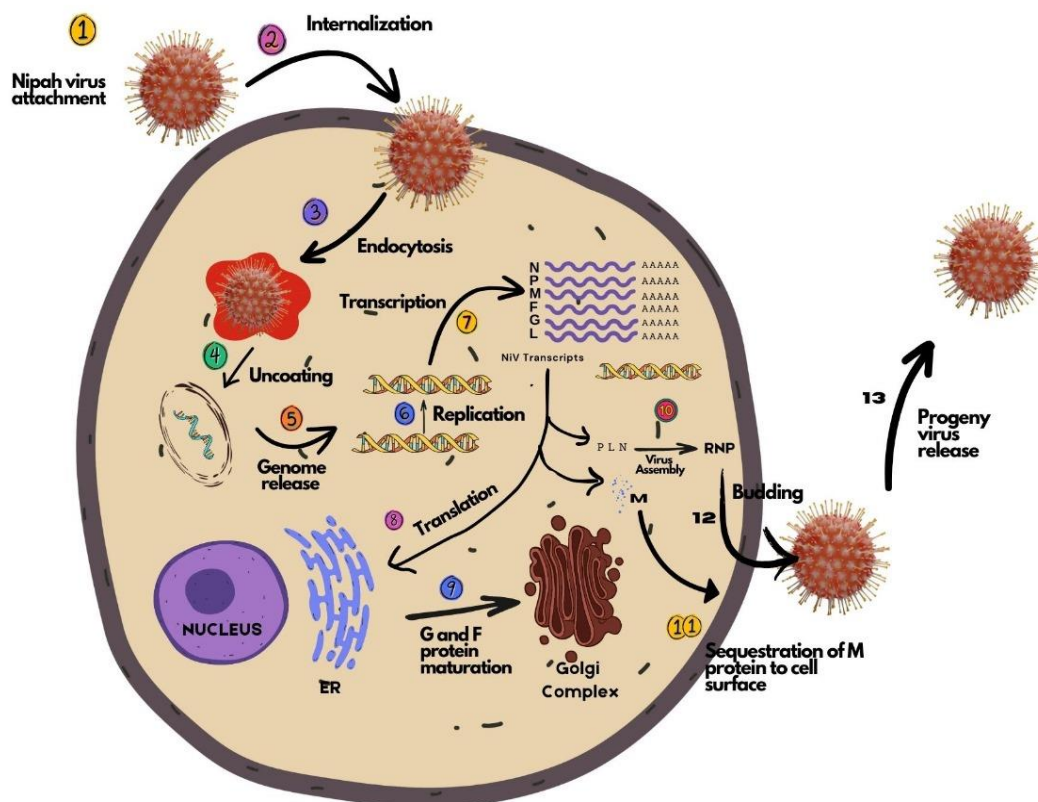


FIG 2. Steps of NiV replication

Fig 2 depicts the replication cycle of the Nipah virus within a host cell.

The process begins with the virus attaching to the host cell membrane via its surface proteins. The virus then enters the cell through endocytosis, a process where the cell engulfs the virus in a vesicle. Once inside the vesicle, the virus is transported within the cell. The viral envelope merges with the vesicle membrane, releasing the viral RNA genome into the cytoplasm, a step known as uncoating. The viral RNA is now free in the cytoplasm and ready for transcription. This RNA serves as a template for replication, producing complementary RNA strands. Subsequently, the viral RNA is transcribed to produce mRNA, which is used to synthesize viral proteins. These proteins, along with new viral RNA, assemble into new virus particles. The mature viruses then bud from the host cell, acquiring a portion of the cell membrane as their envelope, and are released to infect other cells.

Clinical features:

Incubation Period: The incubation period for Nipah virus infection is usually between 4 to 14 days after exposure, with an average of 5 to 7 days.

Initial Symptoms: Nipah virus infection can present with flu-like symptoms, including fever, headache, muscle pain, and fatigue. These initial symptoms can be nonspecific and are often followed by more severe manifestations.

Respiratory Symptoms: In some cases, Nipah virus infection can progress to severe respiratory illness, with symptoms such as cough, shortness of breath, and chest discomfort.

Neurological Symptoms: One of the distinguishing features of Nipah virus infection is its ability to cause encephalitis (inflammation of the brain). Neurological symptoms can include confusion, disorientation, drowsiness, and even coma.

Seizures: Seizures are a common neurological complication of Nipah virus infection.

Atypical Pneumonia: Nipah virus infection can lead to atypical pneumonia, which can be severe and may require mechanical ventilation in some cases.

Other Symptoms: Patients with Nipah virus infection may experience nausea, vomiting, and diarrhea. Some individuals may also develop acute respiratory distress syndrome (ARDS), a life-threatening condition.

Late-Stage Complications: In severe cases, Nipah virus infection can lead to long-term neurological complications, including persistent seizures and cognitive deficits.

Person-to-Person Transmission: People who are in close proximity to someone who has the Nipah virus may be able to spread the illness to others by saliva, respiratory secretions, or other bodily fluids.

Outcome: The case fatality rate of Nipah virus infection can be high, ranging from 40% to 75%, depending on the outbreak and healthcare infrastructure. However, this rate can vary.

It's important to note that the clinical presentation of Nipah virus infection can overlap with other infectious diseases, making diagnosis challenging, especially in areas where Nipah virus is not commonly encountered. Early recognition of the symptoms and appropriate isolation and infection.

Diagnosis**Laboratory Diagnosis**

A variety of assays can be used in the laboratory to confirm the diagnosis of Nipah virus (NiV) infection during both the acute and convalescent phases. It's crucial to detect and diagnose NiV infection as soon as possible. Samples should be taken as soon as feasible from all patients (suspected or symptomatic with contact with Nipah) while taking all necessary biosafety procedures.

Real-time RT-PCR viral RNA anti-NiV IgM and IgG antibodies will be tested using an enzyme-linked immunosorbent assay to validate the diagnosis.

1. Detection of IgM antibody against NiV in serum or cerebrospinal fluid (CSF).
2. Identification of NiV RNA through RT-PCR from respiratory secretions, urine, or CSF.
3. Isolation of NiV from respiratory secretions, urine, CSF, or other tissues.

Treatment

At present, no approved medications or vaccinations are accessible. The demand for more advanced treatment options for NiV infection is unmet. Any novel medication for illnesses like NiV infection may only be tested in an outbreak scenario while closely following the protocol of the clinical study. Because of this, being ready for any future epidemic is crucial as it arises as an emergency. There are currently relatively few therapy options available. Fig 3 depicts the treatment algorithm of NiV.

General management:

- 1) Initiate symptomatic and supportive treatment promptly.

- 2) Prioritize airway, breathing, and circulation (ABC) management.
- 3) Ensure patient isolation, preferably in a separate ward or room.
- 4) Implement barrier nursing techniques, including:
 - Personal protection using masks, gloves, gowns, shoe covers.
 - Hand-washing with soap and water before and after handling/visiting patients

Ribavirin:

There is only one open-label experiment from Malaysia that supports ribavirin as a treatment for Nipah, and it is not a proven treatment. However, the advantage was noteworthy, since there was a 36% decrease in mortality. As a result, it has been advised for use in cases of proven Nipah infections in the absence of other treatments and in light of its safety profile, which has been demonstrated to work rather well in both the short and long term in Hepatitis C patients. The WHO Guidelines form the basis for the recommended dosages [8].

Dose of Ribavirin

For Adults;

2000 mg loading (10 tabs of 200 mg)

Day (1-4) - 1000 mg 6hrly (5 tabs of 200 mg each 4 times daily for 4 days = 80 tablets)

Day(5-10) - 500 mg 6hrly (200 mg each tablet 3 tab - 3 tab - 2 tab – 2 tab at 6hrs gap daily for 6 more days = 60 tablets)

For Childrens;

Load 30mg/kg, Thereafter,

for Day (1- 4) give 15 mg/kg 6th hourly

Day (5-10) to give 7.5 mg/kg 6th hourly.

On an average, each patient (adult) would require 150 capsules for a 10 days course.

Parenteral dose of Ribavirin.

IV Ribavirin

loading dose of 30 mg/ kg then 15 mg/kg every six hourly for 4 days

Then 7.5 mg/kg every eight hourly for 6 days.

Ribavirin should be diluted in 150 ml of 0.9% Normal Saline and infused slowly

M102.4 Monoclonal Antibody:

M102.4 appears to interfere with the NiV G envelope protein's receptor binding site, preventing it from attaching to the Ephrin B2 protein and preventing the virus from infecting the host cell. With assistance from ICMR, the protocols and SOP (Standard Operating Procedures) were created. However, by then the outbreak had finished, thus it was not deployed. The m102.4 monoclonal antibody is an experimental drug that needs to be used with the assistance of Emergency Research Response & Resources. The research team should adhere to the recognized indications and protocols for m102.4 with appropriate knowledge and training, just like any other clinical investigation, with approval from the Ethics Committee [9].

Follow up:

- Following discharge, patients should stay in isolation at home for four weeks.
- It is recommended that patients see a doctor at 28, 56, and 90 days.
- Patients who have been diagnosed with Nipah virus (NiV) infection should all receive long-term follow-up because of late-onset encephalitis and relapses that have been reported in prior cases.

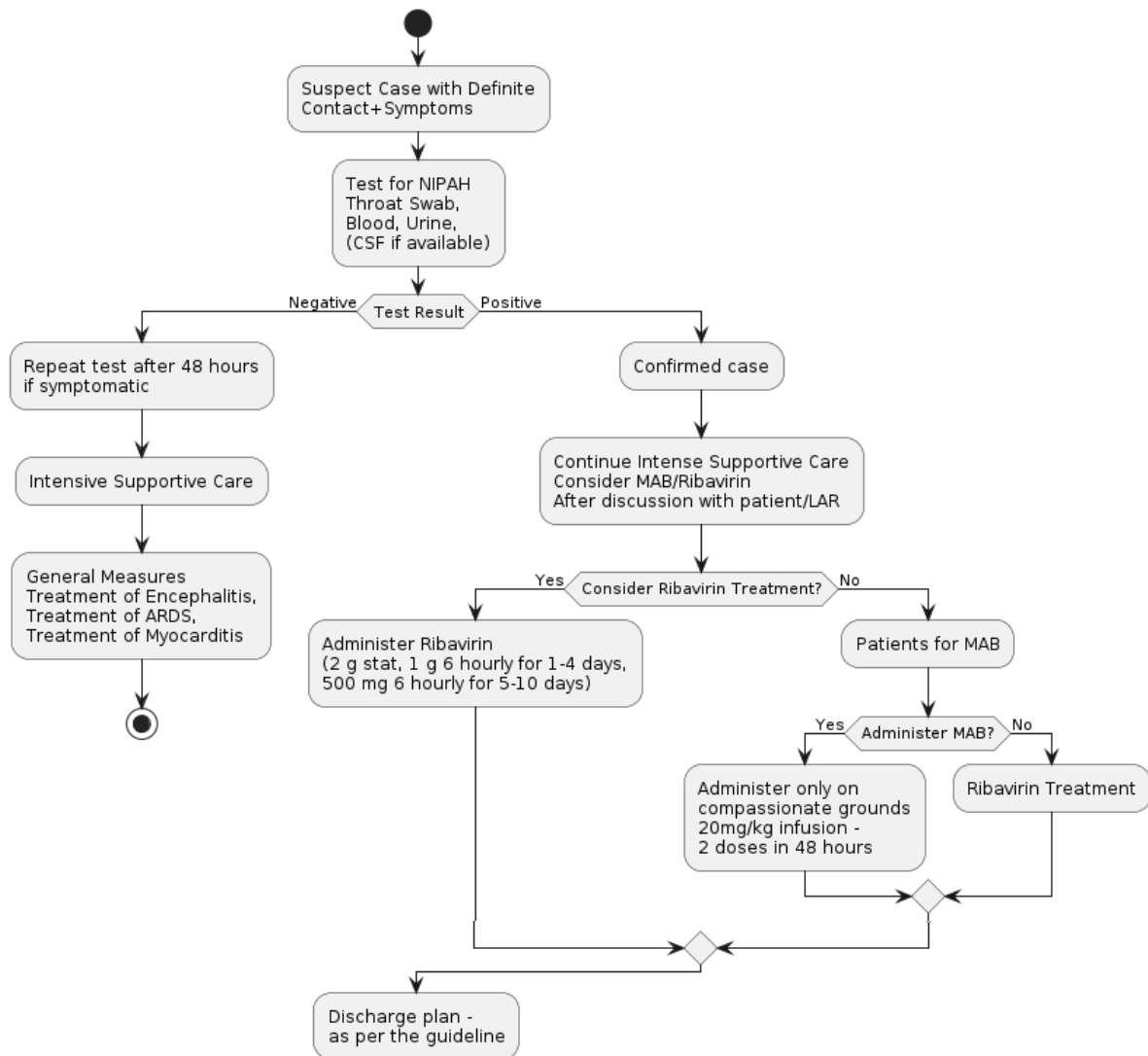


Fig 3 Treatment algorithm

CURRENT RESEARCH

NiV enters target cells via glycoproteins on their surface, mainly proteins G and F. While the fusion protein F initiates the penetration of viral membranes into the host cell, the G glycoprotein helps attachment to external receptors. The NiVG protein can engage with the receptor-activated virus within host cells and perform its complete activity thanks to mutations in the protein. It has recently been found that the nucleolar DNA-damage reaction (DDR) mechanism is used to control mobile devices by viruses. This is accomplished by blocking the nucleolar treacle protein, which raises the production of henipaviral (Hendra and Nipah viruses) viruses. In some fruit juices or mango fruits, the Nipah virus can survive for several days, and in palm milk, it can survive for at least seven days. Many dangerous viruses, such as the Nipah, rabies, and Marburg viruses, are carried by bats. It's interesting to note that these viruses don't seem to have a major negative pathogenic impact on bat populations. To understand the processes of NiV transmission, including the routes from bats to pigs, pigs to humans, and from palm milk to human sources, extensive research is necessary. The ingestion of infected food is the main way that NiV is transmitted. Risk factors include contact in several forms, including as physical contact, nursing, or being around an infected person, which raises the possibility of coming into contact with droplets that are infected with NiV. New experimental studies using dispersed NiV in Syrian hamsters have demonstrated that

aerosolized NiV droplets may also help spread the virus when people are in close proximity to one another. Research utilizing infrared cameras has demonstrated that bats, such as *Pteropus giganteus*, are regular visitors to palm palms and have even been seen licking them on occasion. It has been noted that the virus can survive in sugary solutions—specifically, fruit pulp—for a considerable amount of time. Additionally, it has been shown that *Pteropus* spp. have a high seroprevalence of anti-Nipah virus antibodies, indicating a notable presence of antibodies against the Nipah virus in these bat species. This finding raises the possibility that the virus has evolved to make it easier for *Pteropus* bats to contract it. Vaccinating them against NiV infections becomes essential. Furthermore, as part of comprehensive measures to stop the virus's spread, farm animals like pigs and horses—especially those in permanent habitats—are vaccinated as part of prevention efforts. This implies that the virus has likely undergone adaptations to enable its spread among *Pteropus* bats. To effectively prevent Niv infections, it is crucial to prioritize vaccination for humans. Also, immunization of farm animals that live in permanent habitats—like pigs and horses—should be included in preventative efforts as a crucial way to reduce the danger of transmission. In regions where NiV infection initially spreads through palm milk contamination, it may be challenging to completely prevent outbreaks among livestock. Nevertheless, there is potential for success in such areas if cost-effective cattle vaccination programs are implemented. Despite these possibilities, pharmaceutical agencies often hesitate to contribute in improvising vaccines for rare conditions like NiV, despite their significant mortality rates.

Vaccine Therapy:

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has initiated an early-stage clinical trial to assess an investigational vaccine aimed at preventing Nipah virus infection. This experimental vaccine, developed in collaboration with NIAID’s Vaccine Research Centre, is produced by Moderna, Inc., based in Cambridge, Massachusetts.

The mRNA-1215 Nipah virus vaccine will undergo a dose-escalation clinical trial to determine its safety, tolerability, and ability to elicit an immune response in 40 healthy adults aged 18 to 60. The trial will involve four groups of 10 participants each, with each group receiving two doses of the vaccine via shoulder muscle injection, spaced either four or twelve weeks apart. Group one will receive two 25-microgram (mcg) injections, group two will receive two 50-mcg injections, and group three will receive two 100-mcg injections, all four weeks apart. The dosage for the fourth group will be determined based on interim results from the first three groups and will involve two injections twelve weeks apart.

Participants will be closely monitored through clinical observation and blood collection at specified intervals, and their progress will be tracked by clinical study staff for 52 weeks following their final vaccination ^[10]. Table 1 presents a detailed summary of key studies on Nipah virus (NiV) infection, highlighting the diverse research efforts and findings in this field.

Table 1: Summary of Key Studies on Nipah Virus (NiV) Infection

S. No.	Authors	Year	Title of the article	Study Focus/Objective	Key Insights	Methodology	Conclusion/Recommendations	Limitations	Geographical Focus	Link/DOI
1	Javier Faus-Cotino et al. ^[11]	2024	Nipah Virus: A Multidimensional	The study reviews Nipah virus	The Nipah virus (NiV) is categorized as a	The authors collected and assembled data related	Nipah virus (NiV) is a significant emerging zoonotic	The study did not generate new data or conduct	Spain	https://doi.org/10.3390/v16020179

			nal Update	(NiV) infection determinants, highlighting the lack of approved treatments or vaccines and the urgent need for further research to address high mortality rates. It also emphasizes the importance of low-cost preventive strategies and aligns with WHO and CEPI recommendations to develop tools for NiV in heavily impacted regions.	potentially epidemic-pandemic emerging viral threat. It is prioritized by organizations such as the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) due to its high mutation rate and the possibility of generating more transmissible strains. Clinical presentation of NiV infection encompasses sudden-onset encephalitis, respiratory complications, and flu-like symptoms.	to NiV infection. The methodology of the article primarily involved a comprehensive review and synthesis of existing literature and research findings on Nipah virus (NiV) infection, determinants, potential treatments, and preventive measures.	paramyxovirus, responsible for high mortality outbreaks primarily in South and Southeast Asia, with Bangladesh being a hotspot. The virus primarily resides in Pteropus bat species, with occasional transmission to humans, often through an intermediate mammal host.	original analyses, relying on existing literature and research findings for the update on Nipah virus (NiV) infection. The study focused primarily on NiV infection determinants, therapeutic strategies, and preventive measures, potentially overlooking other aspects of the virus's epidemiology and pathogenesis.		
2	Md. Aminul Islam et al. [12]	2024	Nipah virus transmission: a	The study focuses on the	The emergence of the Nipah virus,	The research paper discusses	The research paper concludes that the Nipah virus	The limitations of the research	Turkey	https://dx.doi.org/10.1097/MS9.00

			<p>persiste nt threat to public health deman ding rapid diagnos is, innovat ive therape utics, vigilan ce, and researc h progres s</p>	<p>Nipah virus (NiV) is a newly discover ed virus that causes fatal encephal itis and serious respirato ry problems in humans, explorin g its transmiss ion, lack of targeted antiviral treatment s, preventiv e measures , genetic classifica tion, symptom s, and challeng es in diagnosis</p>	<p>causing severe respiratory issues and encephalitis with a high fatality rate, highlights the urgent necessity for rapid diagnosis, innovative therapeutics, vigilance, and continued research efforts, emphasizing both the absence of targeted antiviral vaccines or drugs and the importance of exploring therapeutic avenues such as ribavirin and monoclonal antibodies, while also stressing the significance of preventive measures to curb its transmission .</p>	<p>the transmissio n, symptoms, diagnosis, treatment, genetic characteristi cs, and neurologica l impact of the Nipah virus (NiV) through a review of literature and case studies, highlighting the challenges in diagnosis and the absence of specific antiviral treatments, while also exploring the virus's structure, genome compositio n, classificatio n into genotypes, and ethical consideratio ns in research</p>	<p>(NiV) poses a significant public health threat due to its high fatality rate, diverse symptoms, zoonotic nature, and potential for human-to- human transmission, emphasizing the urgent need for rapid diagnosis, innovative therapeutics, vigilance, and continued research progress to effectively control and prevent the spread of the virus</p>	<p>paper include the lack of discussion on specific ongoing research efforts, detailed data on the effectiven ess of preventive measures, and comprehe nsive informatio n on the global epidemiol ogy and impact of the Nipah virus (NiV) beyond the highlighte d outbreaks in Malaysia, Banglades h, and India</p>	<p>00000000 01747</p>	
3	Yvonne Jing Mei Liew et al. [13]	2 0 2 2	The Immun obiolog y of	The primary objective of the article is	The research delves into the cellular immune response to	Literature Review with Pubmed, Google	It highlights the importance of animal models in studying NiV's	The immune responses to NiV infection	Kuala Lumpur 50603, Malaysia	DOI: 10.3390/mi croorganism s1006116 2

			<p>Nipah Virus</p> <p>to provide a comprehensive overview of the immunobiology of Nipah virus (NiV), The research also aims to highlight the challenges in developing vaccines and therapeutics for NiV due to the lack of approved medical countermeasure</p>	<p>NiV infection, highlighting the stimulation of CD4+ and CD8+ T cells in models of NiV infection in humans and animals, suggesting an adaptive immune response.</p>	<p>scholar, Science direct</p>	<p>pathogenesis, given ethical limitations in human testing. Various animal models, such as hamsters, AGMs, swine, ferrets, and mice, mimic human NiV disease, aiding in understanding clinical observations. While these models have provided insights into immune responses to NiV, the exact immunopathogenesis in humans remains unclear</p>	<p>are discussed in detail, the article may not delve deeply into the specific mechanisms of viral entry, replication, and spread within the host cells, which are crucial for a comprehensive understanding of NiV pathogenesis</p>		
4	<p>Naomi Hauser et al. [14]</p>	<p>2021</p>	<p>Evaluation of Nipah Virus Infection: Past, Present and future considerations</p> <p>Analyzing and Understanding the structure, classification, Transmission cycles and spread of the Nipah virus</p>	<p>Human infections show evolving symptoms and modes of transmission. There are currently no approved drugs or vaccines for Nipah virus treatment, The virus's</p>	<p>Literature Review</p>	<p>NiV shows signs of rapid adaptation to other hosts with varying modes of transmission beyond fruit bats. Continuous research into antiviral drug therapies and vaccines for NiV is essential to combat the</p>	<p>Lack of effective therapy or vaccines. High case fatality rate</p>	<p>Baltimore, USA</p>	<p>doi: 10.3390/tropicalmed6010024</p>

				ability to interfere with the immune response, particularly through interferon type I signaling, highlights the challenges in combating its spread and severity		virus effectively. public health measures encompassing education, hygiene practices, and animal husbandry practices are necessary to prevent potentially larger outbreaks in the future.			
5	Althaf Ali et al. [15]	2020	Dissecting an Outbreak: A Clinico-epidemiologic Study of Nipah Virus Infection in Kerala, India, 2018	The rapid spread of infection revealed shortcomings in the healthcare system's ability to implement effective infection control measures, including fever, altered sensorium, tachycardia, hypertension, myoclonus, sweating, and shortness of breath.	The rapid spread of infection revealed shortcomings in the healthcare system's ability to implement effective infection control measures,	The outbreak of NiV highlighted deficiencies in healthcare infection control, necessitating a universal adoption of rigorous protocols across hospitals to prevent future epidemics. "One Health" strategy integrating animal surveillance is essential for early detection of zoonotic diseases like NiV, emphasizing the urgent need for effective treatments, vaccines, and diagnostics to	The study's small sample size of 23 patients could limit the generalizability of the findings to larger populations, impacting the study's overall representativeness	Kerala, India	doi: 10.4103/jgid.419

							mitigate its high fatality rates and socioeconomic impact			
6	Raj Kumar Singh et al. [16]	2019	Nipah virus: epidemiology, pathology, immunobiology and improvements in diagnosis, vaccine development and control strategies – a diverse review	Nipah virus epidemiology, pathology, immunobiology, diagnosis, vaccine development, control strategies, Focus on understanding transmission, disease progression, diagnostics, vaccines, and treatments.	The paper provides a comprehensive review on the epidemiology, pathology, immunobiology, diagnosis, vaccine designing, and control strategies of Nipah virus.	Phylogenetic analysis used to study NiV clades based on gene sequences. Diagnostic methods include ELISA and PCR for NiV detection.	Urgent need for effective NiV vaccine and treatment regimens worldwide, focus on developing broad-spectrum antivirals and small interfering RNAs.	Expensive nature of antibody drugs, lack of vaccines or therapeutics for NiV	pune, india	https://doi.org/10.1080/01652176.2019.1580827
7	Aditi et al. [17]	2019	Nipah virus infection: A review	Nipah virus infection, transmission, prevention, and control strategies. Emphasis on One Health approach	NiV is a lethal bat-borne pathogen causing severe disease, quick diagnosis and infection check measures are vital for	Literature search conducted using PubMed, Google Scholar, and Cochrane Library. MeSH terms used: Nipah Virus Infection, Epidemiology, Clinical	NiV is a deadly zoonotic disease, lack of easily available low-cost diagnostic tests.	No effective treatment or prophylaxis readily available, difficulties in diagnosis and management in new affected areas.	Delhi, India	https://doi.org/10.1017/S0950268819000086

				for management and prevention.	containment .	features, Diagnosis, Surveillance, Vaccine, and country-specific terms.				
8	Govindakarnavar Arunkumar et al. [18]	2018	Outbreak Investigation of Nipah Virus Disease in Kerala, India, 2018	Investigating the characteristics of transmission of nipah virus in kerala during the months May-June 2018	There was news of South India's first NiV epidemic. The recent outbreak produced 23 cases and a 91% case-fatality rate over its roughly one-month duration (2–29 May 2018). The high death rate and clinical signs resembled those of previous NiV epidemics in Bangladesh and India. The latest outbreak's NiV sequence analysis showed 97% similarity to the NiV-B lineage.	NiV is detected in real-time by reverse transcription polymerase chain reaction examination of specimens from the brain, blood, urine, and throat swab. In addition, the viral genome underwent phylogenetic analysis and sequencing. To characterize the outbreak and clarify the dynamics of NiV infection, an epidemiologic study was carried out.	This is the first NiV epidemic in South India that has been noted. The outbreak was controlled with quick test confirmation and public health action. There was a reported NVD outbreak in South India with widespread nosocomial transmission, along with a thorough account of the transmission episodes that shed details on NiV nosocomial transmission.	Initially, as the inquiry was carried out under a public health emergency, comprehensive data about every case was not gathered. Furthermore, there could have been participant recall bias.	Kerala, India	https://doi.org/10.1093/infdis/jiy612

9	Vijay k. chattu et al. [19]	2018	Southern India's Nipah virus pandemic and the importance of the "One Health" concept to guarantee the security of global health	In order to secure global health, emphasize the "One Health" strategy. For early detection, fortify the animal health surveillance system.	NiV is a global public health threat transmitted zoonotically. One Health strategy crucial for world health safety against NiV.	Literature Review	Global health security is prioritized through the One Health concept. absence of particular medications and vague symptoms make diagnosis difficult. bolster the system for monitoring animal health Stress the One Health strategy.	No specific drugs or vaccines for NiV infection available. Challenges in outbreak detection due to nonspecific symptoms.	India	https://www.doi.org/10.4103/JFMPC.JFMPC13718
10	Vikrant Sharma et al. [20]	2018	Emerging trends of Nipah virus: A review	Research on Nipah virus encompasses understanding transmission routes, host reservoirs, outbreaks, and treatment strategies, alongside investigating genetic variations, replication dynamic	Nipah virus outbreaks have been associated with fruit bats, pigs, and human transmission, yet there are currently no specific antivirals or vaccines available for the virus.	Efforts include surveilling animal reservoirs and high-risk communities for Nipah virus while concurrently developing strategies to manage livestock effectively in proximity to bat habitats.	Nipah virus outbreaks present a significant public health threat due to their high mortality rates, necessitating the implementation of comprehensive strategies involving surveillance, education, and vaccination for effective control.	The absence of vaccines and effective antivirals for Nipah virus is compounded by limited data availability, primarily due to the stringent requirements of high containment facilities.	New Delhi, India.	https://doi.org/10.1002/rmv.2010

				s, and underlying mechanisms.						
1 1	Brenda S. P. Ang et al. [21]	2018	Nipah Virus Infection	The article highlights the importance of vigilance and preparedness in managing NiV outbreaks due to its high fatality rate and potential for human-to-human transmission.	Preventing Nipah virus outbreaks involves controlling the spread from animal reservoirs to humans and minimizing human-to-human transmission. Strategies include avoiding exposure to bats, implementing strict biosecurity measures in pig farms, and using protective equipment in healthcare settings. Public health education and awareness campaigns are crucial in endemic areas.	the authors effectively compiled and presented a broad and detailed overview of Nipah virus infection, drawing from a wide range of existing research to inform healthcare professionals and guide future research efforts.	Nipah virus (NiV) emerged as a new virus, causing severe illness and death in humans and animals. It devastated the pig-farming industry in Malaysia. Since then, outbreaks have continued to occur in Bangladesh and India. The virus is carried by fruit bats, and since these bats are found in many countries, there's a risk of outbreaks happening in new regions.	The review is limited by the quality and scope of the existing studies it includes. If the available research is sparse, biased, or methodologically flawed, these issues can affect the reliability and completeness of the review's conclusions.	Malaysia-Singapore and Bangladesh-India	https://doi.org/10.1128/JCM.01875-17
1 2	Benjamin A. Satterfield et al. [22]	2015	The immunomodulating and antiviral properties of Wprote	To investigate and understand the role of	To Understand the functions of the V and W proteins of Nipah	BSR-T7/5 cells, Vero 76 cells, and HEK 293T/17 cells were	The findings confirm that the V protein of Nipah virus (NiV) has a vital role in	There was a Statistical limitations due to BSL-4	Texas, USA	https://doi.org/10.1038/ncomms8483

	<p>ins of Nipah virus determine disease course</p>	<p>the V and W proteins of Nipah virus in modulating the host immune response and how these proteins contribute to the pathogenesis and progression of Nipah virus infection</p>	<p>virus in modulating the host immune response. The V protein is a major determinant of pathogenesis in Nipah virus whereas W protein modulates inflammatory host immune response affecting disease course.</p>	<p>maintained in specific culture media supplemented with fetal bovine serum (FBS). The Nipah virus genomic sequence was used to construct recombinant NiVs. Mutations were introduced into these clones to generate specific variants of NiV. Various experimental procedures were conducted to characterize the generated rNiVs and evaluate their behavior in different cell types and animal models. These procedures included western blot analysis to detect viral</p>	<p>figuring out the severity and outcome of NiV infection. This study presents a novel finding that the W protein of NiV also significantly influences the disease course. Specifically, the absence of W expression leads to a delayed and altered disease progression in infected ferrets. Importantly, this study bridges the gap between in vitro observations and in vivo disease outcomes, providing valuable insights into the pathogenic mechanisms of NiV.</p>	<p>constraints, Data presented as mean from replicate samples, not assays, Data presented as mean from replicate samples, not assays</p>		
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					protein expression, virus growth kinetics assays to assess viral replication in different cell lines.					
13	Stephen P. Luby et al. [23]	2013	The pandemic potential of Nipah virus	The study aims to provide a comprehensive assessment of the pandemic potential of Nipah virus and to inform public health authorities, policymakers, and researchers about the risks posed by this virus and the measures needed to mitigate them.	Comparison of the characteristics and potential of Nipah virus with other known pandemic-causing pathogens, such as influenza viruses or coronaviruses. Discussion of potential strategies for preventing and controlling a Nipah virus pandemic, including surveillance systems, vaccine development, antiviral treatments, and public health interventions.	The author effectively compiled and analyzed existing research to present a detailed assessment of the pandemic potential of Nipah virus. This approach ensures that the review is comprehensive, systematic, and provides valuable insights for both researchers and public health officials.	while the potential for prophylaxis against Nipah virus exists, overcoming the socioeconomic and healthcare infrastructure challenges in Bangladesh is crucial for its successful implementation.	Malaysia, Singapore, Bangladesh, and India.	http://dx.doi.org/10.1016/j.antiviral.2013.07.011	
14	Stephen P. Luby et al. [24]	20	Transmission of	Identify pathways of Nipah	NiV transmission from bats	Literature Review	Prevent transmission by reducing bat	Person-to-person transmissi	Atlanta, Georgia, Bangladesh,	10.3390/v16020179

		09	Human Infection with Nipah Virus	virus transmission in Bangladesh. Focus on prevention strategies to reduce human infection transmission	through date palm sap in Bangladesh. Person-to-person transmission accounts for half of NiV cases.		access to date palm sap. Reduce exposure to infected patients' saliva to prevent transmission. Decrease bat access to date palm sap. Reduce exposure to infected patients' saliva.	on accounts for half of recognized Nipah cases. Efforts focus on reducing bat access to date palm sap.		
15	Stephen P. Luby et al. [25]	2006	Foodborne Transmission of Nipah Virus, Bangladesh	The primary objective is to identify the specific food sources and practices that contribute to the spread of the virus, particularly examining the role of date palm sap contaminated by fruit bats, which are known carriers of the virus.	Nipah virus transmitted through drinking raw date palm sap. Fruit bats (Pteropus giganteus) likely source of transmission.	A case-control study done with 11 case-patients and 33 controls.	Drinking fresh date palm sap might spread the Nipah virus. There is a strong correlation between drinking raw date palm sap and sickness. Prevent the Nipah virus by abstaining from raw date palm sap. Implement measures to deter fruit bats from contaminating sap.	Bias against finding association with date palm sap consumption and Nipah virus not isolated from date palm sap.	Bangladesh	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3291367/
16	V. Guillaume et al. [26]	20	Nipah Virus: Vaccination	In the investigation of	Vaccination with Nipah virus	Expression of Nipah virus	Both vaccination and passive	The lower limits of antibody	Malaysia	10.1128/JVI.78.2.834-840.2004

		04	ation and Passive Protection Studies in a Hamster Model	vaccination and passive protection against Nipah virus in hamsters, research focused on studying Nipah virus glycoproteins to understand their role in both active and passive immunity.	glycoproteins or passive transfer of antibodies from immunized animals both conferred protection against fatal infection in hamsters.	glycoproteins in vaccinia virus recombinants provided protection, while passive transfer of antibodies from immunized animals also conferred defense against Nipah virus infection.	transfer of antibodies offer protection against lethal Nipah virus infection	protection in vivo and the effect of passively immunizing animals post infection remain undetermined in the context of Nipah virus research.		
17	Emily S. Gurley et al. [27]	2004	Nipah virus transmission from person to person in a Bangladeshi community	Person-to-person transmission of Nipah virus, risk factors and infection control strategies in resource-poor settings	Evidence found for person-to-person transmission of Nipah virus, contact with 1 patient carried highest risk for infection	Case-control study conducted to determine risk factors for infection. RT-PCR testing used to confirm Nipah virus contamination.	Person-to-person transmission of Nipah virus confirmed, infection control strategies crucial for resource-poor settings highlighted.	No formal institutional review due to outbreak investigation protocols, no reported Nipah virus illness cases among healthcare workers.	Bangladesh	https://www.doi.org/10.3201/EID1307.061128
18	Kaw Bing Chua et al. [28]	2003	Nipah virus outbreak in Malaysia	Investigating the epidemiology of Nipah virus outbreak	In 1998, the new paramyxovirus known as Nipah virus—which is	Literature Review	There was initial consideration for developing a vaccine against Nipah virus for	The limitation of the paper is its lack of focus on preventive	Malaysia	DOI: 10.1016/s1386-6532(02)00268-8

			<p>s, including the spread and transmission dynamics of the virus in affected regions. Assessing the clinical manifestations and outcomes of Nipah virus infection in humans and animals, particularly focusing on severe febrile encephalitis in humans and encephalitis/respiratory diseases in pigs</p>	<p>linked to the Hendra virus— appears in Malaysia. Its high fatality rate was caused by acute febrile encephalitis in people. The outbreak resulted in a significant number of cases and fatalities, particularly affecting individuals involved in pig farming. Surveillance and control efforts were crucial in containing the spread of the virus.</p>		<p>livestock, the focus shifted towards cost-effective measures such as surveillance and culling. This approach, coupled with a better understanding of wild animal reservoirs, is deemed more pragmatic for preventing the re-emergence of the virus. Research efforts are directed towards developing simpler, more sensitive, and specific laboratory tests for rapid diagnosis and surveillance of Nipah virus infection.</p>	<p>measures and future strategies for managing potential Nipah virus outbreaks.</p>			
19	<p>Kum Thong Wong et al. [29]</p>	<p>2020</p>	<p>Nipah virus: Pathology and pathogenesis of emergi</p>	<p>The present research is based on the clinical and postmort</p>	<p>It discusses the pathogenesis of Nipah virus infection based on the pathological</p>	<p>Analysis of the relative value of many laboratory techniques, such as viral isolation,</p>	<p>The distribution of distinctive viral inclusions and their histological and ultrastructural</p>	<p>no limitations</p>	<p>malaysia</p>	<p>10.1007/s00281-002-0106-y</p>

			ng paramyxoviral zoonosis	em results of thirty-two people who died from infection with the Nipah virus.	findings, which include tissue immunolocalization of viral antigens and electron microscopy.	IHC, and serology, for the diagnosis of this newly developing infectious illness	appearances can assist the diagnosis of Nipah virus infection. Nevertheless, as other paramyxoviral infections can also exhibit similar inclusions, only laboratory techniques like IHC, virus isolation, PCR, and serology can provide a definitive diagnosis.			
20	Kay-Sin TAN MRCP al. [30]	1999	Epidemiological aspects of Nipah virus infection	The study likely aims to provide a comprehensive understanding of the epidemiological characteristics of Nipah virus infection, which can inform public health efforts to prevent and control	Evaluation of surveillance systems for detecting Nipah virus outbreaks, as well as public health interventions implemented to control the spread of the virus, and their effectiveness in mitigating transmission.	This methodology provides a comprehensive approach to understanding the epidemiological aspects of Nipah virus infection, contributing valuable knowledge for preventing and controlling future outbreaks. For specific details, one would need to refer	the conclusion of the study would likely underscore the importance of understanding the epidemiological aspects of Nipah virus infection for effective public health response and highlight the need for continued research and collaboration to address this emerging infectious disease threat.	Limitations in generalizing the findings to other populations or settings due to variations in epidemiological factors, healthcare infrastructure, and cultural practices.	Malaysia, Bangladesh, and India	https://www.neurologya.org/articles/19992077.pdf

			outbreaks of the disease.		directly to the article.				
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Future prospects

1. Research and Surveillance

- **Enhanced Surveillance:** Establishing comprehensive surveillance systems in high-risk regions is crucial for early detection and outbreak management. This involves developing advanced diagnostic tools and streamlined protocols for rapid intervention.
- **Ecological and Epidemiological Studies:** Conducting detailed studies on the natural reservoirs and transmission mechanisms of NiV, particularly focusing on bats and other wildlife, is essential to understand and mitigate spillover events.

2. Vaccine Development

- **Innovative Vaccine Research:** Significant progress in vaccine research against NiV is ongoing, with various candidates such as recombinant protein vaccines, viral vector vaccines, and mRNA vaccines under development.
- **Clinical Trials and Production:** Continued investment in clinical trials to assess the safety and effectiveness of these vaccines is vital. Regulatory approvals and large-scale production will be necessary for widespread immunization efforts.

3. Therapeutic Interventions

- **Antiviral Drugs:** Developing specific antiviral drugs that target NiV can provide treatment options for those infected. Research into broad-spectrum antivirals that are effective against NiV and other related viruses is also promising.
- **Monoclonal Antibodies:** Exploring the use of monoclonal antibodies that can neutralize NiV and offer passive immunity to infected patients or those at high risk.

4. Public Health Preparedness

- **Strengthening Healthcare Systems:** Building robust healthcare infrastructures capable of responding effectively to NiV outbreaks, including training healthcare workers and ensuring an adequate supply of personal protective equipment (PPE).
- **Community Education and Awareness:** Increasing awareness about NiV transmission and prevention in communities, especially in areas where the virus is endemic or likely to emerge, is essential.

5. Global Collaboration

- **International Cooperation:** Enhancing collaboration between countries and international health organizations to share data, resources, and expertise in managing NiV outbreaks.
- **One Health Approach:** Adopting a One Health approach that integrates human, animal, and environmental health efforts to address the complex interactions involved in NiV transmission.

6. Technological Innovations

- **Advanced Diagnostic Tools:** Developing rapid, sensitive, and specific diagnostic tests that can be used in field settings to quickly identify NiV infections.
- **Genomic Surveillance:** Utilizing genomic sequencing technologies to monitor virus mutations and understand the evolutionary dynamics of NiV, which can inform vaccine and therapeutic development.

7. Policy and Regulatory Frameworks

- **Formulating Policies:** Governments and health organizations need to create and implement policies that support research, surveillance, and response efforts for NiV.
- **Ethical Considerations:** Addressing ethical issues related to vaccine and drug trials, particularly in vulnerable populations, and ensuring equitable access to healthcare resources.

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