



## Review Article

# The Nipah Virus: A Review of Epidemiology, Pathophysiology, and Management

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The zoonotic pathogen Nipah virus (NiV) has emerged as a significant global health threat, provoking outbreaks characterised by high mortality and substantial transmission potential. First identified in 1998–1999 in Malaysia and Singapore in association with pig farms and fruit bat reservoirs, NiV is now recognised as a member of the genus *Henipavirus* within the family *Paramyxoviridae*. This review article provides a comprehensive synthesis of current knowledge on NiV, including its epidemiology, molecular virology, clinical features, diagnostic approaches, therapeutic strategies, and public health management. We examine outbreak patterns in Southeast Asia, assessing reservoir hosts (predominantly *Pteropus* spp. fruit bats), intermediate animal hosts (notably pigs), and documented human-to-human transmission events. In terms of virology, NiV possesses a negative-sense single-stranded RNA genome (~18 kb) encoding six major structural proteins (N, P, M, F, G, and L). The viral glycoprotein fusion complex interacts with Ephrin-B2/B3 cellular receptors to mediate entry, enabling broad tissue tropism including endothelial and neuronal cells. The pathophysiological cascade involves endothelial damage, vasculitis, micro-infarction, blood–brain barrier penetration, and fulminant encephalitis or respiratory failure. Clinically, incubation periods of 5–14 days (occasionally longer) precede prodromal flu-like symptoms, followed by neurological decline, seizures, and acute respiratory distress in severe cases; relapsing or delayed-onset encephalitis has also been described. Diagnostic modalities include real-time RT-PCR, serology (IgM/IgG ELISA), virus isolation (BSL-4), and newer point-of-care assays under development. Management remains largely supportive, as there is currently no licensed antiviral or vaccine for NiV. Experimental therapeutics such as ribavirin, favipiravir, monoclonal antibodies (e.g., m102.4), and viral-vectored vaccine candidates are in varying phases of research. From a public health perspective, the adoption of One Health approaches, rigorous surveillance, bat and livestock monitoring, infection control in healthcare settings, and public education are critical to prevention. Recent outbreaks in India (particularly the state of Kerala in 2018 and 2023) and Bangladesh demonstrate both the ongoing threat and the effectiveness of rapid containment when robust systems are in place. Future challenges include elucidating spill-over mechanisms, refining diagnostics and therapeutics, and developing broadly protective vaccines. In conclusion, given the high case-fatality rate, propensity for human transmission, and absence of licenced countermeasures, NiV demands sustained global vigilance, research investment, and integrated human-animal-environmental health strategies.

**Keywords:** Nipah virus, zoonosis, *Henipavirus*, encephalitis, bats, outbreak, management.

## INTRODUCTION

The Nipah virus (NiV) is an enveloped, negative-sense RNA virus of the genus *Henipavirus* and family *Paramyxoviridae*. It emerged as a zoonotic pathogen of grave concern when it was first identified in the 1998-1999 outbreak in Malaysia and Singapore, in which pig farms and the fruit-bat reservoir were implicated (Chua et al., 2000; Luby & Gurley, 2012).

The public health significance of NiV arises from its high case-fatality rate ranging from approximately 40 % to as much as 75 % or more in certain outbreaks (Luby et al., 2009; Hsu et al., 2004) its documented capacity for human-to-human transmission, and its classification by the World Health Organization (WHO) as a priority disease under the R&D Blueprint for emerging pathogens (WHO, 2023). Outbreaks occurring nearly annually in South and Southeast Asia

(notably Bangladesh, India, Malaysia, and the Philippines) highlight the potential for wider spread, especially given bat reservoirs and increasing ecological interface between wildlife, livestock, and humans (Rahman et al., 2012; Lo & Rota, 2018).

**This review article aims to provide a scholarly, evidence-based synthesis of current knowledge on NiV. Specifically, we examine:**

- (1) The historical discovery and major outbreaks of niv
- (2) The virology and molecular structure of the virus
- (3) The epidemiology of niv including global distribution, outbreak drivers, and transmission dynamics
- (4) The pathophysiology of infection and organ involvement
- (5) Clinical manifestations and diagnostic modalities
- (6) Therapeutic strategies and vaccine development
- (7) Public health measures and preventive efforts
- (8) Recent outbreak experiences and lessons learned
- (9) Future directions and remaining challenges; and
- (10) In conclusion, the imperative for integrated control and research.

By synthesising findings from peer-reviewed literature (2010–2025) and major surveillance reports, this review seeks to inform clinicians, public health professionals, virologists, and policy-makers about the critical aspects of NiV and the necessary preparations for future emergence.

## 2. History and Discovery

The first recognized outbreak of Nipah virus occurred between September 1998 and May 1999 in Malaysia and Singapore, centred on pig-farm communities. The index cluster in Malaysia involved 265 human cases and 108 deaths, with a case-fatality rate (CFR) of approximately 40.8 % (Chua et al., 2000; WHO, 2001). The investigation revealed that domestic pigs acted as an amplifying intermediate host, with the reservoir implicated as fruit bats (genus *Pteropus*) that contaminated pig feed or housing with excreta (Chua et al., 2002). The outbreak spread to Singapore via pig imports, prompting > 1 million pigs to be culled. Following this initial outbreak, subsequent NiV outbreaks have occurred in Bangladesh since 2001, with nearly annual seasonal events (Luby et al., 2009;

Hossain et al., 2008). The first major Indian outbreak occurred in Siliguri, West Bengal, in 2001 (Masrour et al., 2001), followed by another in Nadia district in 2007 (Gurley et al., 2007). In 2018, the state of Kerala, India, reported 23 confirmed and probable cases (17 deaths, CFR ~74 %) in May–June 2018, marking the first southern India outbreak (Joseph et al., 2019; Recurrent ... Kerala, 2023). Additional outbreaks have occurred in 2021, 2023, 2024 and 2025 in Kerala, reaffirming the region as a hotspot. Key milestones in NiV research include: the identification of the virus in pigs and bats in Malaysia (Chua et al., 2002); recognition of human-to-human transmission in Bangladesh (Gurley et al., 2007; ICDDR, B, 2008); detailed elucidation of viral receptor interactions (Bonaparte et al., 2005); development of monoclonal antibodies and animal models (Bossart et al., 2008); and recommendation of NiV as a priority pathogen by WHO (WHO, 2015). Over the past two decades, NiV has transitioned from a primarily zoonotic pig-borne event to a pathogen with documented human-to-human and nosocomial transmission, thereby elevating its pandemic potential (Ang et al., 2018). In summary, the discovery and historical outbreak chronology of NiV depict an evolving zoonosis with significant human health implications, necessitating continuous vigilance and research.

## 3. Virology and Molecular Structure

The Nipah virus is classified as genus *Henipavirus*, family *Paramyxoviridae*. It is closely related to the Hendra virus (HeV) and shares features with paramyxoviruses such as measles and mumps viruses, though with notable differences in genome length and host range (Wang et al., 2003). NiV is an enveloped virus possessing a non-segmented, negative-sense single-stranded RNA genome of approximately 18 kb in length, which encodes six major structural proteins: nucleoprotein (N), phosphoprotein (P), matrix protein (M), fusion protein (F), attachment glycoprotein (G), and the large polymerase (L) (Diederich et al., 2016).

### 3.1. Genome organisation and proteins

- N (nucleoprotein) binds viral RNA to form the ribonucleoprotein complex.
- P (phosphoprotein) serves as a non-enzymatic co-factor for L, also giving rise to non-structural

proteins (V, W, C) via RNA editing that modulate host immune responses (Rodriguez et al., 2011).

- M (matrix protein) orchestrates virus assembly and budding at the cellular membrane.
- G (glycoprotein) mediates receptor binding, while F (fusion protein) promotes membrane fusion between viral envelope and host cell membrane.
- L (polymerase) is responsible for viral RNA synthesis and replication.

### 3.2. Mechanism of cell entry and replication

NiV utilises the cellular receptors Ephrin-B2 and Ephrin-B3 on host cells (Bonaparte et al., 2005; Negrete et al., 2006). These receptors are highly conserved across mammalian species and are abundantly expressed in endothelial and neuronal tissues, explaining the virus's broad tropism and severe neuropathology. The G protein binds Ephrin-B2/B3, triggering conformational changes that activate F protein, resulting in fusion of the viral and host membranes and release of the ribonucleoprotein complex into the cytoplasm. Viral replication proceeds via the polymerase L complex and produces mRNAs, antigenome, and progeny genomes; subsequent assembly at the plasma membrane involves M protein and budding of new virions.

### 3.3. Comparison with related viruses

Although measles virus and mumps virus (Paramyxoviridae) also use F and H/HN glycoproteins for entry, NiV has a broader host range and higher pathogenicity. In contrast to HeV, which primarily infects equines and humans (Australia), NiV has a broader zoonotic spectrum and more frequent human-to-human transmission. Genome variation studies indicate two major lineages of NiV: the Malaysia strain and the Bangladesh strain, with the latter associated with higher mortality and more frequent human-to-human spread (Luby et al., 2009).

### 3.4. Mutational diversity and implications for virulence

Although henipaviruses have relatively stable genomes compared to influenza or HIV, some sequence variation has been identified between outbreak strains. The differences in non-structural proteins (V, W) may influence interferon antagonism and thus virulence (Lo & Rota, 2018). Genomic surveillance (Twenty-five years review) has documented 754 human NiV cases and 435 deaths globally (CFR ~58 %) but also highlighted limited mutational drift to date (Twenty-five years ... 2024). From a public-health perspective, the relative genome stability is reassuring for vaccine and therapeutic design, but the capacity for adaptation remains a concern. In sum, the molecular biology of NiV offers insight into its pathogenic potential (broad receptor usage, tissue tropism, immune evasion mechanisms), and underpins the rationale for antiviral and vaccine development.

## 4. Epidemiology

### 4.1 Global Distribution and Outbreak Patterns

The global distribution of NiV is predominantly within South and Southeast Asia, with spillover risk zones overlapping with the range of *Pteropus* spp. fruit bats. The first large outbreak occurred in Malaysia and Singapore in 1998–1999, with 265 human cases and 108 deaths. In Bangladesh, outbreaks have been recorded almost annually since 2001, often in the “date-palm sap” season (Luby et al., 2009; Hossain et al., 2008). In India, major outbreaks occurred in Siliguri (2001), Nadia (2007), and Kerala (2018, 2021, 2023–25) with variable case-fatality rates (Joseph et al., 2019; WHO 2025). Recently, the Philippines reported a NiV or NiV-like henipavirus outbreak (Philippines, 2014) (Gamage et al., 2017). According to a recent review, 754 human NiV cases with 435 deaths (CFR ≈ 58%) were reported globally over 25 years. Table 1 outlines a summary timeline of major outbreaks (country, year, CFR) for reference.

Country	Year(s)	Approximate Case-Fatality Rate
Malaysia / Singapore	1998–1999	~40 % (108/265) (Chua et al., 2000)
Bangladesh	2001–present	~70–90 % in many outbreaks (Luby et al., 2009; Tackling NiV surveillance ... 2021)
India – Siliguri	2001	~68 % (45 deaths)

India – Kerala	2018	~74 % (17/23) (Joseph et al., 2019)
India – Kerala	2023–25	Variable (e.g., 2023: 6 cases, 2 deaths, CFR ~33 %)

Reservoir hosts are fruit bats of genus *Pteropus* (*Pteropus vampyrus*, *P. giganteus*, *P. medius*) which carry NiV asymptotically and can shed virus via urine, saliva, or partially eaten fruit (Wacharapluesadee et al., 2010). Intermediate hosts have included pigs (Malaysia), and in some outbreaks direct bat-to-human or human-to-human transmission has occurred (Hossain et al., 2008; Gurley et al., 2007). Transmission modes include zoonotic (animal-to-human), human-to-human (direct contact, nosocomial), and foodborne (date-palm sap contaminated by bats) (Luby & Gurley, 2012). The geographical risk zones include Bangladesh, eastern India, southern India (Kerala), Malaysia, and potentially neighbouring countries where *Pteropus* bats are present (Gov.UK Nipah guidance 2024).

#### 4.2 Factors Influencing Outbreaks

Environmental and ecological determinants play a major role in NiV spill-over. Deforestation, urban expansion, agricultural intensification, and wildlife habitat fragmentation increase human–bat–livestock contact (Field et al., 2015). Climate factors (particularly drinking of raw date-palm sap in winter months) facilitate bat access to sap containers, thereby increasing foodborne transmission (Rahman et al., 2012). Cultural practices such as consumption of raw date-palm sap in Bangladesh and India have been directly implicated (Luby et al., 2009). Livestock farming practices (pig density, proximity to bat roosts) are significant; the pig-to-human amplification seen in Malaysia underscores this point (Chua et al., 2002). Healthcare-associated transmission is further influenced by inadequate infection prevention and

control (IPC) measures, overcrowded hospitals, delayed diagnosis, and exposure of healthcare workers observed in Bangladesh and Kerala outbreaks (Joseph et al., 2019).

#### 4.3 Transmission Dynamics

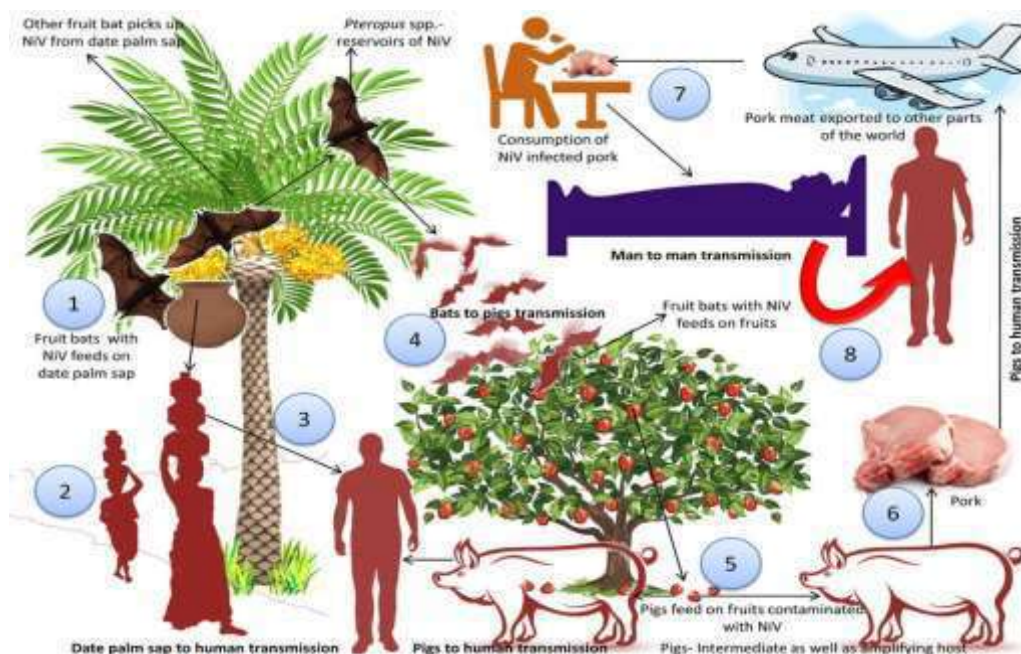
The transmission dynamics of NiV illustrate its capacity for zoonotic spill-over and limited but significant human-to-human spread.

##### 4.3.1. Reservoir-to-human transmission

Fruit bats (genus *Pteropus*) serve as the known natural reservoir of NiV. Humans may be infected through contact with bat urine, saliva, partially eaten fruit or contaminated date-palm sap. In Bangladesh, drinking raw date-palm sap contaminated by bat excreta is a well-documented mode of zoonotic transmission (Luby et al., 2009). In Malaysia, contamination of pig feed or stabling by bats was implicated (Chua et al., 2002). Transmission from bats to humans remains sporadic, but the risk persists in areas with bat–human interface.

##### 4.3.2. Animal-to-human (intermediate host) transmission

Amplification of NiV in intermediate animal hosts increases human risk. In Malaysia, pigs acted as amplifying hosts: infected by bats, then transmitting NiV to farm workers with high virus loads and respiratory shedding (Chua et al., 2002). Similar events have not been widely documented elsewhere, but remain biologically plausible for other livestock species.



**Fig no. 1: Schematic of NiV transmission cycle**

#### 4.3.3. Human-to-human and nosocomial transmission

Unlike many zoonoses, NiV has demonstrated human-to-human transmission, particularly in settings with close contact and respiratory involvement. In Bangladesh, studies of cases from 2001-2014 documented 14 years of investigations, revealing chains of transmission among caregivers and hospital personnel (N Engl J Med Transmission study). In Kerala (2018) the index case transmitted infection to a nurse and multiple other contacts in hospital setting (Joseph et al., 2019). Super-spreader events and nosocomial spread are therefore real concerns. However, the basic reproduction number ( $R_0$ ) for NiV remains below that of pathogens such as measles; modeling studies suggest limited sustained human-to-human transmission (Modelling NiV dynamics 2020).

#### 4.3.4. Shedding, incubation and infectivity

Reported incubation periods of NiV range from 5–14 days, with some documented up to 45 days in rare cases (Wikipedia summary). Viral shedding in humans may occur in respiratory secretions, urine, and blood. The duration of shedding and infectivity are not fully characterised, but longer shedding in respiratory secretions may correlate with transmission risk (Hassan et al., 2020). Understanding of environmental survival (on fomites, in sap) remains

incomplete. In summary, the transmission dynamics of NiV encompass zoonotic spill-over, animal-to-human amplification, and human-to-human transmission under facilitating conditions. While the  $R_0$  remains modest, the high mortality and outbreak potential elevate NiV to a pathogen of concern.

### 5. Pathophysiology

The pathophysiology of NiV infection reflects its broad cellular tropism, potent endothelial and neuronal involvement, and capacity for multisystem disease.

#### 5.1. Viral entry and tissue tropism

NiV binds to cellular receptors Ephrin-B2 and Ephrin-B3, which are expressed on endothelial cells, neurons, smooth muscle cells, and certain epithelial tissues (Bonaparte et al., 2005). This receptor distribution (especially in brainstem, lung, vasculature) explains the neurotropic and vasculitic manifestations of NiV. Following binding, membrane fusion mediated by the F glycoprotein facilitates viral entry. Once inside, NiV replicates in the cytoplasm, assembles new virions, and budding occurs at the plasma membrane. Endothelial infection leads to vascular injury, micro-infarcts, and haemorrhagic lesions.

#### 5.2. Mechanism of disease progression

NiV primarily causes severe disease via a cascade of vascular and neurological injury:

- Endothelial damage: infection of vascular endothelium results in vasculitis, increased permeability, micro-haemorrhages and micro-infarctions (Wong et al., 2002).
- Blood–brain barrier penetration: the virus infects brain endothelial cells and neuronal tissue, causing necrosis, syncytia formation, and encephalitis (Wong et al., 2003).
- Cytokine dysregulation: NiV infection induces high levels of pro-inflammatory cytokines and chemokines (IL-6, TNF- $\alpha$ ) that contribute to tissue injury and systemic manifestations (Wong et al., 2019).
- Multi-organ involvement: Although neurological and respiratory systems predominate, renal, cardiovascular (myocarditis, arrhythmia) and hepatic involvement have been reported (Thompson et al., 2014).

### 5.3. Neuropathology and histopathological findings

Autopsy findings from NiV-infected humans and animals demonstrate widespread vasculitis, necrotising lesions, syncytia in endothelial and neuronal tissues, micro-infarction, and evidence of viral antigen in brainstem medullary regions (Ng et al., 2004). Key features include:

- Necrotising arteritis and perivascular cuffing in the brain.
- Syncytial giant cells in infected tissues.
- Micro-haemorrhages and infarcts in grey matter and white matter.
- Pneumonitis with alveolar damage in respiratory predominant cases.

### 5.4. Comparison with Hendra virus

While both NiV and HeV share similar mechanisms (Ephrin-B2/B3 receptor usage, endothelial/neuronal tropism), NiV tends to cause more frequent human-to-human transmission and has a broader geographic distribution. HeV outbreaks are primarily equine-to-human in Australia, and human-to-human spread is not documented. The relative severity of NiV may be linked to greater viral shedding in human respiratory

secretions and wider host adaptability (Middleton et al., 2014).

In conclusion, the pathophysiology of NiV involves viral entry via ephrin receptors, endothelial injury, neuroinvasion, immunopathology and multisystem collapse, thereby explaining the clinical severity and rapid progression seen in many patients.

## 6. Clinical Manifestations

### 6.1. Incubation period

Reported incubation periods for NiV infection typically range from 5 to 14 days, although longer periods (up to 45 days) have been documented in rare instances (Luby et al., 2009; Wikipedia summary).

### 6.2. Early symptoms

The initial clinical presentation often resembles an influenza-like illness, with fever, headache, myalgia, vomiting, and sore throat. Patients may also experience fatigue and dizziness (Thakur & Bailey, 2019).

### 6.3. Progressive neurological and respiratory manifestations

In many cases, the disease rapidly progresses to involvement of the central nervous system (CNS) and/or the respiratory system:

- Neurological: Dizziness, confusion, altered consciousness, seizures, encephalitis. A systematic review of neurological signs in NiV detailed frequent features of altered mental status, focal deficits, seizures, and abnormal neuroimaging findings.
- Respiratory: Cough, shortness of breath, pneumonia, acute respiratory distress syndrome (ARDS) in severe cases (Luby & Gurley, 2012).
- Multi-organ: Some patients develop cardiovascular dysfunction (arrhythmia, myocarditis), acute kidney injury and elevated liver enzymes.

### 6.4. Severe cases and chronic/relapsing manifestations

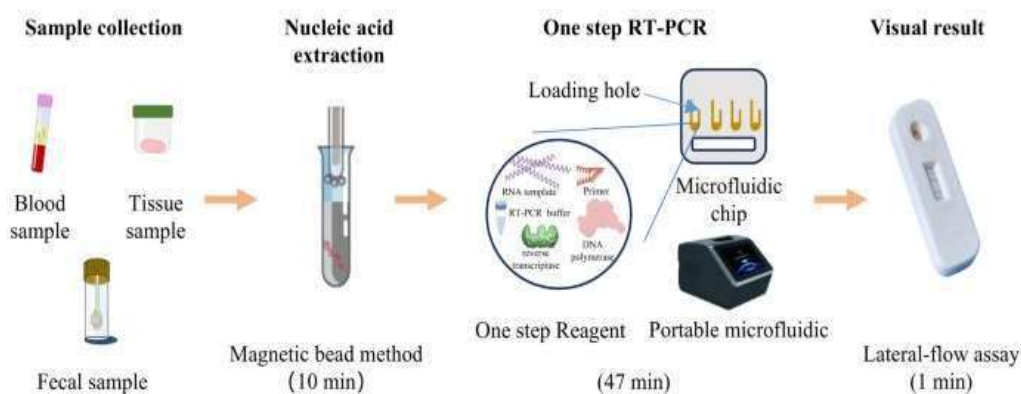
Severe NiV infection may lead to coma, multi-organ failure, and death within days of neurological onset (Wong et al., 2002). Importantly, relapsing or late-onset encephalitis may occur months to years after initial recovery; such cases present with altered mental status, seizures and high mortality (Hossain et al., 2008). Survivors may also experience long-term neurological sequelae including personality changes, residual seizures, and cognitive impairment (Neurologic signs review ... 2020).

## 6.5. Differential diagnosis

Clinical presentation of NiV overlaps with other causes of viral encephalitis (e.g., Japanese

encephalitis, Rabies, herpes encephalitis) and severe respiratory viral infections. Key differential features include epidemiological risk (bat exposure, date-palm sap, pig contact), rapid onset of encephalitis plus respiratory involvement, and known outbreak setting. Early recognition of NiV is critical to infection control and management. In summary, NiV infection presents a clinical spectrum from mild febrile illness to fulminant encephalitis and respiratory failure, with potential long-term consequences in survivors, underscoring the need for timely diagnosis and care.

## 7. Diagnosis



**Fig no.2: Diagnostic / Laboratory assay image**

### 7.1. Sample types and biosafety

Diagnosis of NiV infection requires collection of appropriate specimens under strict biosafety conditions (BSL-4 laboratories for virus isolation). Sample types include blood (serum/plasma), cerebrospinal fluid (CSF), throat/nasal swabs, urine and sometimes post-mortem tissue (CDC NiV factsheet). Proper transport, handling and PPE use (gloves, face shield, N95/FFP2, gown) are mandatory to avoid laboratory-acquired infections.

### 7.2. Diagnostic tests

- **RT-PCR:** Real-time reverse transcriptase PCR is the gold standard for detection of NiV RNA in acute infection (Salim et al., 2017).
- **Serology:** IgM and IgG ELISA tests allow retrospective diagnosis of NiV infection in survivors (Goh et al., 2000).

- **Virus isolation:** Reserved for BSL-4 labs; provides live virus but is rarely used for routine diagnostics.
- **Immunohistochemistry (IHC):** Detection of viral antigen in tissues for pathology studies.
- **Next-generation sequencing (NGS):** Used for epidemiological tracing, genomic characterisation of strains (Pathogenesis review ... 2025).
- **Point-of-care tests (POCT):** New rapid diagnostics are under development to improve outbreak response, but none are widely licensed yet (Therapeutics systematic review 2024).

### 7.3. Interpretation and timing

RT-PCR is most sensitive during early viraemic or respiratory shedding periods (first few days of symptoms). Serology becomes positive later in the

course or during convalescence. Negative results do not exclude NiV if samples are collected late or inadequately. Close liaison with reference laboratories is essential for interpretation and confirmation.

#### 7.4. Biosafety and reporting

Given the high-consequence nature of NiV, laboratories must adhere to WHO and CDC biosafety guidelines, including use of BSL-4 containment for virus culture and proper reporting of confirmed cases to public-health authorities (WHO, 2023). In summary, diagnosis of NiV infection relies on molecular and serologic assays conducted under rigorous biosafety frameworks, with emerging advances in rapid/field diagnostics offering promise for faster outbreak response.

### 8. Management and Therapeutic Strategies

#### 8.1 Supportive and Symptomatic Treatment

Currently, there is no licensed specific antiviral therapy or vaccine for NiV. Clinical management revolves around intensive supportive care:

- Management of fever, seizures (anticonvulsants), and altered mental status in encephalitic patients.
- Respiratory support including supplemental oxygen, mechanical ventilation in ARDS.
- Management of shock, arrhythmias, acute kidney injury or multi-organ failure in ICU settings.
- Infection control measures (isolation, standard and droplet precautions) to protect healthcare workers and contacts. Evidence remains limited to case series, and

outcomes are improved when patients receive early intensive care (Wong et al., 2003).

#### 8.2 Experimental Antivirals

A number of candidate therapeutics have been evaluated pre-clinically or in few human cases:

- **Ribavirin:** Initial Malaysian cases received ribavirin; retrospective analysis did not clearly demonstrate efficacy, and results remain mixed (Kumar et al., 2016).
- **Favipiravir (T-705):** Demonstrated efficacy in NiV animal models (Lo et al., 2021) and is under further assessment.
- **Remdesivir:** Preclinical studies suggest activity against henipaviruses; human data is lacking (Therapeutics systematic review, 2024).
- **Monoclonal antibodies:** The humanised m102.4 antibody targets NiV-G glycoprotein and has shown promise in non-human primate models, and compassionate use in human outbreaks (Bossart et al., 2011).
- **RNA interference and fusion inhibitors:** Early-stage research is exploring small interfering RNA (siRNA) and small-molecule fusion inhibitors, but these remain experimental.
- **Combination therapy:** Because of the high fatality risk, combination therapy (antiviral + antibody + ICU support) is proposed though not yet standardised.

#### Key pharmacological agents under investigation

**Table 2. Key pharmacological agents for NiV under study.**

Agent	Mechanism of Action	Status
Ribavirin	Broad-spectrum antiviral nucleotide analog	Retrospective human use; mixed outcomes
Favipiravir (T-705)	Viral RNA polymerase inhibitor	Animal model efficacy demonstrated; human trials pending
Remdesivir	Viral RNA polymerase inhibitor	Preclinical data; no confirmed human trial yet
m102.4 Monoclonal antibody	Neutralises NiV-G glycoprotein	Phase I/compassionate human use
Fusion inhibitors / siRNA	Inhibit viral membrane fusion or replication	Early-stage research

### 8.3 Vaccine Development

Efforts to develop NiV vaccines are progressing though no licenced product yet exists. Major platforms include:

- **Subunit vaccines:** G-glycoprotein-based formulations have shown immunogenicity in animal models (Guillaume et al., 2020).
- **Viral vector vaccines:** Adenovirus (ChAdOx1 NiV-G) and vesicular stomatitis virus (VSV)-based platforms have entered preclinical/early-phase human trials (Broder et al., 2022).
- **mRNA vaccines:** Given the success of mRNA platforms for other viruses, mRNA-based NiV vaccines are under development though limited published data until 2025. Challenges include cross-protection against divergent NiV strains (Malaysia vs. Bangladesh lineage), durability of immunity, cost and feasibility in low-resource settings, and biosafety in vaccine manufacturing. The necessity of human efficacy trials is complicated by the sporadic nature of outbreaks. Pathogenesis review (2025) emphasised these gaps.

In summary, while therapeutic and vaccine development for NiV is active and promising, current management remains supportive and highlights the urgency of further clinical research and global investment.

### 9. Future Directions and Challenges

While considerable progress has been made in understanding NiV, significant gaps and challenges remain, pointing to key directions for future research and policy.

#### 9.1. Gaps in transmission ecology and host adaptation

Understanding the precise mechanisms of spill-over (bat to human, bat to livestock to human) remains incomplete. The influence of climate change, bat migration, deforestation and land-use change on NiV emergence warrants further investigation (Field et al., 2015). The potential for viral adaptation leading to

sustained human-to-human transmission remains a major concern.

#### 9.2. Limitations of diagnostics and treatment

Rapid point-of-care diagnostics for NiV are still not widely validated; improved field-deployable assays are needed, especially in low-resource settings. On the therapeutic front, although monoclonal antibodies and antivirals show promise, the absence of licenced treatments means current case-fatality remains high. Clinical trials are logistically challenging given sporadic outbreak nature.

#### 9.3. Vaccine development and access

Developing broad-spectrum, durable vaccines covering divergent NiV strains (Malaysia vs. Bangladesh lineages) remains a priority. Ensuring equitable access, cost-effectiveness and deployment in resource-constrained regions is essential. Additionally, conducting human efficacy trials in the context of irregular outbreaks presents design challenges.

#### 9.4. Surveillance and global readiness

Given NiV's inclusion on WHO's priority pathogens list, building global surveillance networks, increasing laboratory capacity (especially in endemic zones), ensuring rapid data sharing, and integrating animal-human-environmental health systems remain critical. Integration with pandemic preparedness frameworks is essential.

#### 9.5. Ethical and biosafety considerations

Research involving BSL-4 pathogens such as NiV presents biosafety risks and ethical considerations around dual-use research of concern (DURC). Transparent governance, international collaboration, and rigorous oversight are required. Furthermore, community engagement and trust in outbreak response ('infodemic' management) remain essential in culturally diverse settings. In essence, the future success of NiV control efforts will depend on interdisciplinary strategies integrating virology, epidemiology, ecology, clinical medicine, policy and ethical governance.

## CONCLUSION

The Nipah virus represents a formidable zoonotic pathogen characterised by high mortality, broad tissue tropism, human-to-human transmission potential and lack of approved counter-measures. The global significance of NiV is underscored by its repeated outbreaks in South and Southeast Asia, its reservoir in widely distributed fruit bats, and its capacity to exploit ecological and behavioural interfaces between animals and humans. Our review has synthesised current knowledge of NiV epidemiology, molecular biology, clinical features, diagnostics, therapeutics, vaccine development and public health response. It is evident that effective management of NiV requires an integrated approach—linking epidemiological surveillance, rapid laboratory diagnostics, intensive clinical care, therapeutics and vaccine research, behavioural interventions and One Health coordination. Recent outbreaks, particularly in Kerala and Bangladesh, provide both cautionary lessons and proof of concept that rapid, organised responses can contain NiV. Going forward, the imperative is clear: global collaboration, sustained investment in research and health-system strengthening, ecological monitoring, and community-engaged prevention strategies. Only by marrying molecular insights with public-health action can we hope to mitigate the threat posed by NiV and avert future large-scale outbreaks. Continued vigilance, preparedness and multidisciplinary effort are essential.

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