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Review Article

Nipah Virus (NiV) at the Human-Animal-Environment Interface: Emerging Insights into Spillover Dynamics, Neurotropism, and Future Pandemic Risk

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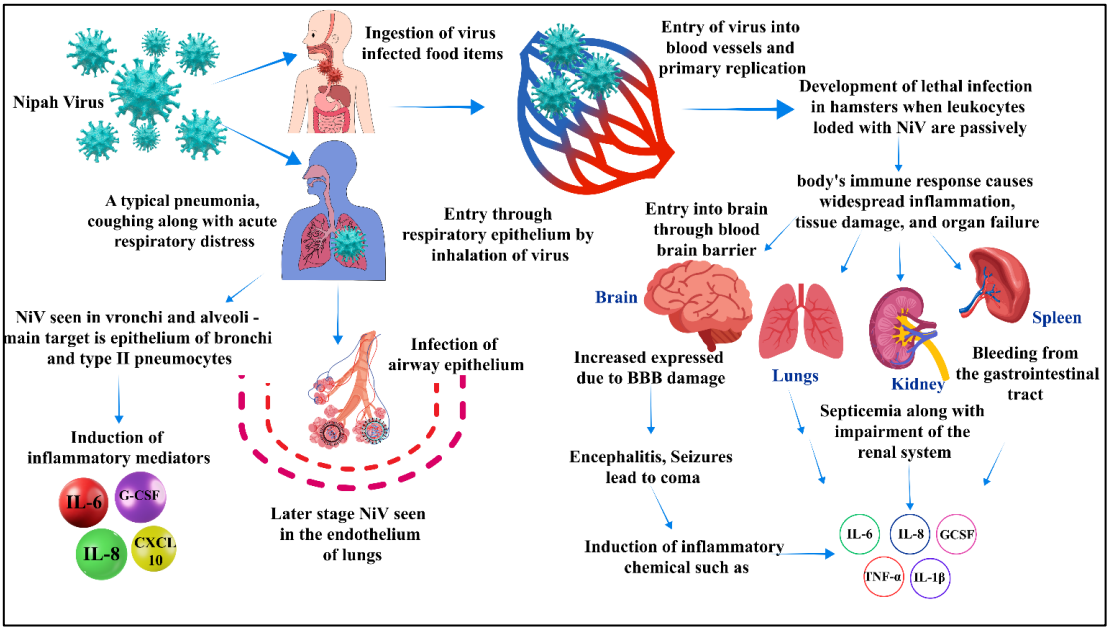
Abstract

Nipah virus (NiV), a highly pathogenic member of the Henipavirus genus within the Paramyxoviridae family, continues to represent a critical zoonotic threat at the intersection of humans, animals, and the environment. First identified in Malaysia in 1998, NiV has since emerged as a paradigm of viral spillover driven by ecological disruption and anthropogenic activities. This review elucidates contemporary insights into the complex interplay governing NiV transmission dynamics, molecular neurotropism, and its potential to precipitate future pandemics. The spillover of NiV from its natural reservoir, Pteropus fruit bats, to intermediate hosts such as pigs, and ultimately to humans, is profoundly influenced by habitat fragmentation, agricultural intensification, and climate-induced alterations in bat foraging behavior. At the molecular level, NiV exhibits pronounced neurotropism and vasculotropism mediated through its interaction with ephrin-B2 and ephrin-B3 receptors, leading to widespread endothelial infection, microvascular damage, and neuronal dysfunction that culminate in fatal encephalitis. Moreover, the virus demonstrates immune evasion strategies that suppress interferon signaling, thereby facilitating systemic dissemination. Despite its high case fatality rate and recurrent outbreaks in South and Southeast Asia, the absence of licensed antiviral therapies or vaccines underscores the urgency of advancing translational research and cross-sectoral surveillance frameworks. The convergence of ecological perturbations, viral adaptability, and limited healthcare infrastructure in endemic regions amplifies the likelihood of future spillover and sustained human-to-human transmission. A unified One Health approach integrating virological, ecological, and epidemiological disciplines is imperative to mitigate NiV's pandemic potential and to strengthen global preparedness against emerging zoonoses.

Keywords: Neurotropism, Nipah virus (NiV), One Health, Pandemic preparedness, Spillover dynamics, Zoonotic transmission.

Graphical abstract:



Highlights:

- ✓ The study elucidates the intricate interactions at the human-animal-environment interface that facilitate Nipah virus (NiV) spillover, emphasizing ecological disruptions, land-use change, and climate variability as pivotal determinants of transmission dynamics.
- ✓ It provides an in-depth interpretation of NiV's molecular neurotropism and vasculotropism, detailing how ephrin-B2 and ephrin-B3 receptor-mediated entry drives endothelial dysfunction, neuronal injury, and fatal encephalitic manifestations.
- ✓ The review identifies anthropogenic factorssuch as agricultural intensification, livestockwildlife overlap, and unsustainable habitat encroachmentas major accelerators of NiV cross-species transmission and outbreak amplification.
- ✓ The analysis underscores the paucity of licensed vaccines or antivirals and highlights deficiencies in regional surveillance, rapid diagnostics, and One Health coordination, which collectively exacerbate the risk of undetected viral spread.
- ✓ It critically evaluates the evolutionary adaptability of NiV, its capacity for sustained human-to-human transmission, and the socio-ecological conditions that may transform localized outbreaks into pandemics.
- ✓ The paper advocates for a unified One Health framework integrating virological, ecological, and epidemiological intelligence to enhance early warning systems, strengthen intersectoral collaboration, and mitigate future spillover risks.

1. Introduction

Emerging zoonoses have repeatedly challenged global health systems, with severe acute respiratory syndrome (SARS), Ebola virus disease, and Coronavirus Disease 2019 (COVID-19) serving as stark reminders of how quickly a localized spillover can escalate into a transnational crisis.[1] The virus was first identified during an outbreak between September 1998 and May 1999 in Malaysia and Singapore, which resulted in 276 confirmed human infections and considerable mortality. Its characteristics, a case fatality rate of up to 75 %, broad host range, pronounced neurotropism, and absence of licensed treatments or vaccines place it among the World Health Organization's Research and Development(R&D) Blueprint priority pathogens.[2] Unlike influenza or corona viruses, NiV outbreaks have remained geographically constrained, largely to Bangladesh, India, and Malaysia.[3] Yet, recurrent re-emergence, human-to-human transmission chains, and ecological changes that increase human-bat interactions raise alarm about its pandemic potential. Recent outbreaks demonstrate both persistence and variability in mortality and outbreak size, underscoring NiV's evolving public health threat. In India, the southern state of Kerala continues to experience repeated spillovers: since 2018, nine outbreaks have been reported in Kerala.[4] The 2018 Kozhikode-Malappuram outbreak involved 23 confirmed and probable cases with a case fatality rate (CFR) of approximately 91 %.[5] In 2019 and 2021, single case outbreaks occurred in Kerala, each resulting in fatality (100 % CFR).[6] More recently, a 2023 outbreak in Kozhikode had six confirmed cases and two deaths, yielding a CFR of ~33.3 %. In mid-2025, from 17 May to 12 July, Kerala reported four confirmed cases of which two were fatal (CFR 50 %) in two districts.[7] Globally, meta-analyses reveal an alarming trend: the NiV mortality rate in the decade 2014-2023 has risen to ~80.1 % (95 % CI: 68.7-88.1 %) from ~54.1 % (95 % CI: 35.5-71.6 %) in 2004-2013.[8] Among individual countries, India has experienced the highest pooled mortality (~82.7 %), followed by Bangladesh (~62.1 %), Philippines (~52.9 %), Malaysia (~28.9 %), and Singapore (~21 %).[9] Additionally, in Bangladesh, since 2001, a total of ~347 human infections have been recorded, with an overall CFR of ~71.7 %.[10]This review explores these recent developments in the ecology, molecular biology, pathogenesis, and clinical spectrum of NiV, while also examining advances in diagnostics, therapeutics, and preparedness frameworks. Our goal is to integrate these perspectives through a One Health lens to highlight how NiV exemplifies the intersection of environmental disruption, pathogen biology, and human vulnerability, especially now, when even small outbreak differences in detection timing, healthcare response, or strain pathogenicity can shift mortality rates dramatically. The Diagrammatic overview of Nipah virus (NiV) structural and genomic organization showing major proteins and their functional roles in viral attachment, fusion, replication, and immune evasion mechanisms are shown in fig. 1.

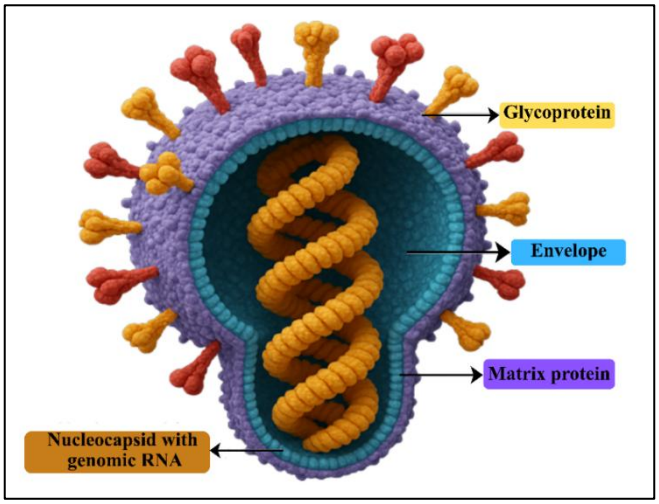


Figure 1: Schematic representation of the structural organization of Nipah virus (NiV)

2. Ecology and Spillover Dynamics

Reservoir hosts: Fruit bats (Pteropus spp.)

Fruit bats of the genus Pteropus are established natural reservoirs of NiV. Viral Ribonucleic Acid (RNA) and antibodies have been consistently detected in multiple Pteropus species across South Asia, Southeast Asia, and parts of Oceania. The wide distribution and migratory behavior of these bats create overlapping zones of risk,

particularly in agricultural landscapes.[11] Importantly, bats show no overt disease from NiV, suggesting long-term co-evolutionary tolerance. Their role as silent carriers is amplified by their ecology large colony sizes, long lifespans, and seasonal feeding migrations enable persistent viral circulation and widespread dissemination. These characteristics make Pteropus bats a critical focal point for surveillance under the One Health framework.[12]

Environmental drivers

Anthropogenic changes such as deforestation, urban expansion, and agricultural intensification disrupt bat habitats and increase opportunities for human-bat contact. Climate change, by altering bat migration and feeding patterns, is expected to intensify spillover risks. Seasonal food scarcity also drives bats closer to human settlements, especially during fruiting seasons.[13] These pressures not only force bats into proximity with humans but also heighten stress within bat populations, which may increase viral shedding. Expansion of livestock farming beneath bat roosts further amplifies spillover risk, as animals can serve as intermediate hosts. Together, these factors illustrate how ecological disruption reshapes the dynamics of pathogen transmission.[14]

Intermediate hosts and direct transmission

The 1998 Malaysian outbreak demonstrated the role of pigs as amplifying hosts, enabling massive viral amplification and occupational exposure.[15]However, in Bangladesh and India, most outbreaks have arisen through direct bat-to-human transmission. A key pathway is the consumption of raw date palm sap contaminated with bat saliva or urine. Direct exposure to bat roosts or contaminated fruit is also implicated.[16]

Human to human transmission

Epidemiological investigations have documented nosocomial transmission, family clusters, and occasional superspreading events. NiV-Bangladesh appears more transmissible between humans than NiV-Malaysia, raising concern about future adaptation. Transmission often occurs via close contact with respiratory secretions, underscoring the virus's dual respiratory and neurological tropism.[17]

One Health perspective

Understanding NiV ecology requires integrating data from wildlife surveillance, veterinary systems, and human health. A One Health approach that considers bat ecology, agricultural practices, and healthcare behavior is essential for designing interventions.[18]The conceptual illustration of the *One Health* framework in the context of Nipah virus (NiV), depicting the interconnectedness between humans, animals, and the environment in facilitating viral spillover, transmission, and control strategies are shown in fig.2.

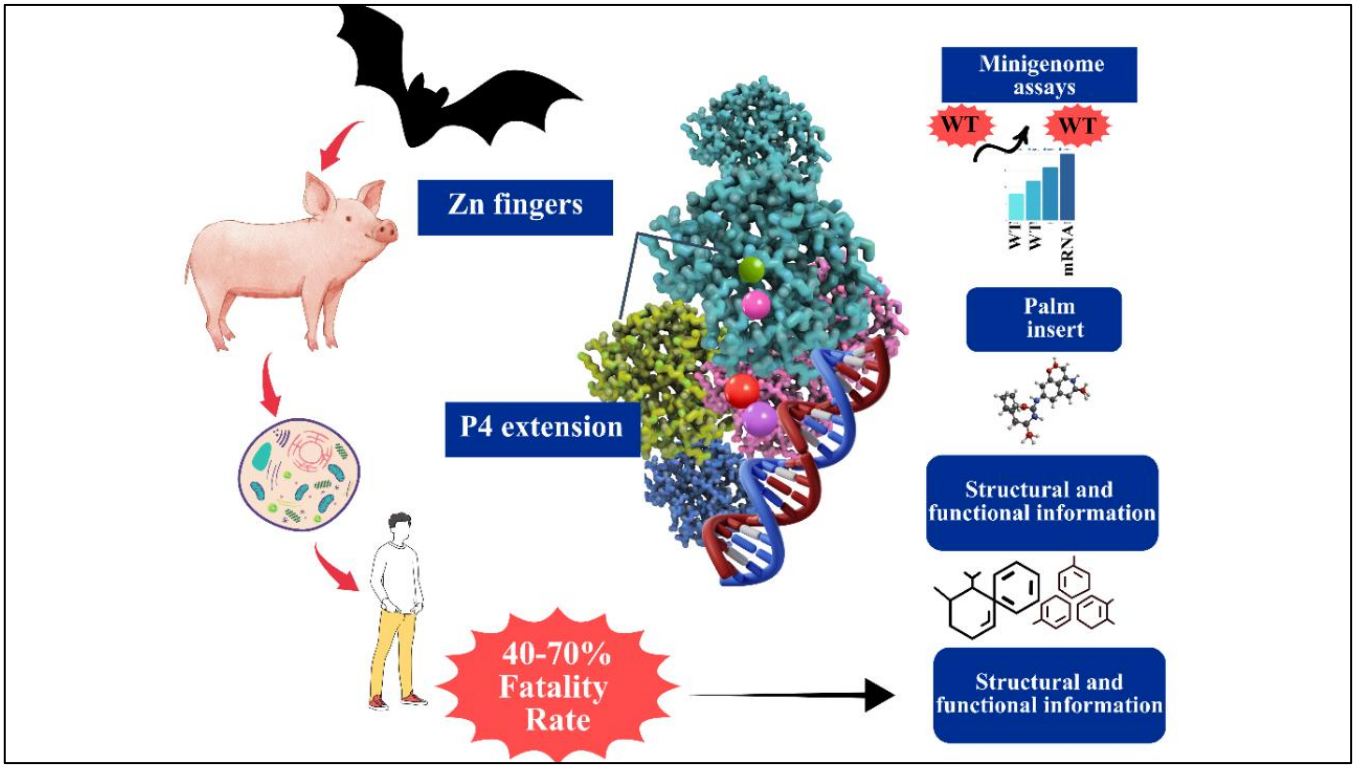


Figure 2: Conceptual illustration of the *One Health* framework in the context of Nipah virus (NiV), depicting the interconnectedness between humans, animals, and the environment in facilitating viral spillover, transmission, and control strategies

3. Viral Biology and Evolutionary Dynamics

NiV belongs to the genus Henipavirus within the family Paramyxoviridae, alongside Hendra virus. Its ~18 kb genome encodes six structural proteins (N, P, M, F, G, L) and three accessory proteins (V, W, C) derived from the P gene. The nucleocapsid (N) protein encapsidates the viral RNA, while the phosphoprotein (P) and large polymerase protein (L) form the RNA-dependent RNA polymerase complex required for replication and transcription. The matrix (M) protein drives viral assembly, while the fusion (F) and attachment glycoprotein (G) mediate host cell entry. Accessory proteins (V, W, C) play key roles in immune evasion, suppressing interferon signaling to facilitate viral persistence.[19]The Schematic representation of the viral biology and evolutionary dynamics of Nipah virus (NiV), illustrating its genomic organization, replication cycle, and adaptive mutations contributing to host tropism and cross-species transmission are shown in Fig 3.

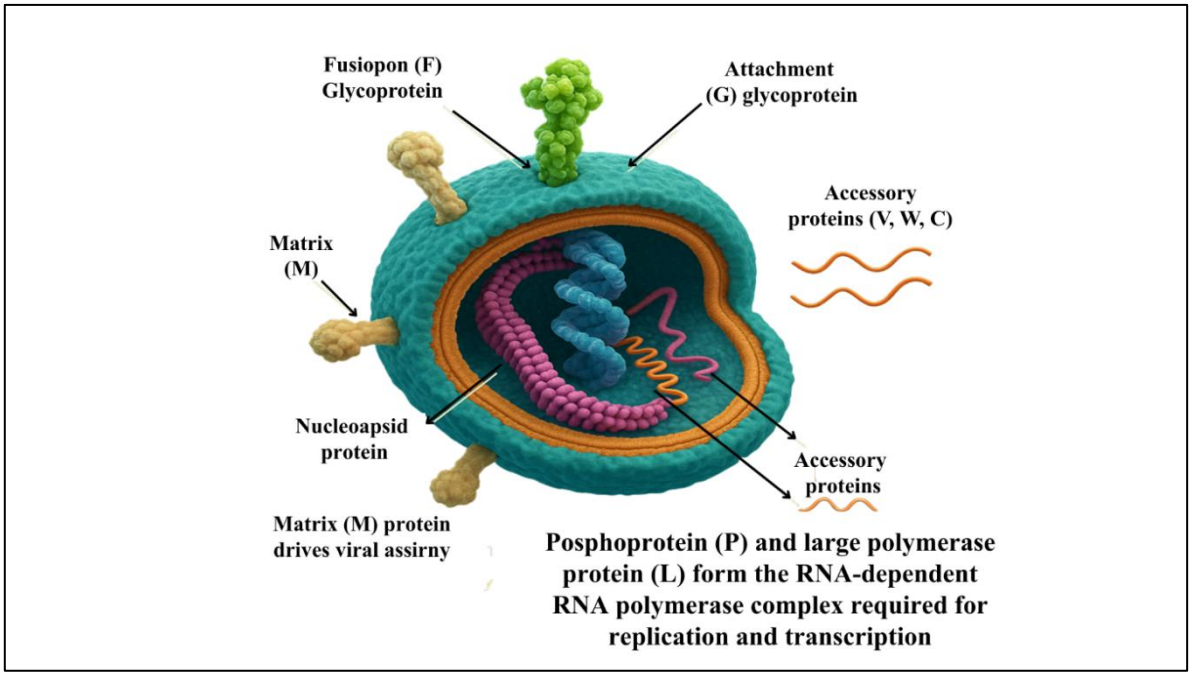


Figure 3: Schematic representation of the viral biology and evolutionary dynamics of Nipah virus (NiV), illustrating its pleomorphic virion architecture with key components including the lipid envelope, matrix (M) protein, fusion (F) and attachment glycoproteins (G), nucleocapsid (N) protein, phosphoprotein (P), and large polymerase (L) protein arranged around the negative-sense single-stranded RNA genome.

Genomic diversity

Two distinct clades circulate: NiV-Malaysia (NiV-M) and NiV-Bangladesh (NiV-B). NiV-M is associated with lower case fatality (~40%) and limited human-to-human spread, while NiV-B shows higher mortality (>70%) and recurrent person-to-person transmission. The differences are thought to reflect both viral genetic variation and ecological contexts of spillover.[20]NiV-M outbreaks largely involved pigs as amplifying hosts, whereas NiV-B is typically transmitted directly from bats to humans or between humans, often through close contact. Genomic comparisons reveal subtle sequence differences that may influence replication efficiency, tissue tropism, and host adaptation. These clade-specific traits underscore the importance of continuous genomic surveillance.[21]

Molecular evolution

Comparative phylogenomic studies show that NiV evolves more slowly than RNA viruses like influenza, under strong purifying selection. However, sporadic mutations may alter viral fitness, tissue tropism, or transmissibility. Recombination events, though rare, could drive adaptation in bat populations. Even modest genomic changes in the fusion (F) or attachment (G) glycoproteins may enhance viral entry efficiency or expand host range. Evidence from sequencing of outbreak strains suggests subtle but recurrent shifts in non-coding and regulatory regions, which could influence replication dynamics. Monitoring these evolutionary trends is crucial, as seemingly minor adaptations may determine whether NiV remains episodic or gains pandemic potential.[22]

Potential for adaptation

Given its receptor usage (ephrin-B2/B3), which is highly conserved across mammals, NiV already has a broad host range, encompassing multiple bat species, domestic animals, and humans. This conserved receptor expression facilitates cross-species infection with minimal adaptation, highlighting the virus's inherent zoonotic potential. Small genetic changes, particularly in the F or G glycoproteins could theoretically enhance respiratory tract infectivity, increase viral shedding, or improve person-to-person transmission efficiency, thereby markedly elevating pandemic risk.[23] Continuous genomic surveillance in both bat reservoirs and human outbreaks is thus crucial, not only to detect emergent variants but also to inform public health interventions

and guide the development of therapeutics and vaccines.[24]

4. Molecular Pathogenesis and Neurotropism

Receptor usage

NiV attaches to ephrin-B2 and ephrin-B3 receptors, expressed abundantly in endothelial cells and neurons. This receptor distribution explains the hallmark features of NiV infection: systemic vasculitis, endothelial disruption, and encephalitis. Endothelial infection leads to widespread vascular damage, increased permeability, and microvascular thrombosis, contributing to multi-organ involvement beyond the central nervous system.[25] In the brain, neuronal infection and associated inflammation result in necrotizing encephalitis, seizures, and altered consciousness.[26] The widespread receptor expression also accounts for respiratory manifestations observed in some outbreaks, as pulmonary endothelial cells can be targeted. Understanding this receptor tropism is critical for elucidating pathogenesis and identifying potential therapeutic targets.[27]

Viral entry and dissemination

After entering via the respiratory tract, NiV spreads through viremia and endothelial infection, reaching the Central Nervous System (CNS) by crossing the blood-brain barrier and via olfactory nerves. The virus's ability to infect endothelial cells facilitates systemic dissemination, allowing it to reach multiple organs, including the lungs, kidneys, and spleen.[28] Within the CNS, NiV infection triggers widespread neuronal apoptosis and inflammation, leading to necrotizing encephalitis. Pathological hallmarks include syncytia formation, vasculitis, microinfarctions, and perivascular cuffing, which together contribute to neurological dysfunction and high mortality. Viral replication in endothelial and neuronal tissues also promotes hemorrhage and edema, exacerbating clinical severity and complicating therapeutic interventions.[29]

Immune evasion strategies

NiV accessory proteins (P, V, and W) inhibit interferon responses by blocking Signal Transducer and Activator of Transcription 1 and 2 (STAT1/STAT2)signaling. This suppression of the host's innate immune defenses allows the virus to replicate efficiently without early antiviral constraints, facilitating systemic dissemination.[30] These proteins also interfere with other immune pathways, including pattern recognition receptor signaling and downstream cytokine production, dampening inflammatory responses that would normally limit infection. By evading interferon-mediated defenses, NiV can establish high viral loads in multiple tissues, including the CNS and endothelial cells. Understanding the precise molecular mechanisms of P, V, and W-mediated immune evasion is critical for developing targeted antiviral therapies and immunomodulatory interventions.[31]

Neurological outcomes

Acute encephalitis is the most severe clinical outcome of NiV infection, often presenting with fever, headache, altered consciousness, seizures, and rapid neurological deterioration, leading to high mortality. However, relapsing or late-onset encephalitis has been documented months to years after initial recovery, indicating that NiV can persist within the central nervous system.[32] This persistence may involve viral latency in neurons or endothelial cells, evasion of immune surveillance, and low-level replication that eventually triggers inflammatory responses. The precise mechanisms underlying latency, reactivation, and CNS tropism remain poorly understood. Elucidating these pathways is essential for developing effective therapeutics, long-term monitoring strategies, and preventive measures for survivors.[33]

5. Clinical Spectrum and Outbreak Features

NiV infection manifests across a wide and heterogeneous clinical spectrum. Many individuals experience mild or asymptomatic infection, often detected only through serological surveys, though the extent to which such cases contribute to transmission remains uncertain. Respiratory involvement is particularly notable in Malaysian outbreaks, where lung pathology facilitated limited airborne spread and amplified exposure risk.[34] The most severe presentation is acute encephalitis, characterized by high fever, altered mental status, seizures, and progression to coma, frequently resulting in death. Case fatality rates vary by outbreak, generally ranging from 40% to 75%. Experiences from Bangladesh and Kerala, India, underscore the heightened vulnerability in settings with constrained healthcare infrastructure, where nosocomial transmission among family members and healthcare workers has amplified the impact of otherwise localized.[35]

6. Diagnostics and Surveillance

Current tools

Molecular diagnostics, particularly RT-PCR, continue to serve as the definitive method for confirming acute NiV infection, while serological techniques such as Enzyme-Linked Immunosorbent Assay (ELISA) and virus neutralization assays are essential for identifying past exposure. However, widespread deployment of these tools is constrained by the requirement for Biosafety Level 4 (BSL-4)laboratory facilities for viral isolation and confirmatory testing, limiting rapid, decentralized response during outbreaks. To address these challenges, emerging diagnostic platforms including Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-based assays, loop-mediated isothermal amplification (LAMP), and portable nanopore sequencing are being developed for field use, enabling timely detection and real-time genomic surveillance.[36]Integrating these human diagnostic efforts with ecological monitoring of bat populations is critical for anticipating spillover events and implementing early interventions. Furthermore, establishing comprehensive genomic databases for NiV can facilitate the rapid identification of viral variants

with altered transmissibility or pathogenicity, supporting both outbreak response and long-term public health preparedness.[37]

7. Therapeutics and Vaccines

Antivirals

Ribavirin, a nucleoside analogue, was used during early NiV outbreaks and demonstrated modest clinical benefit, though robust evidence supporting its efficacy remains limited. Mechanistically, ribavirin is phosphorylated intracellularly to ribavirin triphosphate, which interferes with viral RNA synthesis by inhibiting inosine monophosphate dehydrogenase (IMPDH), thereby depleting intracellular Guanosine Triphosphate (GTP) pools essential for viral replication.[38]Remdesivir, another nucleoside analogue, targets the viral RNA-dependent RNA polymerase (RdRp), incorporating into nascent viral RNA strands and causing premature chain termination, effectively halting genome replication.[39] Favipiravir similarly undergoes ribosylation and phosphorylation to its active form, selectively inhibiting RdRp activity and reducing viral RNA synthesis. In parallel, several novel polymerase inhibitors are under preclinical evaluation, designed to bind specific allosteric or catalytic sites of the NiV polymerase complex, preventing RNA elongation without affecting host polymerases. Collectively, these antiviral strategies aim to suppress viral replication at the molecular level, offering potential therapeutic avenues pending further validation in clinical trials.[40]

Monoclonal antibodies

The human monoclonal antibody m102.4 has shown strong neutralizing activity against NiV both in vitro and in non-human primate models. At the molecular level, m102.4 binds with high affinity to the viral G glycoprotein, blocking its interaction with ephrin-B2 and ephrin-B3 receptors on host cells, thereby preventing viral attachment and entry. Compassionate use in humans has yielded promising outcomes, and ongoing clinical trials are evaluating its safety, pharmacokinetics, and therapeutic efficacy as a targeted post-exposure intervention.[41]

Vaccines

Viral-vectored vaccine platforms, such as Chimpanzee Adenovirus Oxford 1 (ChAdOx1) and vesicular stomatitis virus (VSV)-based constructs, have demonstrated robust immunogenicity in preclinical studies. These platforms function by delivering the gene encoding the NiV glycoproteins primarily the F and G proteins into host cells, enabling in situ expression and presentation of viral antigens to the immune system. This triggers both humoral and cellular immunity, including neutralizing antibodies that block viral attachment and cytotoxic T-cell responses that eliminate infected cells.[42] Similarly, messenger Ribonucleic Acid(mRNA)-based vaccines exploit host cellular machinery to translate the delivered NiV antigen mRNA into protein, eliciting adaptive immune responses analogous to natural infection without exposure to live virus. Translational studies in ferrets, hamsters, and non-human primates provide critical insights into immunogenicity, dosing, and protection against challenge infection.[43] Despite promising efficacy, deployment faces significant barriers, including limited commercial incentive due to the sporadic nature of NiV outbreaks, logistical challenges of stockpiling, and regulatory hurdles for emergency use authorization, which collectively impede rapid global preparedness.[44]The Overview of therapeutic and post-exposure prophylactic agents studied against Nipah virus (NiV), summarizing their mechanisms of action, target pathways, model systems, and efficacy outcomes from experimental and preclinical evaluations are summarize in Table 1.

Table 1: Summary of Pharmacological agents investigated for the treatment and post-exposure prophylaxis of Nipah virus (NiV) infection

Agent	Class	Mechanism of Action	Dose	Route of Administration	Receptor/Enzyme Interaction	Duration	Ref.
Ribavirin	Nucleoside analogue	Inhibits inosine monophosphatedehydrogenase, depleting GTP pools and impairing viral RNA synthesis.	15 mg/kg IV loading dose, then 7.5 mg/kg every 8 hours	Intravenous (IV)	Inosine monophosphate dehydrogenase (IMPDH)	Short-term (acute phase)	45
Remdesivir	Nucleotide analogue	Incorporates into viral RNA by RNA-dependent RNA polymerase (RdRp), causing premature chain termination.	200 mg IV loading dose, then 100	Intravenous (IV)	RNA-dependent RNA polymerase (RdRp)	Short-term (acute phase)	46

			mg daily				
Favipiravir	RNA polymerase inhibitor	Inhibits viral RNA polymerase, reducing viral RNA synthesis.	1600 mg twice daily for 1 day, then 600 mg twice daily	Oral	RNA-dependent RNA polymerase (RdRp)	Short-term (acute phase)	[47]
m102.4	Monoclonal antibody	Binds to NiV G glycoprotein, blocking interaction with ephrin-B2/B3 receptors, preventing viral entry.	5 mg/kg IV once	Intravenous (IV)	Ephrin-B2/B3 receptors	Single dose	[48]

8. Pandemic Preparedness and Policy Perspectives

Nipah virus has been designated a prototype "Disease X" due to its high lethality, zoonotic origin, and potential for sustained human-to-human transmission, highlighting the urgent need for proactive pandemic preparedness.[49]Lessons from COVID-19 emphasize that early intervention, integrated surveillance, and rapid deployment of diagnostics and therapeutics are essential to prevent localized outbreaks from escalating globally.[50] Implementing One Health strategies is central to risk reduction: community-based measures such as covering date palm sap collection sites, minimizing deforestation, and reducing contact between livestock and bat populations can substantially mitigate spillover events. At the policy level, international initiatives including the World Health Organization (WHO),Research and Development(R&D)Blueprint and the Coalition for Epidemic Preparedness Innovations (CEPI) have supported vaccine development and research, yet sustained financial and political commitment remains uneven.[51]Ethical considerations must also guide interventions, ensuring that efforts to control NiV transmission do not stigmatize bat populations or affected communities.[52] Effective management requires balancing conservation priorities with public health imperatives to achieve sustainable, evidence-based prevention strategies.[53]The Infographic representation of the *One Health* framework illustrating the interconnected ecological, clinical, and policy domains relevant to Nipah virus (NiV) prevention and control. The figure highlights cross-sectoral collaboration among wildlife ecology, veterinary surveillance, human healthcare, and public policy systems to strengthen outbreak preparedness and pandemic resilience.

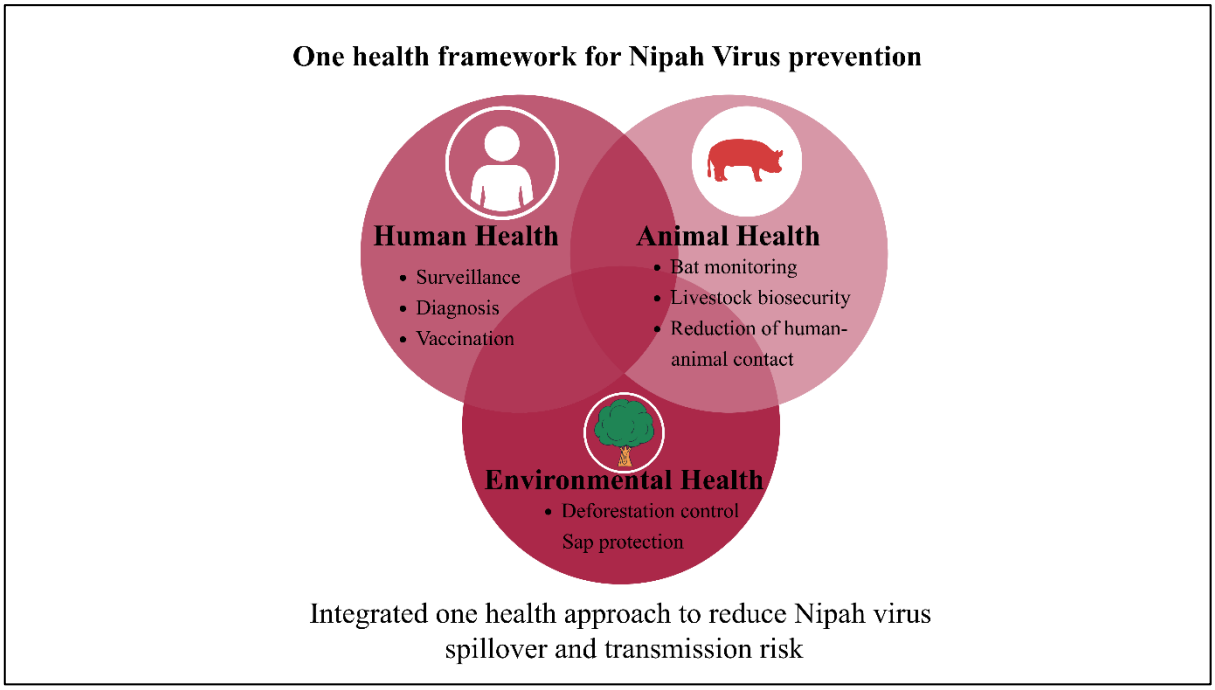


Figure 4: A One Health infographic linking ecological, clinical, and policy domains.

9. Future Directions and Critical Knowledge Gaps

Despite significant advances in understanding Nipah virus, several critical research gaps persist that impede effective prevention and control. The epidemiological role of asymptomatic or subclinical infections remains unclear, limiting accurate modelling of transmission dynamics.[54]Similarly, the mechanisms underlying viral persistence and relapse within the central nervous system are poorly understood, posing challenges for long-term patient management.[55] Predictive models incorporating climate variability and ecological drivers of spillover events are still in early development, restricting the ability to anticipate outbreaks.[56] Translational gaps between animal models and human disease further complicate the evaluation of therapeutics and vaccines, while equitable access to these interventions remains a pressing global health concern. [57]Addressing these challenges will require sustained long-term funding, robust interdisciplinary collaboration across virology, ecology, and public health, and the integration of comprehensive ecological and genomic surveillance networks. Only through such coordinated efforts can the threat of NiV be effectively mitigated and preparedness strengthened.[58]

10. Conclusion

Nipah virus epitomizes the complex and multifaceted threat posed by emerging zoonotic pathogens, situated at the intersection of ecological disruption, viral adaptability, and human vulnerability. Its capacity for high mortality, broad host range, and neurotropism underscores the potential severity of even localized outbreaks, which, when combined with deforestation, climate-driven changes in bat behavior, and expanding human-animal interfaces, heighten the risk of wider dissemination. Effective preparedness requires a strategic shift from reactive outbreak management to proactive investment in surveillance, early detection, and risk mitigation, anchored in One Health principles that integrate human, animal, and environmental health. Advances in molecular diagnostics, antiviral therapeutics, monoclonal antibodies, and vaccine platforms offer tangible promise for controlling NiV. However, the ultimate impact will depend on sustained international commitment, coordinated policy frameworks, and equitable access to medical countermeasures. Without these, Nipah virus may transition from a regional zoonotic threat to a pathogen with global pandemic potential.This review provides a comprehensive synthesis of current knowledge on Nipah virus, spanning its ecology, molecular biology, pathogenesis, clinical manifestations, diagnostics, and therapeutic strategies, offering a valuable resource for young researchers, virologists, and clinical scientists seeking a holistic understanding of this high-consequence pathogen. By highlighting critical knowledge gaps, emerging diagnostic technologies, and novel therapeutic and vaccine platforms, it informs experimental design, translational research, and clinical decision-making. Additionally, the discussion of molecular mechanisms, immune evasion, and viral-host interactions can guide the development of innovative drug delivery systems and targeted antiviral interventions, fostering advancement in both basic science and applied medical research.

List of abbreviations:

BSL-4: Biosafety Level 4

CEPI: Coalition for Epidemic Preparedness Innovations

CFR: Case Fatality Rate

ChAdOx1: Chimpanzee Adenovirus Oxford 1

CNS: Central Nervous System

COVID-19: Coronavirus Disease 2019

ELISA: Enzyme-Linked Immunosorbent Assay

GTP: Guanosine Triphosphate

IMPDH: Inosine monophosphate dehydrogenase

LAMP: Loop-mediated isothermal amplification

mRNA: Messenger Ribonucleic Acid

NiV: Nipah virus

R&D: Research and Development

RdRp: RNA-dependent RNA polymerase

RNA**:** Ribonucleic Acid

RT-PCR: Reverse Transcription Polymerase Chain Reaction

SARS: severe acute respiratory syndrome

STAT1/STAT2: Signal Transducer and Activator of Transcription 1 and 2

VSV: Vesicular stomatitis virus

WHO: World Health Organization

Ethics approval and consent to participate: This manuscript is a review. Hence, no experiments in animals or humans are included in this study, so ethical approval and consent are not required.

Clinical Trial No: The manuscript is a review article (not a part of Clinical trial), hence no Clinical trial no is applicable.

Consent for publication: This manuscript does not contain any personal data. Hence, no consent is required.

Availability of data and material: Data sharing does not apply to this article as no datasets were generated or analyzed during the current study.

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