Nipah Virus: Pathogenesis and Outbreak Preparedness – A Comprehensive Review Paper

[1]Miss Ifshana Shafi, [2]Mr Peerzada Mohammad Idrees, [3]Mr Shaikh Anaitullah, [4]Mr Umar Manzoor

[1,2,3,4]*Sher-i-Kashmir Institute of Medical Sciences*

Abstract**—Nipah virus (NiV) is a highly pathogenic, zoonotic, single-stranded RNA virus belonging to the genus *Henipavirus* within the family *Paramyxoviridae*. First recognized during a large outbreak of encephalitis among pig farmers in Sungai Nipah, Malaysia (1998–1999), the virus has since emerged as a recurrent public health threat in South and Southeast Asia, particularly in Bangladesh and India. The natural reservoir hosts are fruit bats of the genus Pteropus, commonly known as flying foxes, which harbor the virus asymptomatically. Spillover events occur through direct contact with infected bats, intermediate animal hosts such as pigs, or consumption of contaminated food products (e.g., raw date palm sap). Human-to-human transmission has been documented, particularly in healthcare and household settings, raising concerns about outbreak amplification.**

Clinically, Nipah virus infection presents a wide spectrum ranging from asymptomatic infection to acute febrile illness, severe respiratory distress, and fatal encephalitis. Neurological manifestations include headache, dizziness, altered consciousness, seizures, and coma. The case fatality rate varies between 40% and 75%, depending on outbreak context, healthcare access, and surveillance capacity. Some survivors experience long-term neurological sequelae, and relapsing or late-onset encephalitis has been reported months to years after initial infection.

Pathogenesis involves viral entry via respiratory or oropharyngeal routes, followed by systemic dissemination through endothelial and neuronal tissues. The virus targets multiple organ systems, particularly the central nervous system and respiratory epithelium, causing widespread vasculitis, inflammation, and tissue necrosis. Diagnosis is primarily achieved through real-time polymerase chain reaction (RT-PCR), enzyme-linked immunosorbent assay (ELISA), and virus isolation in high-containment laboratories due to its classification as a Biosafety Level-4 (BSL-4) pathogen.

***Index Terms*—Nipah virus (NiV), Henipavirus Zoonotic infection, Emerging infectious disease, Viral encephaliti, Acute respiratory distress, Case fatality rate, Fruit bats Pteropus reservoir, Human-to-human transmission, Spillover infection, Biosafety Level-4 (BSL-4) pathogen, Outbreak surveillance, Monoclonal antibodies, Vaccine development public health preparedness**

I. INTRODUCTION:

Nipah virus (NiV) is a highly pathogenic, zoonotic, negative-sense single-stranded RNA virus belonging to the genus *Henipavirus* within the family *Paramyxoviridae*. Since its initial identification during the 1998–1999 outbreak in Malaysia, NiV has emerged as one of the most lethal viral pathogens affecting humans, with reported case fatality rates ranging from 40% to 75%, and in some outbreaks exceeding 90% [1,2]. The virus is characterized by its broad host range, ability to infect multiple organ systems, and potential for human-to-human transmission, thereby posing a significant threat to global health security.

NiV is maintained in nature by fruit bats of the genus Pteropus, commonly referred to as flying foxes, which serve as the natural reservoir hosts [3]. These bats are widely distributed across South and Southeast Asia, Australia, and parts of Africa, facilitating extensive ecological persistence. Spillover events occur when ecological, agricultural, or behavioural factors increase contact between bats, domestic animals, and humans. Anthropogenic drivers such as deforestation, habitat fragmentation, agricultural intensification, and urban encroachment have been strongly implicated in facilitating zoonotic transmission [4].

From a public health standpoint, NiV has been designated as a priority pathogen by the World Health Organization (WHO) under its Research and Development Blueprint due to its epidemic potential and lack of licensed vaccines or targeted therapeutics [5]. The virus is classified as a Biosafety Level-4 (BSL-4) agent owing to its high lethality and absence of definitive treatment options.

Clinically, Nipah virus infection presents with a spectrum ranging from asymptomatic seroconversion to fatal encephalitis and acute respiratory distress syndrome (ARDS). Neurological manifestations predominate in many outbreaks, reflecting the virus's marked neurotropism and endothelial tropism [6]. The capacity for relapsing or late-onset encephalitis months to years after primary infection further distinguishes NiV from many other viral encephalitides and underscores its complex pathobiology [7].

Currently, there is no licensed antiviral therapy or vaccine specifically approved for Nipah virus infection. Management remains largely supportive, including intensive care for respiratory and neurological complications. Several therapeutic strategies—such as monoclonal antibodies, antiviral agents like ribavirin and remdesivir, and various vaccine candidates (including viral vector and subunit platforms)—are under investigation in preclinical and early clinical studies. Due to its high mortality rate, epidemic potential, and absence of specific countermeasures, Nipah virus is designated as a priority pathogen by global health authorities for urgent research and development. [7].

Strengthening surveillance systems, promoting community awareness to reduce zoonotic transmission, implementing infection control measures in healthcare settings, and advancing vaccine and therapeutic research are critical components of global preparedness. Given increasing human–wildlife interface and environmental changes, proactive strategies are essential to prevent future outbreaks and mitigate the risk of wider regional or global spread. [7].

The epidemiological patterns of Nipah virus outbreaks have evolved over time, demonstrating distinct transmission dynamics in different geographic settings. While the Malaysian outbreak was largely driven by pig-mediated amplification, outbreaks in Bangladesh and India have frequently involved direct bat-to-human transmission and sustained human-to-human spread, particularly in healthcare environments [8,9]. These differences highlight the adaptability of the virus and the importance of context-specific outbreak preparedness strategies.

1.1. Historical Timeline of Nipah Virus Emergence:

1998–1999: Emergence in Malaysia

Nipah virus was first identified during an outbreak of severe febrile encephalitis among pig farmers in peninsular Malaysia between September 1998 and May 1999. Initially misdiagnosed as Japanese encephalitis, the outbreak ultimately resulted in 265 reported human cases and 105 deaths [1]. Epidemiological investigations linked the outbreak to intensive pig farming operations located near fruit orchards, where fruit bats were known to feed. Pigs acted as amplifying hosts, facilitating viral transmission to humans through close occupational exposure. Control measures included mass culling of more than one million pigs, which successfully terminated the outbreak [2].

2001 Onward: Recurrent Outbreaks in Bangladesh

Beginning in 2001, recurrent seasonal outbreaks were reported in Bangladesh, primarily during winter months [8]. Unlike the Malaysian outbreak, these cases were strongly associated with the consumption of raw date palm sap contaminated by bat saliva or urine. Notably, person-to-person transmission became a prominent feature, particularly among family caregivers and healthcare workers. The Bangladesh strain (NiV-BD) demonstrated higher respiratory involvement and greater transmissibility compared to the Malaysian strain (NiV-MY), with case fatality rates frequently exceeding 70% [9].

2001 and Subsequent Outbreaks in India

In 2001, an outbreak occurred in Siliguri, West Bengal, India, characterized by significant nosocomial transmission [10]. More recently, outbreaks in the southern Indian state of Kerala in 2018, 2019, 2021, and 2023 demonstrated rapid public health response, aggressive contact tracing, and effective containment measures, limiting secondary spread [11]. The Kerala outbreaks highlighted the importance of coordinated surveillance, laboratory diagnostics, and intersectoral collaboration.

Global Recognition and Research Prioritization

In response to its epidemic potential, WHO formally included Nipah virus among priority pathogens for urgent research and development in 2018 [5]. Ongoing research initiatives have focused on vaccine development, monoclonal antibody therapies (e.g., m102.4), and antiviral candidates such as remdesivir [12]. However, no licensed vaccine or specific antiviral treatment is currently available for human use.

1.2. Ecological and Socioeconomic Drivers of Emergence

The emergence and persistence of Nipah virus are closely linked to ecological and socioeconomic transformations. Deforestation and agricultural expansion have altered bat habitats, increasing bat-human interfaces. Climate variability may influence bat migration patterns and viral shedding dynamics. Additionally, cultural practices—such as consumption of raw date palm sap in Bangladesh—have contributed to repeated spillover events [4,8].

Globalization and increased mobility further heighten the risk of international dissemination. Although outbreaks have thus far been geographically localized, modelling studies suggest that viral mutations enhancing respiratory transmissibility could substantially increase pandemic risk [13]. The documented capacity for limited human-to-human transmission underscores this concern.

1.3. Public Health Significance and Research Imperatives

Nipah virus exemplifies the challenges posed by emerging zoonotic diseases in the Anthropocene era. The convergence of ecological disruption, densely populated regions, limited rural healthcare infrastructure, and insufficient BSL-4 laboratory capacity complicates outbreak detection and response. Moreover, the virus's ability to cause severe encephalitis with high mortality places significant strain on healthcare systems.

Preparedness strategies emphasize the One Health framework, integrating human, animal, and environmental health sectors. Surveillance of bat reservoirs, rapid diagnostic testing (RT-PCR), isolation protocols, contact tracing, and community risk communication are central to outbreak containment. Nevertheless, gaps remain in vaccine development, therapeutic research, and predictive ecological modelling.

In summary, Nipah virus represents a paradigmatic example of an emerging zoonosis with high mortality, complex pathogenesis, and epidemic potential. A comprehensive understanding of its historical emergence, ecological drivers, molecular biology, and transmission dynamics is essential to inform effective outbreak preparedness and global health security strategies.

II. VIROLOGY AND STRUCTURE

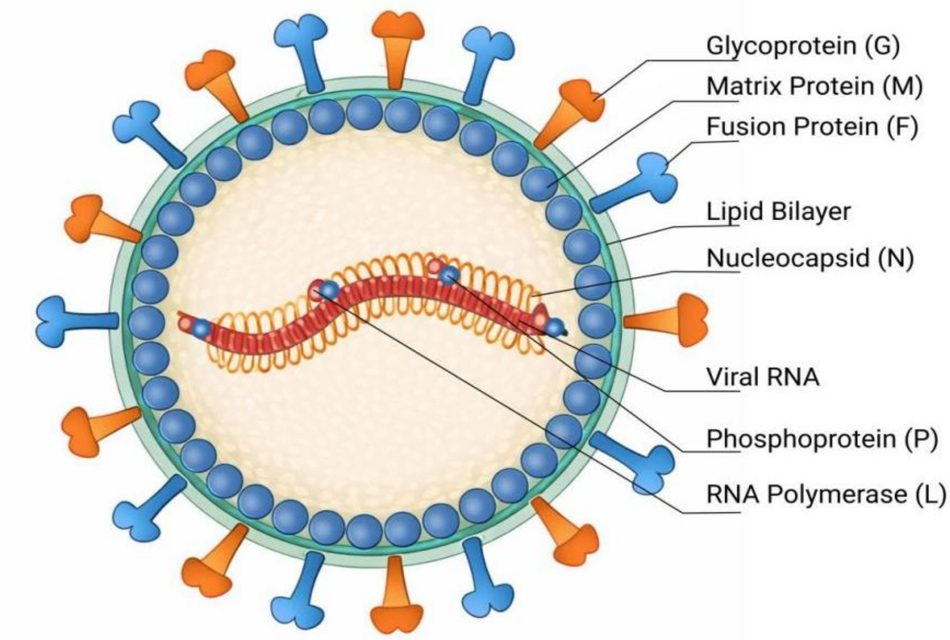
NiV is an enveloped, negative-sense, single-stranded RNA virus.

2.1.Genome Organization

The genome encodes six structural proteins:

• N (Nucleocapsid)
• P (Phosphoprotein)
• M (Matrix)
• F (Fusion)
• G (Attachment glycoprotein)
• L (RNA-dependent RNA polymerase)

The G glycoprotein mediates attachment to host cell receptors ephrin-B2 and ephrin-B3, which are highly expressed in endothelial and neuronal tissues.



2.2.Strains

Two major strains:

• Malaysian strain (NiV-MY):

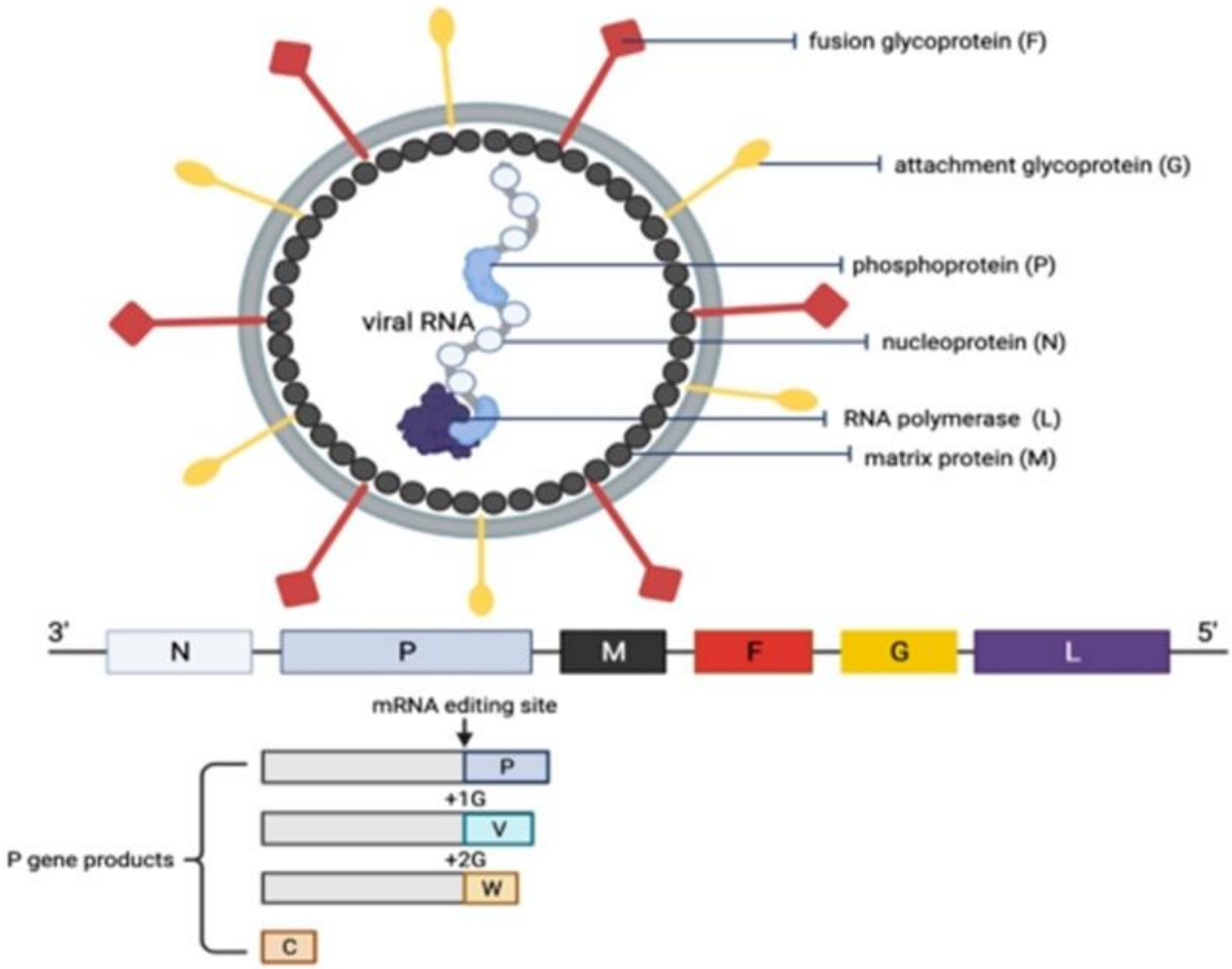
First identified during the 1998–1999 outbreak in Malaysia
Transmission mainly from infected pigs to humans
Limited human-to-human transmission
Lower respiratory involvement compared to Bangladesh strain
Case fatality rate: ~40%

• Bangladesh strain (NiV-BD):

Associated with higher respiratory transmission and case fatality rates.First identified in 2001 in Bangladesh
Also responsible for outbreaks in India
Stronger human-to-human transmission
More severe respiratory symptoms
Higher case fatality rate: 60–75%

Table no.01

Feature	Malaysia Strain	Bangladesh Strain
Main transmission	Pig-to-human	Bat-to-human & human-to-human
Respiratory symptoms	Less common	More common
Mortality rate	Lower (~40%)	Higher (60–75%)
Outbreak pattern	Large farm outbreak	Recurrent seasonal outbreaks



III. EPIDEMIOLOGY

3.1.Reservoir and Transmission

- Natural reservoir: Fruit bats (*Pteropus* species)
- Amplifying host: Pigs (notably in Malaysia outbreak)
- Transmission routes:
  - Bat-to-human (contaminated date palm sap)
  - Animal-to-human
  - Human-to-human (respiratory droplets, close contact)

Table no.02

Year	Location	Key Features
1998–1999	Malaysia	Pig-mediated transmission
2001–Present	Bangladesh	Recurrent outbreaks, person-to-person spread
2001	India	West Bengal outbreak
2018	Kerala	High fatality, rapid containment

Case fatality rate: 40–75%, occasionally higher.

IV. PATHOGENESIS

4.1.Entry and Initial Infection

NiV enters via:

- Respiratory epithelium
- Oropharyngeal mucosa

Attachment is mediated by G glycoprotein binding to ephrin-B2/B3 receptors.

4.2.Viral Replication and Spread

After entry:

1.Fusion protein (F) facilitates membrane fusion.
2.Viral RNA released into cytoplasm.
3.Replication via RNA-dependent RNA polymerase.
4.Budding from host membrane.

Systemic dissemination occurs via:

- Hematogenous spread
- Lymphatic system

4.3.Endothelial Tropism and Vasculitis

NiV shows strong tropism for:

- Endothelial cells
- Neurons
- Smooth muscle cells

Pathological hallmark:

- Systemic vasculitis
- Endothelial syncytia formation
- Microinfarctions

This leads to:

- Blood-brain barrier disruption

• CNS invasion
• Multi-organ failure

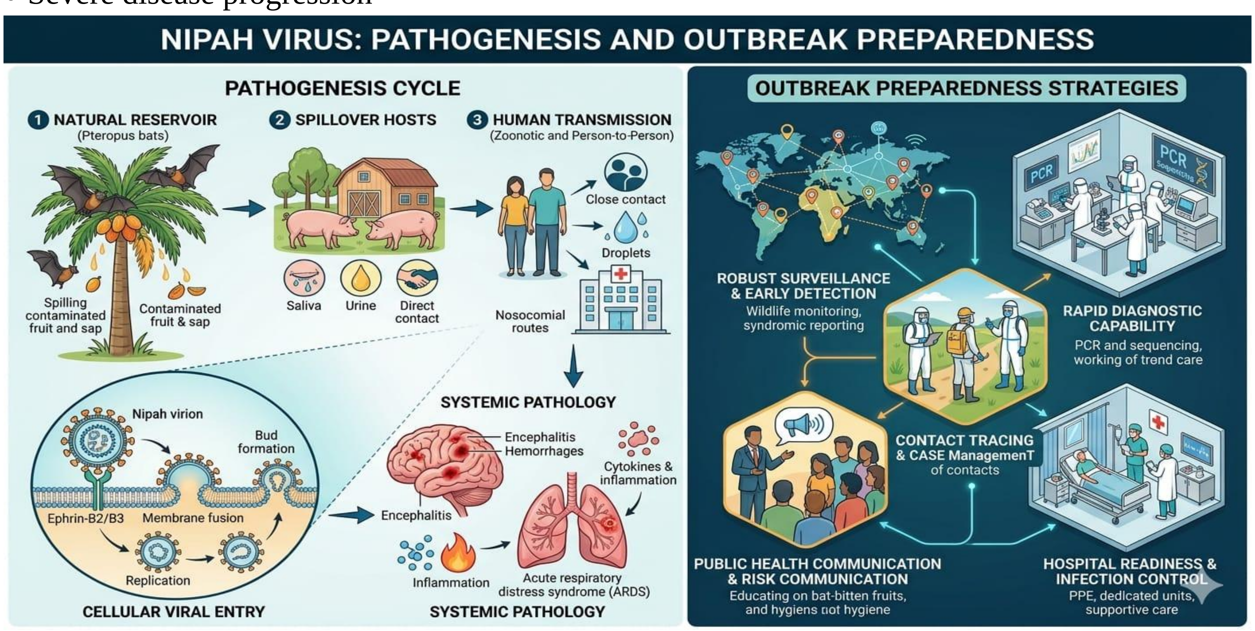
4.4.Central Nervous System Involvement
Mechanisms:
• Hematogenous spread
• Retrograde axonal transport

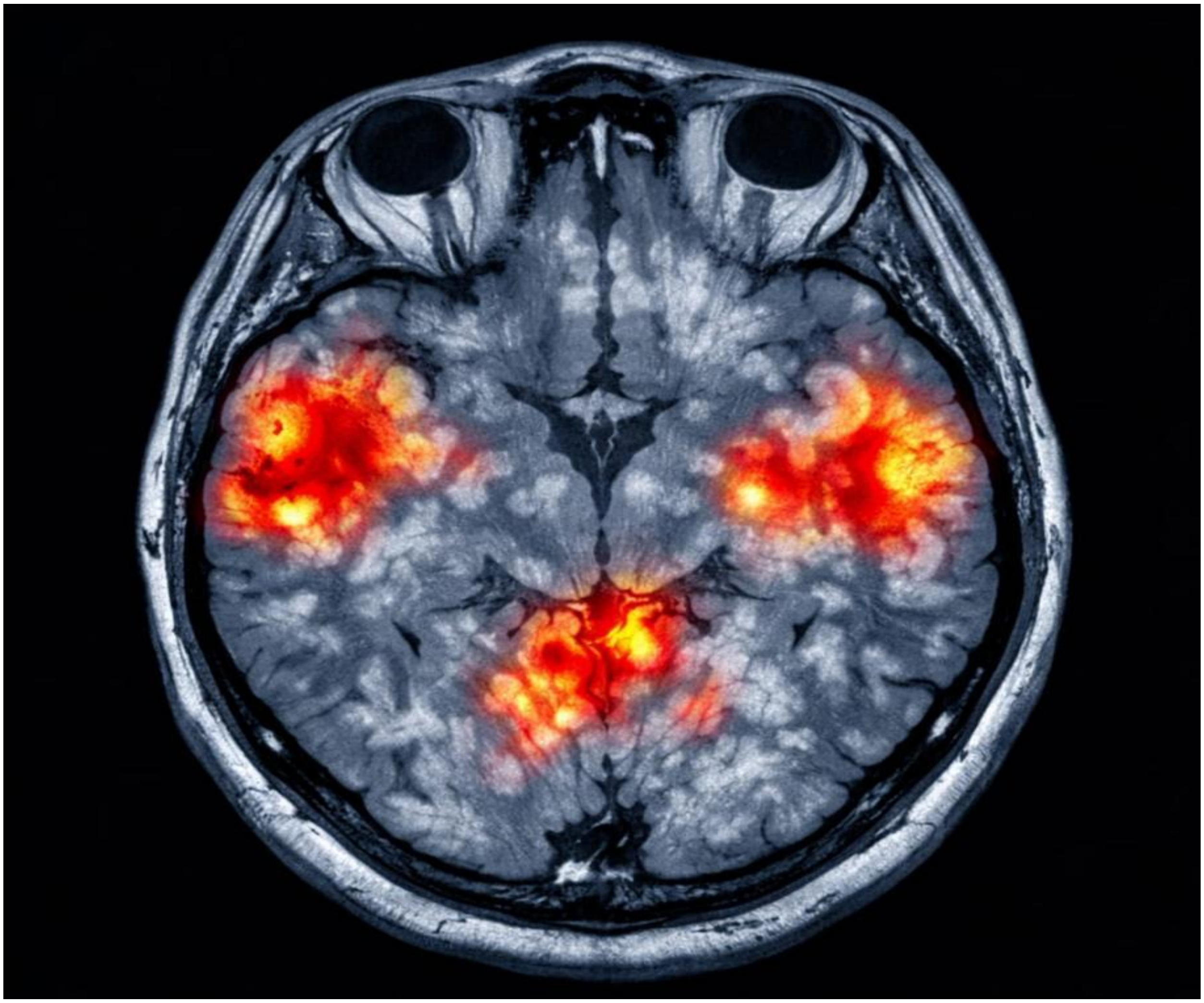
Neuropathology:
• Diffuse encephalitis
• Neuronal necrosis
• Microhemorrhages

MRI findings:
• Multiple small hyperintense lesions in subcortical and deep white matter.

4.5.Immune Evasion
NiV P gene products (V, W, C proteins) inhibit:
• Interferon signaling
• Innate immune response

Result:
• Delayed viral clearance
• High viral load
• Severe disease progression





V. CLINICAL MANIFESTATIONS

5.1.Incubation Period
5–14 days (can extend up to 45 days)

5.2.Symptoms
Early phase:
- Fever
- Headache
- Myalgia
- Vomiting

Neurological phase:
- Altered sensorium
- Seizures

- Acute encephalitis
- Coma

Respiratory involvement (more common in Bangladesh strain):
- Cough
- Acute respiratory distress
- Hypoxia

5.3.Complications
- Relapse encephalitis
- Persistent neurological deficits
- Long-term cognitive impairment

Emergence and Initial Characterization
Nipah virus (NiV) was first identified during the 1998–1999 outbreak of encephalitis among pig farmers in Malaysia. The causative agent was isolated and characterized by Chua KB et al. (2000), who described it as a novel paramyxovirus within the genus *Henipavirus*. The outbreak resulted in over 250 human cases and more than 100 deaths, prompting large-scale culling of pigs to halt transmission. This event marked the recognition of NiV as a zoonotic pathogen capable of crossing species barriers and causing severe neurological disease (Chua et al., 2000).
Following this outbreak, recurrent epidemics were reported in Bangladesh and India, with notably higher case fatality rates (40–75%) compared to Malaysia (World Health Organization, 2023). These outbreaks demonstrated clear evidence of human-to-human transmission, significantly increasing public health concern.

Reservoir Hosts and Transmission Dynamics
Extensive ecological and serological studies have identified fruit bats of the genus Pteropus as the natural reservoir of NiV (World Organisation for Animal Health, 2023). Bats remain asymptomatic carriers, shedding virus in saliva, urine, and excreta.
In Bangladesh, epidemiological investigations led by Luby SP et al. (2009) established a strong association between human infection and the consumption of raw date palm sap contaminated by bat secretions.

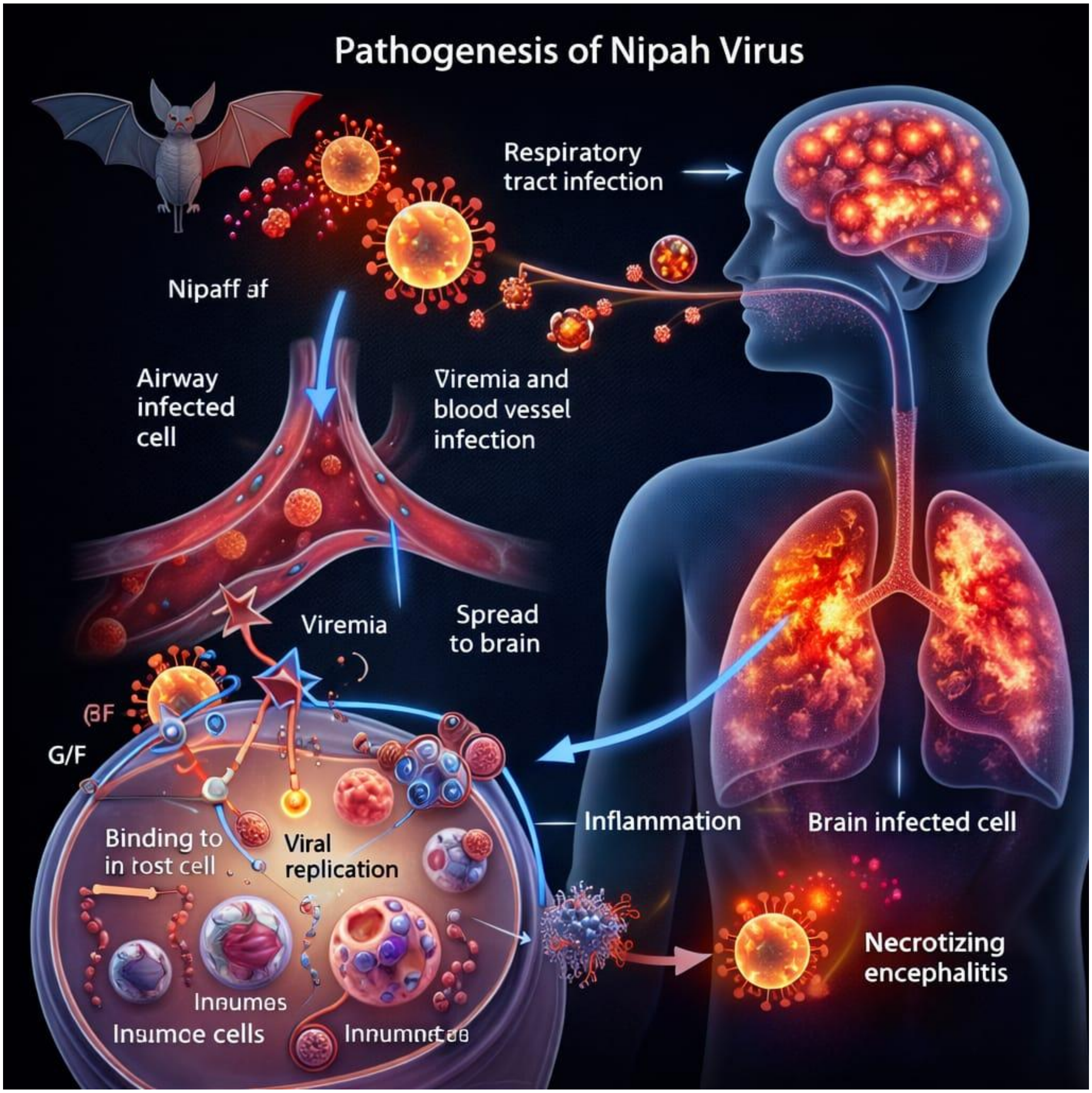
Transmission patterns differ geographically:
- In Malaysia, pigs acted as intermediate amplifying hosts.
- In Bangladesh and India, direct bat-to-human and human-to-human transmission predominated.

Nosocomial transmission has been documented, highlighting gaps in infection prevention and control (IPC) practices (WHO, 2023).

Clinical Features and Pathogenesis

The clinical presentation of NiV infection ranges from asymptomatic infection to acute encephalitis and severe respiratory illness. Common symptoms include fever, headache, altered mental status, seizures, and coma. Respiratory distress appears more frequently in Bangladeshi and Indian outbreaks compared to Malaysian cases (Centers for Disease Control and Prevention, 2024).

Histopathological studies demonstrate systemic vasculitis, endothelial syncytia formation, and neuronal infection, explaining the severe neurological manifestations. Relapsing or late-onset encephalitis has also been reported months to years after initial infection, suggesting viral persistence in certain individuals (CDC, 2024).



Diagnostic Advances

Laboratory confirmation of NiV infection relies primarily on real-time reverse transcription polymerase chain reaction (RT-PCR) for viral RNA detection and enzyme-linked immunosorbent assay (ELISA) for serological testing. Due to its high pathogenicity, NiV is classified as a Biosafety Level-4 (BSL-4) pathogen, requiring specialized containment facilities (WHO, 2023).

Recent advancements in molecular diagnostics have improved early case detection and outbreak response capacity, especially in endemic regions. Rapid identification is crucial for timely isolation and contact tracing to prevent secondary transmission.

Therapeutics and Vaccine Research

Currently, there are no licensed antiviral drugs or approved vaccines for Nipah virus infection (WHO, 2023). Treatment remains supportive, focusing on management of respiratory failure and neurological complications. Ribavirin has been used in some outbreaks, though evidence regarding its efficacy remains inconclusive.

Global initiatives led by the Coalition for Epidemic Preparedness Innovations have prioritized NiV vaccine development. Multiple candidates—including viral vector-based, recombinant subunit, and mRNA vaccines—are in preclinical or early clinical stages (CEPI, 2024). Monoclonal antibodies have also shown promise in experimental animal models.

Public Health Impact and One Health Perspective

Nipah virus is recognized by the World Health Organization as a priority pathogen due to its epidemic potential and high mortality. Increasing deforestation, agricultural expansion, urbanization, and climate variability contribute to greater human–wildlife interaction, enhancing spillover risk (WOAH, 2023).

The literature strongly advocates for a One Health approach integrating human, animal, and environmental surveillance systems. Strategies include bat population monitoring, food safety interventions (e.g., covering date palm sap collection sites), strengthening healthcare infection control measures, and enhancing laboratory capacity in endemic regions.

The existing body of literature establishes Nipah virus as a high-mortality, emerging zoonotic pathogen with demonstrated human-to-human transmission capability. Evidence underscores the importance of early detection, improved IPC practices, vaccine development, and integrated One Health surveillance to mitigate the risk of future outbreaks. Continued interdisciplinary research and global collaboration remain essential to address the evolving threat posed by Nipah virus.

VI. MATERIALS AND METHODS:

Study Design

A descriptive and laboratory-based study was conducted to investigate the epidemiology, clinical characteristics, and molecular detection of Nipah virus (NiV). The study incorporated retrospective analysis of reported outbreaks and prospective laboratory confirmation of suspected cases.

Study Area and Population

Data were collected from reported NiV outbreaks in endemic regions, particularly in Bangladesh and India. The study population included suspected human cases presenting with acute febrile illness, encephalitis, or severe respiratory symptoms, as well as individuals with confirmed exposure to infected animals or patients.

Sample Collection

Clinical specimens, including blood, cerebrospinal fluid (CSF), throat swabs, and urine samples, were collected from suspected patients following standard infection prevention and control (IPC) protocols. Samples were transported under cold chain conditions to designated high-containment laboratories. All laboratory procedures involving live virus were performed in Biosafety Level-4 (BSL-4) facilities.

Laboratory Diagnosis

Viral RNA was extracted from clinical specimens using commercially available viral RNA extraction kits according to the manufacturer's instructions. Detection of Nipah virus RNA was performed using real-time reverse transcription polymerase chain reaction (RT-PCR) targeting the N and G genes. Serological testing was conducted using enzyme-linked immunosorbent assay (ELISA) to detect NiV-specific IgM and IgG antibodies. Viral isolation, where applicable, was carried out in Vero cell lines under strict biosafety conditions.

Epidemiological Investigation

Demographic, clinical, and exposure data were collected using standardized case investigation forms. Contact tracing was performed to identify and monitor close contacts for 21 days following exposure. Environmental investigations included assessment of potential zoonotic sources, such as bat exposure and consumption of raw date palm sap associated with fruit bats of the genus Pteropus.

Data Analysis

Collected data were entered into a secured database and analyzed using statistical software. Descriptive statistics were used to summarize demographic and clinical variables. Case fatality rates were calculated, and associations between exposure history and clinical outcomes were assessed using appropriate statistical tests, with significance set at $p < 0.05$.

6.1.Laboratory Diagnosis

- RT-PCR (gold standard)
- ELISA for IgM/IgG antibodies
- Virus isolation (BSL-4 labs)

Clinical Samples for Testing:

- Blood (serum or plasma) – reflects systemic viral load
- Cerebrospinal fluid (CSF) – important for patients with neurological symptoms (encephalitis)
- Urine – non-invasive sample, sometimes shows viral shedding
- Throat or nasal swabs – detects virus in respiratory secretions

Note: Proper collection, storage, and transport under cold-chain conditions are critical to prevent RNA degradation.

Detailed Procedure

1. Sample Collection

- Collect blood (serum/plasma), CSF, urine, throat swab, or nasal swab
- Use sterile techniques and place samples in viral transport media
- Maintain cold chain (2–8°C) during transport
- Handle under BSL-4 conditions due to high pathogenicity

2. RNA Extraction

- Use commercial RNA extraction kits or standard phenol-chloroform method

Steps:

1.Lyse virus particles to release RNA
2.Bind RNA to silica columns or magnetic beads
3.Wash away contaminants
4.Elute purified RNA in RNase-free water

Goal: Obtain pure, intact viral RNA for amplification

3. Reverse Transcription (cDNA Synthesis)

- Mix RNA with reverse transcriptase enzyme, primers, dNTPs, and buffer
- Incubate under conditions that allow RNA → complementary DNA (cDNA) conversion
- Optional: use gene-specific primers for higher specificity

4. PCR Amplification

Add cDNA to a PCR mix containing:
NiV-specific forward and reverse primers (commonly target N or G gene)

DNA polymerase
Buffer and dNTPs

- Thermocycler steps:

1.Denaturation: DNA strands separate (94–95°C)
2.Annealing: primers bind to target cDNA (50–60°C)
3.Extension: DNA polymerase synthesizes new strand (72°C)

- Repeat for 30–40 cycles to amplify target sequence

5. Detection of Amplified Product
- Conventional PCR:
  - Run amplified DNA on agarose gel with ethidium bromide or safe dye
  - Visualize under UV light → presence of specific band = positive

- Real-Time PCR (qRT-PCR):
  - Use fluorescent probes
  - Amplification monitored in real time
  - Ct (cycle threshold) value indicates viral load

Precautions
- Requires BSL-4 laboratory for handling samples due to high mortality and transmissibility of NiV
- Strict biosafety protocols must be followed to protect laboratory personnel

Advantages of RT-PCR

1.High Sensitivity and Specificity
- Can detect even low levels of viral RNA.
- Specific primers ensure no cross-reactivity with other viruses.

2.Early Detection
- Viral RNA can be detected within 3–5 days of infection, often before symptom onset.

3.Quantitative Possibility
- Real-time RT-PCR allows viral load estimation, which can correlate with disease severity and prognosis.

4.Rapid Results
- Turnaround time can be as short as a few hours, compared to virus isolation which may take days.

Interpretation of Results:

Table no.04

Result	Meaning
Positive	Viral RNA detected → NiV infection confirmed
Negative	No viral RNA detected → may be early infection or sample issue
Inconclusive	Repeat testing recommended

6.2.Imaging
- MRI brain for encephalitic changes

6.3.Differential Diagnosis
- Japanese encephalitis
- Herpes simplex encephalitis
- COVID-19 (respiratory cases)

VII. TREATMENT

Currently no approved specific antiviral therapy.

7.1.Supportive Care
- Mechanical ventilation
- Management of raised intracranial pressure
- Seizure control

7.2.Investigational Therapies
- Ribavirin (limited evidence)
- Monoclonal antibody m102.4
- Remdesivir (experimental data)

Vaccine candidates are under development (subunit, viral vector, mRNA platforms).

VIII. OUTBREAK PREPAREDNESS

8.1.Surveillance Systems
- Integrated Disease Surveillance Programs
- Zoonotic monitoring of bat populations
- Sentinel hospital reporting

8.2.One Health Approach
Collaboration between:
- Human health sector
- Veterinary services
- Environmental agencies

8.3.Rapid Response Measures
- Isolation of suspected cases
- Contact tracing
- Quarantine protocols
- Use of PPE (N95 masks, gloves, gowns)

8.4.Laboratory Preparedness
- BSL-3/BSL-4 containment
- Trained personnel
- Specimen transport protocols

8.5.Risk Communication
- Public awareness campaigns
- Avoidance of raw date palm sap
- Safe burial practices

8.6.Hospital Infection Control
- Negative pressure isolation rooms
- Standard + droplet precautions
- Strict biomedical waste disposal

8.7.International Collaboration
Organizations such as:
- World Health Organization
- Centers for Disease Control and Prevention
- Indian Council of Medical Research

Play Key Roles In:
- Technical guidance
- Outbreak investigation
- Research funding

IX. CHALLENGES IN PREPAREDNESS

- Lack of licensed vaccine
- Limited BSL-4 facilities
- Underreporting in rural regions
- Human-bat ecological interface
- Climate change impacts on bat migration

X. FUTURE DIRECTIONS

- Accelerated vaccine trials
- Monoclonal antibody stockpiling
- Ecological modeling of bat reservoirs

- Genomic surveillance
- Strengthening primary healthcare systems

XI. CONCLUSION

Nipah virus remains a significant emerging zoonotic threat with high mortality and epidemic potential. Its pathogenesis involves endothelial infection, systemic vasculitis, and severe encephalitis driven by immune evasion mechanisms. In the absence of specific therapeutics, preparedness strategies centered on surveillance, rapid containment, and One Health collaboration are essential to prevent large-scale outbreaks. Continued global research and coordinated response mechanisms are critical to mitigating future NiV epidemics.

Nipah virus continues to represent a serious and re-emerging zoonotic threat with substantial public health implications (World Health Organization, 2023; Centers for Disease Control and Prevention, 2024). Characterized by high case fatality rates, severe neurological and respiratory manifestations, and the ability to transmit from person to person, NiV poses a persistent risk of localized outbreaks with potential for wider regional spread (WHO, 2023). The established ecological reservoir in fruit bats of the genus Pteropus, combined with increasing human encroachment into wildlife habitats and ecological changes, facilitates recurrent spillover events (World Organisation for Animal Health, 2023). Countries such as Bangladesh and India remain particularly vulnerable due to documented outbreaks and sociocultural practices that increase exposure risk (Luby SP et al., 2009).

The absence of approved antiviral therapies and licensed vaccines significantly limits disease-specific management options (Coalition for Epidemic Preparedness Innovations, 2024). Current treatment strategies remain largely supportive, emphasizing intensive care for respiratory distress and neurological complications (CDC, 2024). Therefore, outbreak containment relies heavily on rapid case identification, laboratory confirmation, strict infection prevention and control (IPC) measures, effective isolation protocols, and comprehensive contact tracing (WHO, 2023). Strengthening diagnostic capacity, particularly molecular detection methods such as RT-PCR, is essential for timely intervention (CDC, 2024).

Long-term prevention strategies must focus on a One Health approach that integrates human, animal, and environmental health systems (WOAH, 2023). Surveillance of bat populations, monitoring of high-risk animal–human interfaces, public education to discourage consumption of potentially contaminated food products, and improved healthcare infrastructure are critical to reducing transmission risk (WHO, 2023). Additionally, sustained investment in vaccine research, monoclonal antibody development, and antiviral therapeutics is urgently needed to enhance preparedness and response capabilities (CEPI, 2024).

In conclusion, Nipah virus exemplifies the growing challenge of emerging zoonotic diseases in an interconnected world. Proactive global collaboration, interdisciplinary research, community engagement, and strengthened public health systems are imperative to mitigate future outbreaks, reduce mortality, and prevent potential epidemic escalation (WHO, 2023).

REFERENCES

[1] K. B. Chua *et al*., "Nipah virus: A recently emergent deadly paramyxovirus," *Science*, vol. 288, no. 5470, pp. 1432–1435, 2000.
[2] Centers for Disease Control and Prevention (CDC), "Outbreak of Hendra-like virus—Malaysia and Singapore, 1998–1999," Morbidity and Mortality Weekly Report (MMWR), vol. 48, pp. 265–269, 1999.
[3] J. M. Yob et al., "Nipah virus infection in bats (order Chiroptera) in peninsular Malaysia," Emerging Infectious Diseases, vol. 7, no. 3, pp. 439–441, 2001.
[4] J. R. Pulliam et al., "Agricultural intensification, priming for persistence and the emergence of Nipah virus," Journal of the Royal Society Interface, vol. 9, pp. 89–101, 2012.
[5] World Health Organization, 2018 Annual Review of Diseases Prioritized Under the R&D Blueprint. Geneva, Switzerland: WHO, 2018.
[6] K. T. Wong et al., "Neuropathology of Nipah virus infection," Journal of Neuropathology and Experimental Neurology, vol. 61, pp. 736–746, 2002.
[7] C. T. Tan et al., "Relapsed and late-onset Nipah encephalitis," Neurology, vol. 59, pp. 153–156, 2002.
[8] S. P. Luby et al., "Recurrent zoonotic transmission of Nipah virus into humans, Bangladesh, 2001–2007," Emerging Infectious Diseases, vol. 15, no. 8, pp. 1229–1235, 2009.
[9] E. S. Gurley et al., "Person-to-person transmission of Nipah virus in Bangladesh," Emerging Infectious Diseases, vol. 13, pp. 1031–1037, 2007.
[10] M. S. Chadha et al., "Nipah virus-associated encephalitis outbreak, Siliguri, India," Emerging Infectious Diseases, vol. 12, pp. 235–240, 2006.
[11] G. Arunkumar et al., "Outbreak investigation of Nipah virus disease in Kerala, India, 2018," Eurosurveillance, vol. 24, no. 39, 2019.
[12] C. E. Mire et al., "Single-dose recombinant vesicular stomatitis virus vaccine protects against Nipah virus challenge," Science Translational Medicine, vol. 5, p. 205ra138, 2013.
[13] M. K. Lo and P. A. Rota, "The emergence of Nipah virus, a highly pathogenic paramyxovirus," Journal of Clinical Virology, vol. 43, pp. 396–400, 2008.
[14] Centers for Disease Control and Prevention, "Nipah Virus (NiV): Transmission, Symptoms, and Prevention," CDC, 2024.
[15] Coalition for Epidemic Preparedness Innovations (CEPI), "Nipah Virus Vaccine Development Programs," CEPI, 2024.
[16] World Health Organization, "Nipah Virus – Fact Sheet," WHO, 2023.
[17] World Organisation for Animal Health (WOAH), "Nipah Virus Disease," WOAH, 2023.