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NIPAH VIRUS INBENGAL AND INDIA: A COMPREHENSIVE REVIEW OF PAST OUTBREAKS, PRESENT IMPACT, AND FUTURE CHALLENGES

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Abstract

Nipah virus (NiV), a lethal zoonotic paramyxovirus, poses a significant public health threat in South Asia, with the Bengal region as a recurrent epicentre. This review synthesises the historical trajectory, epidemiological impact, and multifaceted challenges of NiV in Bengal and India. It details the outbreak chronology from its initial identification to recurrent emergence, examining the ecology centred on Pteropus bats and spillover via contaminated date palm sap. The clinical spectrum, from asymptomatic infection to severe encephalitis, is critically analysed. The review systematically examines the limitations of current diagnostics and therapeutics, including scarce monoclonal antibodies, and discusses supportive management. Preventive strategies, surveillance strengthening, and infection control are outlined. Future directions emphasise accelerating vaccine development, improving point-of-care diagnostics, and fortifying One Health networks to mitigate anticipated outbreaks driven by the virus's endemicity in bat populations.

Keywords: Nipah virus, Henipavirus, zoonotic spillover, encephalitis, One Health

1. Introduction

Nipah virus (NiV), a member of the genus Henipavirus within the family Paramyxoviridae, represents a paradigm of an emerging zoonotic pathogen with high pandemic potential [1]. Identified first in 1998 during a severe outbreak among pig farmers in Malaysia and Singapore, NiV has since established a distinct epidemiological pattern in South Asia, particularly in Bangladesh and the neighbouring Indian state of West Bengal, collectively forming the Bengal region [2,3]. The virus is classified as a Biosafety Level 4 (BSL-4) agent and features on the World Health Organization's (WHO) Blueprint list of priority pathogens requiring urgent research and development due to its high case fatality rate (CFR), which can exceed 70% in some outbreaks, lack of licensed vaccines or specific antivirals, and potential for human-to-human transmission [4,5].

The ecology of NiV is inextricably linked to fruit bats of the Pteropus genus (flying foxes), which serve as its natural reservoir host without exhibiting apparent disease [6]. Spillover events to humans occur either directly through consumption of bat-contaminated raw date palm sap, a culturally significant practice in Bengal, or indirectly via intermediate amplifying hosts such as pigs, as witnessed in the Malaysian outbreak [7,8]. Subsequent human-to-human transmission, especially in healthcare and household settings, has been a hallmark and major amplifier of outbreaks in India and Bangladesh, posing severe challenges for infection prevention and control (IPC) [9].

India has experienced several discrete NiV outbreaks, primarily in the state of West Bengal (Siliguri in 2001, Nadia district in 2007, and recurrent outbreaks in Kerala in 2018, 2019, 2021, and 2023) [10,11,12]. Each event has tested the nation's public health response, exposed gaps in surveillance, and underscored the need for sustained vigilance. This review aims to provide a comprehensive analysis of the impact of NiV on Bengal and India. The review traverses the past chronology of outbreaks, delineates the present challenges in diagnosis, treatment, and prevention, and projects future directions for research, preparedness, and control within a One Health framework.

2. Past Outbreaks: Chronology and Lessons Learned

The history of NiV is a narrative of recurrent spillover from its bat reservoir, with geographical and epidemiological variations between the initial Southeast Asian outbreak and the subsequent pattern in South Asia.

2.1. The Malaysian/Singapore Outbreak (1998-1999) The index outbreak in Kampung Sungai Nipah, Malaysia, led to the virus's identification. It primarily affected pig farmers and abattoir workers, with pigs acting as the amplifying host. The outbreak resulted in 265 human encephalitis cases and 105 deaths (CFR ~40%) and necessitated the culling of over one

million pigs to contain the virus [13,14]. This event highlighted the role of livestock in zoonotic amplification and the economic devastation accompanying such outbreaks.

2.2. The Emergence in Bengal: Bangladesh and West Bengal, India

Since 2001, Bangladesh has reported near-annual outbreaks of NiV, with a markedly higher CFR (often >70%) and a different transmission dynamic [15]. The primary route identified is the consumption of raw date palm sap (tari or khejurerrosh) contaminated by bat urine or saliva [16,17]. This established a distinct "Bengal basin" epidemiological zone.

- **Siliguri, West Bengal, India (2001):** India's first recognised outbreak occurred in Siliguri, West Bengal, bordering Bangladesh. It involved 66 cases with a CFR of approximately 68% [18]. Notably, this outbreak underscored the potential for efficient nosocomial transmission, with at least 33 cases occurring among hospital staff and visitors, revealing critical gaps in IPC practices [19].
- **Nadia District, West Bengal (2007):** A second outbreak in India was reported in Nadia district, with five confirmed cases and a 100% CFR [20]. Epidemiological investigations again pointed towards the consumption of date palm sap as the likely source.
- **Kerala Outbreaks (2018, 2019, 2021, 2023):** While outside the Bengal region, the recurrent outbreaks in Kerala (Kozhikode and Kochi) are significant for India's NiV narrative. The 2018 outbreak, with a CFR of 91% (17 of 19 confirmed cases), demonstrated the virus's potential to emerge in new geographical areas, possibly via bat migration or virus carriage by travellers [21,22]. These outbreaks tested and refined India's outbreak response capabilities in a new setting.

Table 1: Major Nipah Virus Outbreaks in India

Year	Location (State)	Confirmed Cases	Deaths (CFR)	Primary Suspected Source	Key Feature
2001	Siliguri (West Bengal)	66	45 (~68%)	Unknown, possible nosocomial	Major nosocomial amplification
2007	Nadia (West Bengal)	5	5 (100%)	Consumption of date palm sap	Limited cluster
2018	Kozhikode (Kerala)	19	17 (~89%)	Bat exposure (well contamination suspected)	First South India outbreak
2019	Kochi (Kerala)	1	1 (100%)	Zoonotic exposure (bat)	Isolated case
2021	Kozhikode (Kerala)	1	1 (100%)	Zoonotic exposure (bat)	Isolated case
2023	Kozhikode (Kerala)	6	2 (33%)*	Zoonotic exposure	Lower CFR, improved management

*Case fatality ratio as of confirmed outbreak conclusion.

3. Present Impact and Epidemiology in the Bengal Region

The persistent circulation of NiV in Pteropus bat populations across Bangladesh and eastern India makes the Bengal region a perpetual hotspot [23]. Serological evidence indicates widespread exposure in bat colonies, with seasonal variations in viral shedding potentially linked to bat reproductive cycles [24,25].

3.1. Transmission Dynamics

The primary risk factor remains the consumption of raw date palm sap harvested during winter months (December to April) [26]. Bats access the sap collection pots overnight, contaminating the sap with virus-laden excreta or saliva. Cultural preferences for raw sap pose a significant challenge to behaviour change interventions. Secondary human-to-human transmission occurs through close contact with infected patients' respiratory secretions, saliva, or urine, making family caregivers and healthcare workers particularly vulnerable [27].

3.2. Clinical Presentation and Pathology

NiV infection causes a severe systemic illness. The incubation period ranges from 4 to 14 days [28]. Clinical features encompass:

- **Febrile encephalitis syndrome:** Fever, headache, dizziness, vomiting, and altered mental status progressing to coma within 24-48 hours [29].
- **Respiratory involvement:** Severe acute respiratory infection, including cough, dyspnoea, and atypical pneumonia, is common, particularly in Bangladesh outbreaks [30].
- **Long-term sequelae:** Survivors often face significant neurological consequences, including personality changes, motor deficits, and relapsing encephalitis months or years after initial infection [31].

The pathogenesis involves widespread vasculitis, endothelial cell infection, and syncytia formation in multiple organs, particularly the brain and lungs, explaining the severe clinical manifestations [32].

4. Challenges in Management and Control

Addressing the NiV threat is fraught with multidisciplinary challenges.

4.1. Diagnostic Challenges

Rapid and accurate diagnosis is critical for outbreak containment but remains a challenge in resource-limited settings where outbreaks typically occur.

- **Laboratory Requirements:** Confirmation requires BSL-3/4 facilities for virus isolation, which are limited globally [33].
- **Available Tests:** Real-time reverse transcriptase-polymerase chain reaction
- (RT-PCR) on throat swabs, nasal swabs, cerebrospinal fluid (CSF), or urine is the primary method for early detection [34]. Serological assays (ELISA for IgM and IgG) are useful for convalescent-phase diagnosis and surveillance [35].
- **Point-of-Care Need:** There is an urgent need for validated, rapid diagnostic tests (RDTs) that can be deployed at the point of outbreak to facilitate triage and IPC decisions [36].

Table 2: Diagnostic Methods for Nipah Virus Infection

Method	Specimen	Purpose	Timeframe	Advantages	Limitations
Virus Isolation	CSF, throat swab, tissue	Gold standard for confirmation	Days to weeks	Definitive diagnosis	Requires BSL-4 lab; slow; hazardous

Method	Specimen	Purpose	Timeframe	Advantages	Limitations
RT-PCR (real-time)	Throat/nasal swab, CSF, urine	Early diagnosis, detection of viral RNA	Hours	High sensitivity/specificity; rapid	Requires specialised lab equipment
IgM ELISA	Serum, CSF	Detection of recent infection	From end of first week	Useful for acute diagnosis	Cannot detect very early infection
IgG ELISA	Serum	Detection of past infection, serosurveys	Convalescent phase	Useful for surveillance	Not for acute case management
Immunohistochemistry	Tissue (autopsy)	Post-mortem confirmation	Post-mortem	Confirms infection in deceased	Invasive; not for patient management

4.2. Treatment Challenges

Management is primarily supportive, focusing on managing cerebral oedema, seizures, and respiratory failure [37]. Specific therapeutic options are extremely limited.

- **Ribavirin:** This broad-spectrum antiviral was used empirically during the Malaysian outbreak, with some observational studies suggesting a potential mortality benefit [38]. However, subsequent in vitro and in vivo data have been conflicting, and its efficacy remains unproven in randomised controlled trials [39].
- **Monoclonal Antibodies:** The most promising therapeutic is m102.4, a human monoclonal antibody that neutralisesNiV. It has shown high efficacy in animal models and has been used under compassionate use protocols in Australia and during the Kerala outbreaks [40,41]. However, it remains an investigational product with limited global availability and high cost.
- **Other Antivirals:** Favipiravir and remdesivir have shown in vitro activity, but clinical data are lacking [42,43].

Table 3: Therapeutic and Prophylactic Options for Nipah Virus

Agent	Type	Stage of Development	Key Notes
Supportive Care	Medical management	Standard of care	Mainstay of treatment; includes ICU support for encephalopathy & respiratory failure.
Ribavirin	Antiviral (nucleoside	Used off-label/empirically	Efficacy not conclusively proven; potential teratogen.

Agent	Type	Stage of Development	Key Notes
	analogue)		
m102.4	Human monoclonal antibody	Phase I trials complete; expanded access use	Highly effective in animal models; used compassionately in outbreaks; supply limited.
Remdesivir	Antiviral (nucleotide analogue)	Preclinical/In vitro activity	Broad-spectrum antiviral; efficacy in animal models of NiV requires further study.
Favipiravir	Antiviral (polymerase inhibitor)	Preclinical/In vitro activity	Shows in vitro promise; clinical data absent.
NiV Vaccines (e.g., HeV-sG, ChAdOx1 NiV)	Vaccine	Phase I/Preclinical	Several candidates in pipeline (based on Hendra G glycoprotein or viral vectors); none licensed.

4.3. Infection Prevention and Control (IPC) Challenges

Controlling nosocomial transmission is paramount. Challenges include:

- Late recognition of index cases.
- Inadequate triage and isolation facilities in primary healthcare settings.
- Shortages of personal protective equipment (PPE).
- Lack of training in standard, contact, and droplet precautions for a high-consequence pathogen [44].

5. Precautions and Public Health Preparedness

A multipronged strategy is essential for prevention and preparedness.

5.1. Community-Level Interventions

- **Date Palm Sap Safety:** Public health campaigns to promote boiling date palm sap before consumption or using bamboo skirt barriers (bana) on collection pots to prevent bat access are crucial, culturally sensitive interventions [45,46].
- **Awareness:** Educating communities, healthcare workers, and traditional healers about NiV symptoms, transmission routes, and the importance of avoiding contact with sick bats or animals and bodily fluids of patients.

5.2. Strengthening Surveillance and One Health Approach

- **Integrated Surveillance:** Establishing syndromic surveillance for acute encephalitis and respiratory illness in outbreak-prone areas [47].
- **One Health Collaboration:** Fostering collaboration between human health, animal health (livestock, wildlife), and environmental sectors to monitor NiV in bat populations, understand spillover risks, and conduct coordinated outbreak investigations [48].
- **National Institute of Virology (NIV) and ICMR Network:** India's NIV and its network of laboratories serve as the central hub for NiV diagnosis and research, requiring sustained strengthening [49].

5.3. Healthcare System Preparedness

- **Protocol Development:** Developing and disseminating national guidelines for case definition, diagnosis, management, and IPC for NiV [50].
- **Simulation Exercises:** Conducting regular training and simulation drills for rapid response teams and hospital staff in outbreak-prone states.

- **Stockpiling:** Exploring options for regional stockpiling of essential PPE and investigational therapeutics like m102.4 for emergency use.

6. The Future: Research Directions and Concluding Remarks

The future of NiV management hinges on advancing research and fostering global collaboration.

6.1. Vaccine Development

The development of a safe and effective vaccine is a critical priority. Several candidates, including subunit vaccines based on the Hendra virus G glycoprotein (which confers cross-protection against NiV) and viral vector platforms (e.g., ChAdOx1), are in preclinical and early clinical development [51,52]. Accelerating these efforts through public-private partnerships and funding mechanisms like CEPI (Coalition for Epidemic Preparedness Innovations) is vital [53].

6.2. Advanced Diagnostics and Therapeutics

Investment in developing field-deployable RDTs and broadening the portfolio of effective antivirals and monoclonal antibodies is necessary. Research into host-directed therapies also holds promise.

6.3. Ecological and Epidemiological Research

Further studies are needed to understand the drivers of viral shedding in bats, identify high-risk interfaces for spillover, and model the potential impacts of climate and land-use change on NiV distribution [54,55]

Table 4: Key Future Research and Preparedness Priorities

Priority Area	Specific Objectives
Vaccine Development	Advance lead candidates through clinical trials; establish correlates of protection; develop deployment strategies for at-risk populations (e.g., healthcare workers).
Therapeutics	Conduct clinical trials for m102.4 and other candidates; develop affordable, scalable production methods for monoclonal antibodies; explore combination therapies.
Diagnostics	Develop, validate, and deploy rapid point-of-care antigen or molecular tests for field use in outbreak settings.
Ecology & Spillover	Longitudinal studies on bat ecology and viral dynamics; identify environmental and behavioural risk modifiers; map high-risk zones using geospatial tools.
Health Systems	Strengthen integrated One Health surveillance networks; institutionalise simulation training; develop regional stockpiling strategies for countermeasures.

7. Conclusion

Nipah virus represents a formidable and persistent zoonotic threat to public health security in the Bengal region and India. Its high case fatality rate, capacity for human-to-human transmission, and the absence of licensed vaccines or specific antivirals underscore its classification as a priority pathogen of pandemic potential. The historical pattern of outbreaks, from the initial spillover in Malaysia to the recurrent, often devastating, events in West Bengal, Bangladesh, and Kerala, provides critical lessons. These episodes have starkly revealed vulnerabilities within health systems, particularly regarding infection prevention and control in healthcare settings and the challenges of interrupting entrenched environmental transmission pathways, such as the consumption of raw date palm sap.

The present landscape is characterised by significant challenges in rapid diagnosis, limited therapeutic arsenals, and the constant ecological pressure of a virus endemic in widespread bat populations. While supportive care remains the cornerstone of management, and investigational agents like the monoclonal antibody m102.4 offer promise, these tools are not yet accessible or scalable for widespread use. Therefore, the future of NiV management must

be fundamentally proactive rather than reactive. This necessitates a dual-track approach: firstly, the acceleration of research and development to deliver effective vaccines, scalable therapeutics, and field-deployable diagnostics; and secondly, the robust strengthening of foundational public health and One Health systems.

Sustained success hinges on moving beyond siloed responses. It requires the deep integration of human, animal, and environmental health surveillance to predict and prevent spillover. It demands continued community engagement to promote sustainable, culturally acceptable risk-reduction behaviours. Ultimately, mitigating the cyclical threat of Nipah virus depends on unwavering political commitment, sustained international collaboration, and significant investment in building resilient health infrastructure. Only through such a comprehensive, forward-looking, and collaborative strategy can the recurring spectre of NiV outbreaks be effectively contained and the health security of populations in at-risk regions be assured.

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