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Mini-Narrative Review

Navigating Nipah virus: Insights, challenges, and recommendations

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ABSTRACT

Nipah virus (NiV), a zoonotic pathogen with global implications, poses multifaceted challenges. Highlighting the virus's diverse strains and recurrent outbreaks, we explore the rapid course of infections, diagnostic limitations, and the pressing need for therapeutic advancements. Emphasizing the complex dynamics of viral transmission; the urgency for comprehensive biosecurity measures and early detection systems is highlighted. This advocates for a robust global response to address the evolving landscape of NiV, emphasizing the need for collaborative efforts to mitigate its impact on public health.

1. Introduction

Nipah virus (NiV) was discovered in 1999, is a biosafety level 4 and category C pathogen belonging to the *Paramyxoviridae* family and *Henipavirus* genus, sharing genetic similarities with Hendra, Cedar, and Mojiang viruses. Structurally, it is a single-stranded enveloped RNA virus approximately 18 knt in length, with a helical nucleocapsid, measuring 40–1900 nm. [1,2]. Viral RNA mutates rapidly, and if a human-adapted strain infects communities in South Asia, the high population density and global interconnectedness would quickly spread the infection among humans, potentially initiating a pandemic similar to COVID-19 [3,4].

Phylogenetically, NiV exhibits two distinct clades, NiV-Malaysia (NiV-MY) and NiV-Bangladesh (NiV-BD), causing respiratory tract illness and fatal encephalitis, respectively. The Malaysian and Bangladeshi strains differ genetically in the number of their nucleotides, having 18,246 and 18,252 nucleotides, respectively. Notably, NiV-MY proves more virulent than NiV-BD, highlighting genotypic variations [5].

NiV infections range from mild to severe, with an incubation period of 4–14 days. Initial symptoms include fever, headache, and respiratory distress. Subsequent encephalitis may lead to drowsiness, disorientation, progressive coma, and death. Survivors face potential long-term effects, such as persistent seizures or behavioral changes. The virus's multiorgan involvement stems from vasculitis-associated thrombosis. Diagnostic investigations involve early real-time polymerase chain reaction (RT-PCR) from nasopharyngeal swabs, blood, cerebrospinal fluid (CSF), and urine, and later in the disease, an ELISA test can be conducted to check antibodies. There are no targeted vaccines or specific antiviral treatments available yet. Care is supportive i.e. oxygen and fluids supplementation, antipyretics, anti-convulsants, and nutritional support. The absence of a definitive cure and its transboundary prowess make NiV a formidable health threat [6].

Family	*Paramyxoviridae*
Genus	*Henipavirus* genus
Morphology	Non-segmented, negative-sense, single-stranded RNA, helical nucleocapsid, enveloped, can be filamentous or spherical.
Number of strains	Two; NiV-Malaysia (NiV-MY) and NiV-Bangladesh (NiV-BD).
Primary host	Pteropid fruit bats, including Pteropus vampyrus (large flying fox), and Pteropus hypomelanus (small flying fox).
Intermediate host	Pigs

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(*continued*)

Family	*Paramyxoviridae*
Mode of transmission	Close contact with infected animals or their body fluids, contaminated food
Human-to-human transmission	Through respiratory droplets or contact with the body fluids of an infected person
Incubation period	4–14 days
Clinical presentation	Fever, headache, cough, sore throat, encephalitis.
Case fatality rate	40–75 %
Diagnosis	In the early stage, real-time polymerase chain reaction **(RT-PCR)** on urine, blood, throat, nares, or CSF samples. In the later stages and following recovery, an enzyme-linked immunosorbent assay **(ELISA).**
Treatment	Supportive care; rest, hydration, and treatment of symptoms.

2. Literature search

A comprehensive literature search using PubMed, Google Scholar, Science Direct, and Cochrane Library was carried out from inception to February 2025, using the search string Nipah Viruses OR Virus, Nipah OR Nipah henipavirus OR Henipavirus. Articles reporting significant data on the epidemiology, clinical presentations, transmission, management, therapeutic advancements, and hurdles faced while controlling the Nipah virus globally were considered. Furthermore, the bibliographies of selected articles were manually examined to identify any relevant articles. No language restriction was applied.

3. Epidemiology

The epidemiology of NiV unfolds with distinct manifestations in various regions, shaped by diverse breeding practices and dietary habits. Fruit bats, also known as flying foxes, are widespread in regions of Southeast Asia, East Africa, Central and South America, and some parts of Australia, and serve as the primary carriers. The disease's origins trace back to West Malaysian pig farms, causing a significant outbreak in 1998–99, where the virus finds an intermediary host in pigs and is transmitted through bat-bitten fruits, subsequently affecting humans through contact with pig secretions and consumption of raw pork. The first outbreak resulted in 265 cases of acute encephalitis and 105 deaths [7]. Significantly, Malaysia and Singapore have been free from NiV outbreaks since 2001, while several parts of Asia, particularly Bangladesh and India, witness annual episodes between December and May, where transmission occurs via bat saliva or excreta-contaminated palm fruit sap, with subsequent human-to-human transmission through respiratory droplets or contact with bodily fluids of an infected person [2].

The epidemiological landscape includes notable outbreaks, such as those in West Bengal, India, recorded in 2001 and 2007. Bangladesh documented 14 outbreaks from 2001 to 2012. The Philippines faced a fatal outbreak in 2014, marked by an alarming 82 % mortality rate. In 2018, Kerala, India, experienced a NiV outbreak resulting in 21 fatalities. From April 2001 to December 2021, Bangladesh reported a total of 322 human NiV cases, with a case fatality rate of 71 % [1,8]. Recent cases in 2023 alone highlight the persistent threat, with eight reported cases in Bangladesh resulting in five fatalities [2]. These outbreaks follow a seasonal pattern, occurring from December to April, aligning with the date palm sap collection period. These epidemiological insights underscore the need for sustained vigilance and strategic interventions to curb the impact of the Nipah virus on public health.

4. Challenges

Due to the worldwide distribution of bats, new spillovers and reports cannot be dismissed. Human activities like deforestation, agricultural expansion, and urbanization increase human-wildlife contact, facilitating zoonotic spillovers. The Virion reservoir is suspected to extend to the African and Australian regions. The disease is challenging to identify due to its rapid course and high fatality rate following infection, especially in areas with insufficient diagnostic facilities [9]. Viral isolation, immunohistochemistry, serology, and other molecular diagnostic techniques for detecting the presence of NiV infection are absent in remote areas where outbreaks are more likely to occur. A limited understanding of pathogenesis, transmission, and long-term effects due to limited human studies hinders the development of effective measures. Small recurrent outbreaks help the virus adapt into a more deadly strain than the previous one [10], with fatality rates for recent strains approaching 40–75 %. Continuous viral transmission modes among different hosts and geographical areas are concerning treatment development. Additionally, the long incubation period of up to 45 days can lead to extremely high infection rates in densely populated areas, as it is still unknown whether viral transmission occurs from asymptomatic or symptomatic patients [6]. Currently, the improvement in hygiene and feeding habits of individuals living in endemic or high-risk areas is the only strategy, but we need to have a solid base for disease prevention on a large scale.

5. Recommendations

The recurring outbreaks of the Nipah virus highlight the unpredictable nature of emerging infectious diseases and emphasize the need for proactive measures to reduce their impact. A key component in preventing disease outbreaks is biosecurity, which is designed to lower the risk of transmission to both humans and animals, especially for diseases where no specific treatment is available. Contamination of crops and other eateries is another risk factor for zoonotic diseases. It is best practice for agricultural and livestock staff in countries where outbreaks have occurred (Bangladesh, India, Singapore, and Malaysia) and worldwide to use personal protective equipment (PPE) such as masks, gloves, protective goggles, gowns, and boots whenever anticipating an outbreak. These items need to be cleaned properly and sanitized with 70 % alcohol after each usage [11]. Early detection systems in the Nipah reservoir areas could be an effective measure for preventing the spread. Surveillance plans need to be employed continuously since undetected reservoirs are at risk of experiencing spillovers. Hospitals should be the primary sites for the screening. Since healthcare workers and the attendants of patients are at high risk, wearing masks and patient isolation for at least 21 days would be effective measures to cope with this [7]. Monoclonal antibodies hold significant potential to prevent deadly outcomes in patients with early symptoms and close contacts [9]. Monoclonal antibody m102.4 has completed phase 1 trials with convincing results [6]. The effectiveness of the antiviral drug Remdesivir as a post-exposure prophylaxis in non-human primates, exhibiting 100 % survival in African studies on monkeys, should be investigated for further human and clinical trials. Ribavirin, a nucleoside analog, showed partial benefits regarding neurological deficits; the administration reported a 36 % decrease in mortality in the Malaysian outbreak, providing a base for further research. Further research on drugs to target specific aspects of the NiV cycle is crucial to achieving appreciable benefits. Branda et al. argues that genomic surveillance provides invaluable insights into a virus's evolution, and the emergence of new strains, enabling more effective outbreak responses. Public awareness campaigns are the major contributor to preventing virus spread in resource-limited regions. Since bats are the primary animal reservoir for the virus, awareness of this could prevent virus transmission. Studying the ecology of fruit bats might produce significant knowledge of their ability to hoard and transmit infection. Possible measures include avoiding eating bat meat and fallen fruits, and preventing contact with animals such as pigs, that could encounter fruit bats [1]. Comprehensive studies on agent virological factors and patient immunological factors increasing susceptibility to NiV are crucial for effective countermeasures against it. Vaccine development remains the cornerstone for combating

viral illness. Several candidate vaccines (mRNA vaccine, peptide vaccine) have been developed and are being tested in various animal models in preparedness for a looming pandemic threat [7]. Several vector-based vaccines, mainly employing B-cell and humoral immune responses, have been showing promising results in pre-clinical trials. However, there is a need to expedite the ongoing projects related to anti-NiV drugs and immunization through global collaboration and sustained funding [12].

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CRediT authorship contribution statement

Muhammad Hassan Hafeez: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Hafsa Ajmal:** Data curation, Conceptualization. **Amna Nadeem:** Data curation, Conceptualization. **Shehroze Tabassum:** Funding acquisition, Formal analysis, Data curation, Conceptualization. **Aymar Akilimali:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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The authors declare that there no conflict of interest.

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