

Brief Communication

Understanding the dynamics of nipah virus (NiV) transmission and outbreaks in India from Kerala's perspective

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ABSTRACT

This comprehensive analysis delves into the series of Nipah virus (NiV) outbreaks across India, with a particular focus on occurrences in Kerala. NiV, which belongs to the Paramyxoviridae family and Henipavirus genus, originated in Malaysia in 1998 and has consistently posed significant global health threats. In India, NiV outbreaks have sporadically emerged since the initial case in West Bengal in 2001, often with alarming mortality rates. The 2018 resurgence in Kerala exhibited an astonishing case fatality rate of 89%, emphasizing the need for tailored diagnostic and management strategies due to substantial variability in the incubation period and clinical manifestations. Understanding the predominant person-to-person transmission underscores the importance of comprehending transmission dynamics. Early detection, facilitated by the Integrated Disease Surveillance Program (IDSP), remains vital, as treatment options are currently confined to supportive care, necessitating the exploration of more effective therapeutics. The sporadic nature of NiV outbreaks, exemplified by the recent Kerala episode, emphasizes the urgency for robust response mechanisms, while collaborative efforts and capacity-building initiatives are essential for effectively managing these occurrences. Continued focus on prompt detection, advanced laboratory testing, accessibility to cutting-edge facilities, and heightened infection control measures remains imperative to mitigate future incidents.

Keywords: Nipah virus, NiV outbreaks, Kerala, Transmission dynamics, Infectious diseases, Public health emergencies

INTRODUCTION

The Nipah virus (NiV), a pleomorphic pathogen classified within the Paramyxoviridae family and Henipavirus genus, was first discovered in Malaysia in 1998 and subsequently manifested in Singapore by 1999.¹ Its initial outbreak in India occurred in Siliguri, West Bengal, in 2001, showcased a dire 68% mortality rate. This grim scenario worsened with a catastrophic event in 2007 in the Nadia district of West Bengal, which recorded an overwhelming 100% mortality rate.¹ NiV's inclusion in the World Health Organization's (WHO) 2018 Research and Development Blueprint among the top 10 priority diseases was justified due to its propensity to cause substantial public health crises.¹ The resurgence of NiV in May 2018 in the Kozhikode district of Kerala, India, exhibited an alarming case fatality rate of 89%, resulting in 17 tragic fatalities among 18 confirmed cases within a month.² The most recent NiV epidemic, occurring on September 5, 2021, in Kozhikode district, Kerala, resulted in the unfortunate demise of a 12-year-old boy, attributed to his consumption of rambutan fruits procured along the riverbank by his father.³

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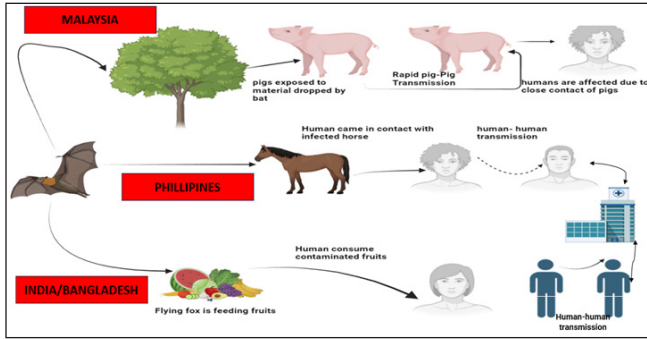


Figure 1: Transmission dynamics of Nipah virus. (Adapted and modified with permission with Creative Common License CC BY 4.0, Open Access Article of 2022) (Created with Bio render).

The transmission dynamics of NiV [Figure 1]⁷ is based on the direct contact with infected humans or animals or eating food or fruits that have come into contact with the bodily fluids of diseased animals, such as pigs and bats.³ G Arunkumar *et al.*¹ has demonstrated the transmission dynamics in their research and they had shown that the transmission is happening through close contact of the infected individual. So, contact tracing is a key factor in this scenario. G Arunkumar *et al.*¹ has also mentioned, “Of the 60 environmental samples including partially eaten mangoes, guava and areca nuts with bite marks of bats were collected from the surroundings of the residence and potential work places of the index case, none had evidence of NiV RNA by real time PCR. His pet rabbits and ducks tested negative for NiV” So, origin of this disease is still not clear, but direct transmission picture is quite clear. So, isolation of cases and contact tracing, both are crucial in this disease.

DISCUSSION

The incubation period of NiV disease spans a wide spectrum across different geographical regions, ranging from as short as 4 days to as long as 2 months.^{3,4} Clinical manifestations of the viral infection exhibit significant variability, encompassing instances predominantly characterized by fever and severe cases involving acute encephalitis. Notably, cases in Kerala showcased psycho-neural symptoms such as behavioral distortions, disorientation, and reduced consciousness.⁵ Throughout India, including recent occurrences in Kerala, all NiV outbreaks have propagated through person-to-person transmission. Substantial evidence supports the correlation between the emergence of bat-related viral infections, which are contagious to both humans and animals and the loss of natural habitats for bats.⁵

Following the confirmation of the 2018 outbreak by the National Institute of Virology (NIV) in Pune, the information

was swiftly relayed to the World Health Organization (WHO) on May 23, 2018.⁴ The Medical College Hospital (MCH) in Kozhikode emerged as the central facility for admitting suspected NiV cases, with regional healthcare providers explicitly instructed to adhere to strict protocols and it is crucial to manage the cases at designated tertiary care hospitals with appropriate infrastructure.⁶ In response to the NiV infection situation, a multidisciplinary central team, guided by the Union Health Minister, was deployed to conduct a comprehensive review and formulate a response strategy. Comprising experts from diverse healthcare specialties and reputable organizations, this team was well-equipped to address the exigencies of the situation.⁵

Efforts to contain the spread and reduce the fatality rate of Nipah Virus Disease (NiVD) focus on early detection, vigilant monitoring, and swift response to outbreaks that are prone to epidemics. The Government of India, through the Integrated Disease Surveillance Program (IDSP), plays a pivotal role in early detection by offering technical and financial support to all states under the National Health Mission (NHM). Diagnostic techniques, including virus isolation, neutralization, immunohistochemistry, molecular and serological assays, enzyme-linked immunosorbent assays (ELISA), and polymerase chain reaction (PCR) have been extensively employed for NiV detection, with successful NiV isolation achieved through Vero cell culture. The WHO officially declared the cessation of the epidemic status within the state of Kerala by July 1, 2018.⁴

The comprehensive examination of the 2018 Kerala NiV outbreak revealed a staggering 91% case-fatality rate, resulting in 21 mortalities and only two survivors. The majority of the cases were among males with a median age of 45 years. The median incubation period was meticulously determined to be 9.5 days.⁴

CONCLUSION

Efforts to elucidate the origin of NiV infection involved meticulous sampling from incarcerated bat specimens, utilizing techniques such as mitochondrial cytochrome b gene polymerase chain reaction (PCR) for species classification.

Currently, treatment options [Table 1] for NiV primarily focus on supportive care and symptomatic management, particularly in cases involving various complications. The Department of Health and Family Welfare, Government of Kerala, has recommended drugs such as ribavirin, human monoclonal antibody M102.4, remdesivir, and favipiravir for treatment, with details provided in Table 1. In a study by Pallivalappil *et al.*, Ribavirin was administered to over 40% of patients, while 15% initially received intravenous acyclovir, which was subsequently

Table 1: Nipah Virus (NiV) treatment options in India: Drugs, dosages, and potential side effects.

Drug	Type	Recommended dose	Short-term side effects	Long-term side effects
Ribavirin	Antiviral	1200 mg/day (in 6 divided doses) for 14 days in survivors	Nausea, vomiting, anemia, fatigue, headache	Hemolytic anemia, potential teratogenic effects
Monoclonal antibody M102.4	Monoclonal antibody	Administered as per healthcare provider's guidance	Hypersensitivity reactions, fever, chills, fatigue	Not well-defined due to limited use in NiV treatment
Remdesivir	Antiviral	Administered as per healthcare provider's guidance	Nausea, vomiting, increased liver enzymes, rash	Not well-defined due to limited use in NiV treatment
Favipiravir	Antiviral	Administered as per healthcare provider's guidance	Gastrointestinal symptoms, increased liver enzymes	Not well-defined due to limited use in NiV treatment

switched to Ribavirin at a dosage of 1200 mg/day (administered in 6 divided doses) and continued for 14 days in survivors.⁴ Convalescent plasma may emerge as a potential therapeutic recourse in severe cases where proven treatment options are unavailable. Preventive measures focus on identifying and isolating infected individuals, promoting rigorous hand hygiene, and advocating the meticulous use of personal protective equipment (PPE) in endemic areas.⁶ Recommendations to combat the situation are highlighted in Table 2.

The recent Nipah Virus Disease (NVD) outbreak highlights the sporadic nature of NiV spillover into the human population, emphasizing the prevalence of NiV infections among the *Pteropus medius* bat population. The swift and efficient confirmation of the outbreak in India was facilitated by seamless coordination between Virology Research and Diagnostic Laboratories (VRDL) and the Department of Health and Family Welfare, Government of Kerala, within a mere 12 hours of notification.

Table 2: Key recommendations for Nipah Virus (NiV) outbreak management in India.

Recommendation	Rationale
Enhance early detection and surveillance systems	Early detection is crucial for a swift response and containment of NiV outbreaks. Implement robust surveillance systems, including monitoring of potential reservoirs (bats) and identifying unusual health patterns.
Strengthen coordination between government agencies and health organizations	Seamless coordination between government agencies, research institutes, and health organizations is essential to quickly confirm and manage NiV outbreaks. This coordination ensures timely information sharing and resource allocation.
Implement rigorous laboratory confirmation	Invest in well-equipped and accessible diagnostic laboratories, capable of conducting a diverse range of diagnostic tests, including virus isolation, neutralization, immunohistochemistry, and molecular assays. This will help in rapid and accurate confirmation of NiV cases. Proper infrastructure like ELISA, PCR, viral isolation cell culture should be present. Labs should be well equipped and well-staffed.
Develop and update treatment protocols	Continuously update treatment protocols based on the latest research and available drugs. Consider drugs such as Ribavirin, monoclonal antibodies, Remdesivir, and Favipiravir for symptomatic management. Research and develop new treatments. Updating and maintain standard operating protocols (SOPs) is crucial.
Promote infection control practices	Emphasize the importance of infection control measures, including the use of personal protective equipment (PPE) and rigorous handwashing, especially in endemic areas.
Study and monitor bat populations	Conduct ongoing studies and monitoring of bat populations, particularly <i>Pteropus medius</i> , to understand and predict potential spillover events. This can aid in early intervention and prevention.
Promote public awareness and education	Raise awareness among the public about NiV, its transmission, and preventive measures. Educate people on safe practices, like avoiding exposure to bats and their habitats. From district administrative level, different awareness program should be conducted.
Invest in capacity building initiatives	Strengthen initiatives for capacity building in areas like laboratory diagnosis, epidemiology, and response preparedness. Collaborate with organizations and international agencies for support and training.
Encourage research and collaboration	Foster research on NiV transmission and outbreaks and collaborate with national and international research organizations. Share findings and insights to improve understanding and response strategies.
Drug availability	Ribavirin should be available in the outbreak areas. The stock should be present beforehand for the preventive purpose. Other treatment options should be available also.

ELISA: Enzyme-linked Immunosorbent Assay, PCR: Polymerase Chain Reaction.

Capacity-building initiatives under numerous programs, notably the National Centre for Disease Containment's Integrated Disease Surveillance Program and India's Global Health Security Agenda, significantly contributed to the successful containment of this outbreak. Continuous efforts to promote early diagnosis, ensure rigorous laboratory confirmation, provide access to top laboratories, and enhance infection control procedures are critical for identifying and managing future instances of NVD.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of AI-assisted technology for assisting in the writing of the manuscript and no images were manipulated using AI.

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