

Nipah Virus Spillover and Transmission in Asia for Targeted Management Strategies: A Systematic Review Protocol

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Abstract

Introduction: Nipah virus (NiV) is a zoonotic pathogen that poses a significant public health threat in Southeast and South Asia, with case fatality rates ranging from 40% to 100%. This systematic review aims to identify key transmission and spillover patterns and management strategies to help in prioritizing resource allocation and intervention.

Methods and analysis: This systematic review will be conducted following PRISMA guidelines. The search will encompass multiple electronic databases, including PubMed, Embase, and Scopus, up to 2024. Study selection, data extraction, and quality assessment will be performed by three independent reviewers, with a fourth reviewer resolving any disagreements. Data will be synthesized to identify patterns in transmission dynamics and inform targeted management strategies.

Ethics and dissemination: Ethical approval was not required as no human participants were involved.

Registration details: This systematic review has been registered on PROSPERO with registration ID CRD42024546848.

Keywords: Asia; Nipah Virus; Outbreak; Transmission; Zoonotic spillover

Introduction

Nipah virus (NiV) is a zoonotic pathogen posing a major public health threat in Southeast and South Asia, with case fatality rates ranging from 40% to 100%¹. From 1998 to 2015, more than 600 cases were

reported globally², with recent severe outbreaks in India and Bangladesh, including a notable outbreak in Kerala, India, in 2018, which resulted in 18 confirmed cases and 16 deaths^{3,4}. Bangladesh reported 322 confirmed cases between 2001 and 2021, with a 71% case fatality rate⁵.

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NiV transmission primarily involves spillover from bats to intermediary hosts, such as pigs, and subsequently to humans. Key transmission routes include contact with infected bat saliva, urine, droppings, or consumption of contaminated fruits⁶. Factors such as encroachment into bat habitats, agricultural practices, and land use changes increase spillover risk⁷. Human-to-human transmission, often through respiratory secretions or close contact, along with nosocomial spread, further sustains outbreaks^{8,9}.

Despite ongoing research, there is a need to synthesize existing evidence on NiV transmission dynamics and their implications for outbreak management. The major risk factors have been previously reported. But the interplay between various risk factors and how they shape the spillover and transmission dynamics is yet to be known. Understanding the complex interactions among bats, intermediate hosts, and humans shaped by ecological and human activities is crucial for effective control measures. This systematic review aims to identify key patterns and trends in NiV transmission dynamics. This includes investigating the relative importance of different stages of transmission and the respective ecological management strategies. This will help in prioritizing resource allocation and interventions where they are needed the most.

Objective

To characterize the spillover events of Nipah virus (NiV) from bats to intermediate hosts, followed by transmission to humans, and investigate the diverse modes of NiV transmission.

Research question: What are the spillover and transmission dynamics of NiV in Asia and how can this understanding inform targeted management strategies for NiV outbreaks?

Methods

The protocol has been written according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses for systematic review protocols (PRISMA-P)¹⁰ and registered on the PROSPERO database with registration ID CRD42024546848.

Eligibility criteria

Studies will be included if they report outbreak investigation on Nipah. Studies about spillover events will also be included. They should provide primary data on NiV transmission dynamics, including but not limited to epidemiological investigations. Reviews, Systematic reviews, commentaries, etc will be excluded. Only studies published in English language will be included. Detailed eligibility criteria is given below:

Population:

All patients who had Nipah virus infection during an outbreak and general population in case of management strategy studies will be included. There will be no differentiation on the basis of age, gender, ethnicity, etc.

Intervention:

Any intervention in case of management strategies for prevention or treatment of NiV will be included.

Comparator:

If applicable.

Outcomes:

- Incidence and categorisation of Nipah virus cases and their sources
- Spillover stages of NiV transmission
- Modes of NiV transmission

Study design:

All observational and analytical study designs, surveillance reports, hospital records will be included. For effectiveness of management practices, RCTs maybe included.

Search strategy

Search will be conducted in PubMed, Embase, CINAHL, Scopus, Science Direct, and Web of Science. Search strategy will be made keeping in mind 4 concepts namely: Nipah, Outbreak investigation, Risk factors or sources of exposure, Management guidelines or practices. Grey literature relevant to Nipah virus will also be searched across various sources, including Google Scholar, Shodhganga and ProQuest.

Study selection

For the study selection process, Rayyan software will be utilized to ensure a systematic approach¹¹. After importing all identified studies into the software, duplicates will be removed. Subsequently, three independent reviewers will screen titles and abstracts to assess relevance against pre-defined inclusion and exclusion criteria. Eligible studies will include research focused on Nipah virus outbreaks and management strategies, with any relevant information on transmission. Full-text versions of potentially eligible studies will undergo assessment by three independent reviewers, with proper documentation of inclusion and exclusion. Any disagreements will be solved through discussion with a fourth reviewer.

Assessment of methodological quality and risk of bias

Assessment of the articles will involve a thorough examination for quality using the Joanna Briggs Institute (JBI) Critical Appraisal checklist appropriate to the study's design¹² and Mixed methods appraisal tool (MMAT) version 2018.

Data extraction

A standardized data extraction form will be developed, capturing key variables including:

- Study characteristics (author, publication year, study design, etc)
- Population demographics (age, sex, geographic location, etc)
- Nipah virus outbreak details (index case, location, duration, etc)
- Transmission pathways (zoonotic spillover, human-to-human transmission etc)
- Source of infection
- Ecological management interventions implemented (surveillance, quarantine measures, infection control practices, etc)

Two independent reviewers will perform data extraction, with discrepancies resolved through discussion or consultation with a third reviewer if necessary. The extracted data will be synthesized and analysed to identify patterns, trends, and gaps in the literature, informing the synthesis of findings

and development of recommendations for future research and practice.

The studies will be categorised into 4 groups depending on whether they report risk factors, spillover, transmission or ecological management strategies. These four groups will be compared and thematic analysis will be done.

Discussion

The study aims to elucidate the stages of spillover and transmission of Nipah virus, including the pathways through which the virus is transmitted from its natural reservoir to humans. Understanding these transmission dynamics is crucial for developing targeted interventions and preventive measures. By quantifying the number of cases and identifying sources of infection at each stage, we can gain insights into the epidemiological patterns of Nipah virus transmission and inform targeted surveillance and management efforts. If certain stages show higher case numbers or greater importance, our review will guide decision-makers on where to allocate resources and prioritize interventions. It will also inform the development of guidelines that address the ecological and epidemiological complexities of NiV transmission.

Limitations

The inclusion of studies with varying methodologies and quality levels may introduce heterogeneity into the analysis, potentially impacting the synthesis of findings. Geographical and temporal variability in Nipah virus outbreaks may limit the generalizability of the findings. Also studies published only in English language will be considered which might lead to selection bias.

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Conflicts of interest

The authors declare that they have no conflicts of interest. No organization or person with a financial interest in the subject matter was or will be a part in this manuscript.

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