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The rising threat of Nipah virus: a highly contagious and deadly zoonotic pathogen

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Abstract

The Nipah virus (NiV) is a highly virulent zoonotic infectious agent that poses a significant threat to public health. The virus is characterized by its pleomorphic structure and a single-stranded negative-sense RNA genome. It encodes six structural proteins and three nonstructural proteins. Attachment glycoproteins play a crucial role in allowing the virus to attach to the host cell surface. The matrix protein facilitates the encapsidation of the viral genome and proteins, enabling the formation of mature viral particles. The virus can spread via different routes, including zoonotic spillover and human-to-human transmission. Clinical manifestations include mild respiratory illness and severe and fatal encephalitis. The case fatality rate of Nipah virus infection varies widely, ranging from 40 to 75%, and is regulated by factors such as healthcare availability and quality, the patient's condition, and the virulence of the infecting strain. NiV has been reported in Malaysia, Bangladesh, and India, with fruit bats serving as natural reservoirs. Early detection and prompt response are crucial for controlling outbreaks; however, these efforts are hindered by diagnostic challenges and delayed recognition. The World Health Organization has categorized NiV as a priority pathogen owing to its epidemic potential, recurrent outbreaks, and alarming mortality rates. The persistent transmission dynamics and genetic stability of the Nipah virus among fruit bats require immediate attention and coordinated global action. The present study reviews the epidemiology, clinical features, and modes of transmission of Nipah virus infection, its geographical distribution, and endemic regions, highlighting the challenges in managing disease outbreaks.

Keywords Geographical distribution, Mortality, Nipah virus, Outbreaks, Transmission, Zoonotic

Introduction

The emergence of new infectious diseases poses a significant threat to global public health [9, 18, 19]. Nipah virus (NiV) is a highly fatal and contagious pathogen that causes severe outbreaks with high morbidity and mortality rates. It is a pleomorphic virus endemic to the Western Pacific and Southeast Asia. It belongs to the family Paramyxoviridae and genus Henipavirus. The genetic architecture of the virus comprises a single-stranded negative-sense, unsegmented RNA that encodes six genes: nucleocapsid (N), phosphoprotein (P), matrix (M), fusion protein (F), glycoprotein (G), and RNA polymerase (L) [21]. The first cases of Nipah virus infection were reported in 1998, during an outbreak of neurological and respiratory illnesses in pig farms in Malaysia. The

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outbreak infected 265 humans and claimed 108 lives [17]. NiV was later reported in Bangladesh during the winters of 2001, 2003, and 2004 [23, 50]. NiV-specific IgM was observed during an outbreak of febrile illness associated with altered sensorium in Siliguri, West Bengal, India, in 2001 [7]. It is suspected that fruit bats of the *Pteropus* genus are its natural reservoir [1]. Evidence of NiV infection has been documented in bats in Malaysia, Bangladesh, and Cambodia [13, 52]. In Malaysia, NiV spreads to pigs and most human cases occur through direct contact with infected pigs [12]. The Nipah virus can spread through different routes. Zoonotic spillover can occur when people consume food contaminated with bat saliva or urine, such as raw date palm sap, or when there is direct contact with bats [24]. Human-to-human transmission has also been documented in detail, particularly in hospitals. Transmission of the virus occurs through respiratory droplets or bodily fluids in such environments [27]. The potential for massive outbreaks increases owing to the ability of the virus to be transmitted from person to person, especially in areas with a high population density and weak health care [28]. This scenario has made NiV a condition of growing concern not only for health officials but also for researchers, especially because recent outbreaks continue to occur in certain regions of South and Southeast Asia.

The manifestations of Nipah virus infection vary greatly, ranging from subclinical to severe respiratory diseases and fatal encephalitis [31]. Nonspecific symptoms, including fever, headache, and myalgia, often become severe. It may result in seizures, coma, and encephalitis, with a high risk of death (https://www.who.int/news-room/fact-sheets/detail/nipah-virus). Although the Nipah virus has the potential to cause mass outbreaks, there is no licensed vaccine or targeted antiviral drugs against it [31]. Early detection and prompt response are crucial for controlling outbreaks; however, these efforts are hindered by diagnostic challenges and delayed recognition, as NiV symptoms mimic those of many other febrile illnesses [1]. This study examines the epidemiology and transmission dynamics of the Nipah virus, its clinical presentation, and the challenges associated with diagnostics and treatments. It also explores strategies to reduce the risk of future outbreaks, including vaccine development, improved surveillance systems, and robust public health measures. The insights gained from past Nipah virus outbreaks will be vital for strengthening preparedness and response strategies, offering valuable lessons for the global community in addressing the threats posed by emerging infectious diseases.

This review provides a comprehensive analysis of the Nipah virus (NiV), covering its structure, replication, epidemiology, and the latest advancements in therapeutics and vaccines. It stands out by integrating cutting-edge computational vaccine design, regulatory approval strategies, and the challenges of clinical trials due to sporadic NiV outbreaks. The importance of this work lies in its timely synthesis of emerging research that offers valuable insights for scientists, policymakers, and healthcare professionals. This serves as a crucial resource for guiding future research, enhancing outbreak preparedness, and accelerating the development of effective medical countermeasures against NiV.

Virus structure

Nipah virus (NiV) is a pleomorphic virus with a size range of 120–150 nm (nm) in diameter, which is significantly larger than most other paramyxoviruses [39]. The viral surface is characterized by a single layer of surface projections averaging approximately 17 nm in length. The NiV nucleocapsid had a diameter of approximately 5 nm and a pitch of 17 nm. Notably, the presence of reticular cytoplasmic inclusions near the endoplasmic reticulum distinguishes NiV from other viruses within the Paramyxoviridae genus, rendering its morphology and nomenclature unique [3]. NiV has a helical nucleocapsid and a negative-sense, single-stranded non-segmented RNA with a total genome size of approximately 18.2 kbp [40]. The RNA genome from the 3'-5' region is encoded by three non-structural and six structural proteins: nucleocapsid (N), phosphoprotein (P), matrix protein (M), fusion glycoprotein (F), attachment glycoprotein (G), and long RNA polymerase protein (L) [45, 47]. The P gene of the NiV encodes not only the phosphoprotein (P) but also three non-structural proteins, namely the C, V, and W proteins (Fig. 1). These accessory proteins are generated through alternative open reading frames and RNA editing mechanisms, allowing for the diversification of protein functions and contributing to the complex biology of NiVs. All of these factors are important for the development and progression of viral diseases [29, 43, 47]. Depending on the viral strain, the NiV genome sequence contains six genes that vary in length from approximately 18,246 to 18,252 nucleotides [8, 20]. The viral matrix protein shell is composed of a lipid membrane [45]. The Nipah virus possesses two envelope glycoproteins, the attachment protein (G/RBP) and the fusion protein (F), which work in tandem to facilitate viral entry into the host cells [6]. The G protein is thus crucial for allowing the virus to attach to the host cell surface by interacting with conserved ephrin B family members, such as B1,B2, and B3, which are proteins present in mammals [23]. The G and F proteins are mainly involved in the processes of binding and fusion to the host cell during the initial viral life

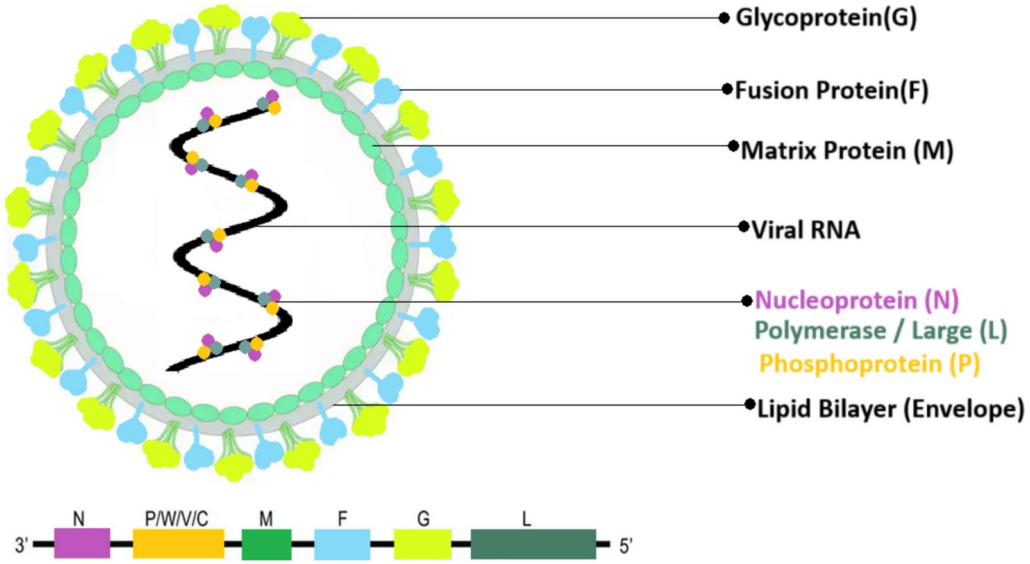

Fig. 1 Schematic representation of the Nipah virus structure and genome organization: Encoding three non-structural (C, V, and W) and six structural proteins (N, P, M, F, G, L)

cycle in the host body [41]. The anti-G protein is necessary for the neutralization of Nipah virus activity [5]. The matrix (M) protein of Nipah virus (NiV) plays a pivotal role in the final stages of viral assembly [43]. Specifically, the M protein facilitates the encapsidation of the viral genome and proteins, enabling the formation of mature viral particles. Furthermore, the M protein mediates the budding process, allowing newly assembled viral particles to exit the host cell and initiate subsequent rounds of infection [39].

The extracellular region of the G attachment glycoprotein, a tetrameric type II membrane protein, forms a six-bladed ((B1–B6)) β-propeller in its receptor-free state but changes the shape of the G/Ephrin-B3 complex [43]. Each blade, stabilized by a disulfide bond, contained a four-stranded β-sheet. Ephrin-B3 binds to the upper face of the β-propeller and interacts with multiple G-loops. The G/Ephrin-B2 complex features a large interface with Ephrin-B2 residues 107–125. The F protein, a trimeric class I membrane protein, is synthesized as F0 and then cleaved into F1 and F2, which aids in membrane fusion. In the pre-fusion state, six F trimers form a stable hexameric structure [43]. NiV exhibits extensive cell tropism, infecting a variety of cell types including endothelial cells, alveolar pneumocytes, and smooth muscle cells. However, their ability to target non-vascular tissues, particularly neurons in the brain, plays a critical role in disease progression, often resulting in severe neurological complications [16].

Replication

The G protein of the Nipah virus attaches to the host cells in a direct manner to the respective receptors that are found on the host cell membrane (Fig. 2). The G protein of the Nipah virus specifically attaches to the EFNB2 and EFNB3 receptors [4]. There are also roles for the F protein in envelope-virion binding, which permits the virus envelope to fuse with the host cell membrane. This primary fusion event brings the viral RNA genome into the cytoplasm of the host cell [51]. It is the structural change in the F protein caused by the binding of the G protein to its receptor, which leads to fusion. Following entry into the host cell, the negative-sense single-stranded RNA of NiV unwinds in the presence of the bound N protein. The L protein combines with the P protein to form an RNA-dependent RNA polymerase that is involved in the transcription and replication of viral RNA. This enzyme generates positive-sense RNA that serves as a template for the transcription of mRNA and replication of the new genome. The produced mRNAs are later translated into viral proteins, and positive-sense RNA templates are used to produce new negative-sense genomic RNA [51]. Within such a short period, mRNAs synthesized by viruses are translated by host cell ribosomes into both structural and non-structural proteins. The important proteins produced by viruses include nucleoprotein (protects the viral RNA), phosphoprotein (Supports RNA dependent RNA polymerase activity and participates in the formation of the virus), matrix protein (assembles and buds new

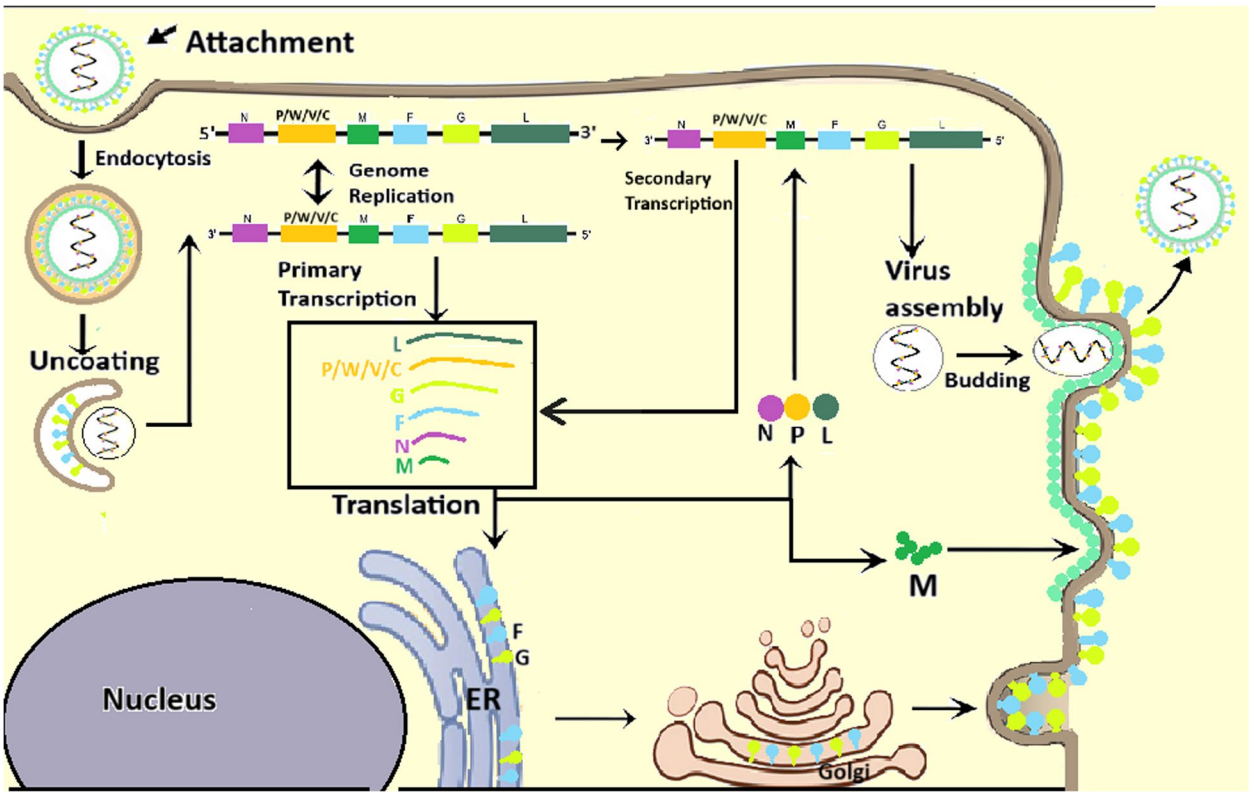

Fig. 2 Replication of NiV: (1) Attachment to the cell surface receptor; (2) Fusion; (3) mRNA synthesis; (4) Translation; (5) Endocytosis; (6) Replication; (7) Interferon inhibition; (8) Assembly; (9) Budding

virions), fusion protein (infect host cells), glycoprotein (associated with attachment of the virus to receptors on host cells), and large protein (catalytic subunit of RNA-dependent RNA polymerase and has a role in the synthesis of RNA) [20]. Newly synthesized viral proteins and RNA genomes are assembled on the host cell membrane. Subsequently, with the formation of new virions, it buds off from the host cell membrane, obtaining its envelope from the host lipid bilayer. As the M protein interacts with the cytoplasmic tails of the F and G proteins, these proteins are included in new virions. This step allows the NiV to acquire its envelope, which is crucial for the formation of infectious particles [51]. Following assembly, newly formed Nipah virions can either damage the host cell or bud from its surface, releasing infectious particles that can infect neighboring cells and perpetuate the disease process. The release of virions facilitates both localized and systemic dissemination within the host, significantly contributing to disease progression and high transmissibility of Nipah virus (NiV). Effective release of the virus is crucial for its widespread dissemination throughout the host and population, underscoring the importance of this step in the viral life cycle.

Geographic distribution and endemic regions

Sun et al. [44] documented 749 human cases of Nipah virus infection across Bangladesh, India, Malaysia, Singapore, and the Philippines (Fig. 3a). Of the patients with demographic data, 89% (358 of 402) were adults aged 15–59, with men making up 74% (391 of 530) and 26% (139 of 530) of the cases, respectively. Livestock practitioners were the most common occupational group, accounting for 68% (238 of 351) of cases. Among the 489 patients with known exposure, 69% (336) had animal contact, 26% (127) had exposure to infected individuals, and 5% (26) had exposure through date palm-related activities. Epidemiological patterns such as sex, exposure, and disease timing varied across the five countries. The crude case fatality rate of Nipah virus infection in humans is 55% [44]. The Nipah virus was also detected in 425 bats from seven countries: Thailand, Cambodia, Malaysia, Indonesia, Timor-Leste, Bangladesh, and India. Figure 3b highlights the countries with incidences of Nipah virus infection in humans and animals. Sun et al. [44] used population data to map regions at risk of Nipah virus infection (Fig. 4a), identifying 185,312 km^2 areas as potential endemic zones, mostly in densely populated regions (Fig. 4b). Their model suggested broader at-risk

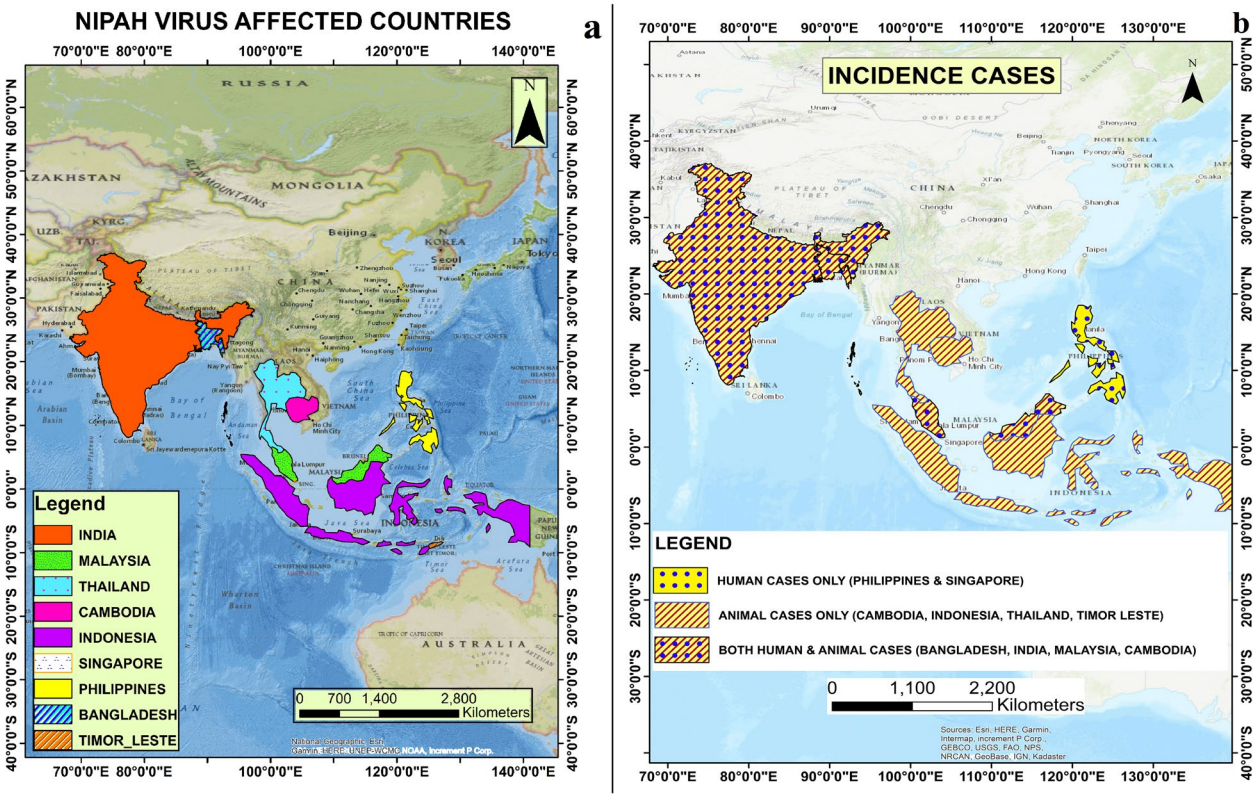

Fig. 3 Geographical distribution of Nipah virus. **a** Nipah virus affected countries across the world and percentage of human fatality. **b** Global incidences of Nipah virus infection in human and animals. (Data adapted from [44])

regions compared with areas reporting human infections and reservoir hosts, aligning with previous studies that indicated that South and Southeast Asia are potentially vulnerable based on the presence of *Pteropus* bats.

Transmission

Nipah virus is mostly associated with fruit bats, mainly from the genus *Pteropus* of the family *Pteropodidae* (Fig. 5). These animals are generally not infected, but can transfer the virus through saliva, urine, or excreted form through their faces [24]. Direct transmission involves contact with infected bats or their contaminated excreta, whereas indirect transmission occurs through an intermediate host such as pigs.

The initial outbreak of NiV in Malaysia was linked to extensive pig farming, which facilitated the transmission of the virus from bats to pigs and subsequently to humans [11]. Human-to-human transmission of the Nipah virus is a significant concern because it can spread through direct contact with infected bodily fluids. This mode of transmission has been observed in hospitals and among close family members of infected patients, highlighting the risk of hospital outbreaks and human-to-human infections. However, studies of outbreaks in Bangladesh and India have demonstrated that implementing appropriate precautions can significantly reduce the spread of secondary infections [28]. Food-borne and waterborne transmission of NiV have been identified as significant risk factors, particularly in Bangladesh. Epidemiological investigations have revealed a strong association between the consumption of contaminated food products, such as fresh date palm sap, and transmission of the virus. It is likely that the sap becomes contaminated with the virus during the harvesting process when it comes into contact with the infected bats. Therefore, avoiding potential sources of infection, especially through contaminated food products, is crucial for preventing the spread of Nipah virus [24]. Sun et al. [44] analyzed 66 complete Nipah virus genome sequences from 43 human patients, 14 bats, 8 pigs, and 1 dog, with data spanning from 1999 to 2021 (GenBank). Five countries contributed to the sequences, with the majority from Bangladesh (41, 62%), followed by Malaysia (15, 23%), India (8, 12%), Thailand (1, 2%), and Cambodia (1, 2%). Phylogenetic analysis revealed two clades: the Malaysian clade (including strains from Malaysia, Thailand, and Cambodia) and the Bangladeshi clade (covering strains from Bangladesh, India, and Thailand). Phylogeographic analysis estimated

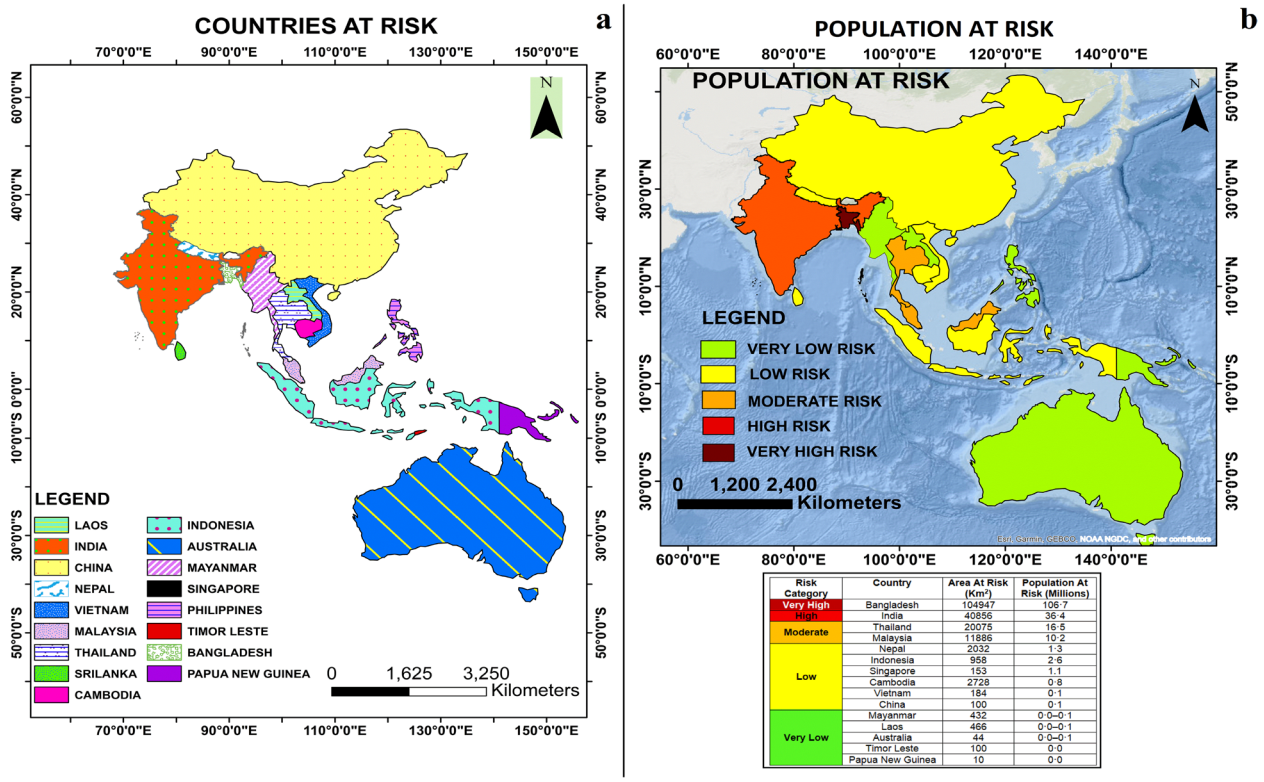

Fig. 4 Endemic zones of Nipah virus infection. **a** Countries at risk of Nipah virus infection across the world. **b** Population at risk of Nipah virus infection across the world. (Data adapted from [44])

that the common ancestor of the virus emerged around 1853 (95% CI 1687–1966), with the Malaysian clade emerging around 1960 (1910–91) and the Bangladeshi clade around 1971 (1929–96). Transmission patterns showed that the Malaysian clade spread from Malaysia to Bangladesh and Cambodia, while the Bangladeshi clade spread from Bangladesh to India and Thailand (Supplementary Material: Figure S1). In India, the sequences were further divided into two subclades: one from Bangladesh, a single sequence from West Bengal, and another from other regions in India. This study identified 195 Nipah virus occurrences across nine countries, with the highest in Bangladesh (130), followed by Malaysia (22), India (19), and Thailand (16) [44].

Symptoms

The Nipah virus causes acute and rapidly progressive disease, primarily affecting the respiratory central nervous system. Symptoms begin 3–14 d after exposure to the pathogen. The clinical manifestation is characterized by rapid progression of symptoms. Initially, patients typically experience high fever, weakness, and headache, which is quickly followed by mental confusion (https://www.who.int/news-room/fact-sheets/detail/nipah-virus). This confusion can deteriorate into a coma within a remarkably short period, often just a few days. While encephalitis is a significant risk factor associated with NiV infection, early symptoms may also include respiratory complications such as atypical pneumonia in some cases. Additional symptoms observed in some patients include respiratory distress, cough, sore throat, vomiting, convulsion, headache, altered mental status, and myalgia [22, 48]. Critically ill patients may rapidly progress to encephalitis and seizures within 24–48 h, ultimately resulting in coma (https://www.who.int/news-room/fact-sheets/detail/nipah-virus). Furthermore, research has shown that the contagiousness of the virus is significantly higher among patients with respiratory difficulties than among those without respiratory symptoms [27].

NiV infection causes a range of symptoms in different species. In young swine, especially those under six months in age, the "one-mile cough" or porcine respiratory and encephalitis syndrome (PRES) is well noted to cause respiratory disease in this group of young pigs. The impact on young animals can involve mild to severe respiratory problems associated with labored breathing and rapid respiration with a dry coughing fit. Although mortality is usually low, it is often much higher in piglets [11, 32]. Some neurological signs in pigs include muscle tremors, weakness of the back legs, and flaccid

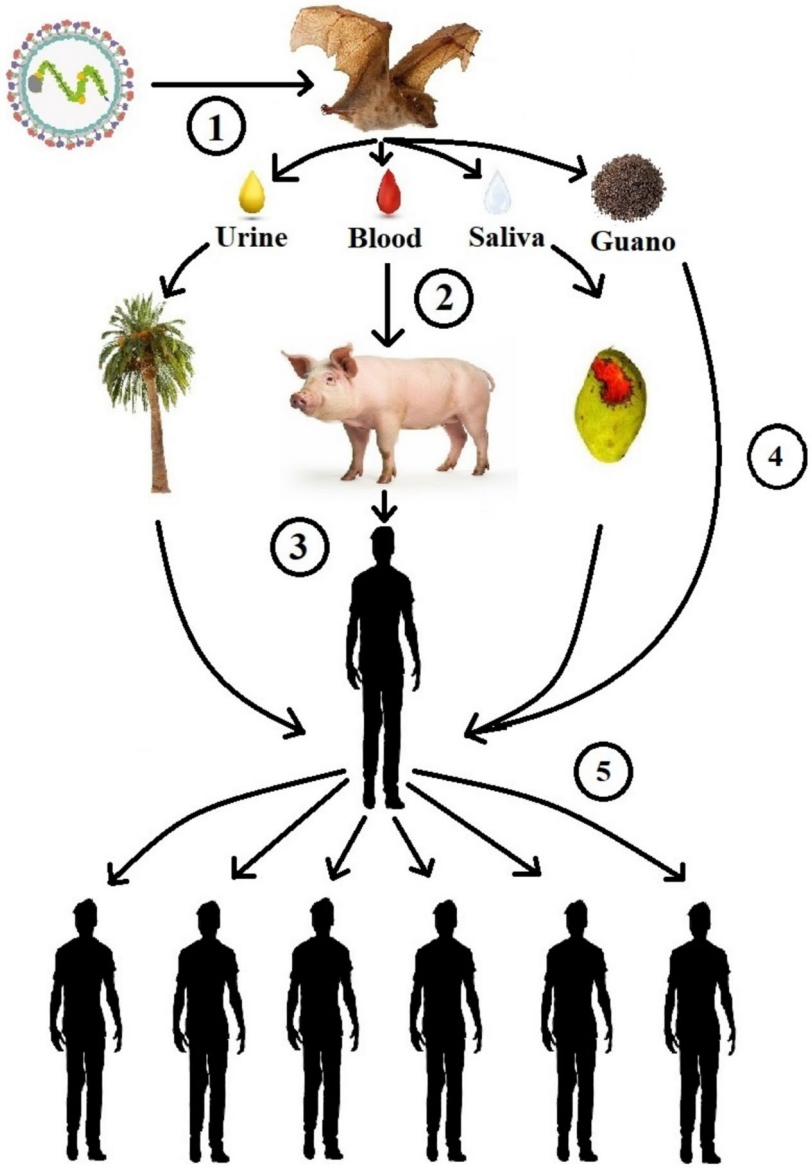

Fig. 5 Transmission of NiV: (1) Fruit bats are often the natural reservoirs of NiV; (2) The saliva, urine, blood or excreta can transmit the pathogen to pigs or to fruits or date palm sap; (3) Human can get infected either with the direct interaction with pigs or through consumption of contaminated fruits; (4) Bat guano may come in contact with human; (5) Human-to-human transmission of the Nipah virus occurs through body fluids

or spastic paresis accompanied by possible seizures and nystagmus in both males and females [11, 26]. In dogs, the infection causes interstitial pneumonia, whereas in cats, the infection may be associated with inflammation of blood vessels and syncytial cell formation in organs. Experimental infections in hamsters, guinea pigs, and African green monkeys resulted in CNS tissue lesions, but in mice and rats, the reasons for such infections remain unknown [26, 49].

Prevention and control

Staying away from pigs and farm animals, avoiding raw date palm sap, and drinking a good amount of potable water can reduce the chance of NiV infection [1]. Fruit bat roosting trees should be planted away from livestock farms and grazing areas [40]. Personal protective equipment (PPE) is recommended for medical professionals during NiV treatment [42]. Active surveillance, contact tracing, and proper diagnosis are essential for curbing the spread of NiV. Vaccine development for NiV faces

significant challenges, including the sporadic nature of outbreaks, limited understanding of protective immunity, lack of private sector involvement, and insufficient BSL-4 laboratories for preclinical testing. Priorities include diagnostics, immunotherapies, vaccines, and antiviral drugs [40]. In countries without prior NiV outbreaks, advanced preparations for potential urban and rural spread can aid in prevention [15]. Understanding the role of bats in transmitting pathogens is critical for preventing cross-species spillover, particularly that of deadly viruses between humans and animals. For example, in Zimbabwe, bat guano are collected from caves for use as manure or for hunting, highlighting the need for monitoring and surveillance of bats in areas with high zoonotic transmission potential [40].

The National Center for Disease Control reports that treatment is primarily supportive, focusing on rest, hydration, and symptom management. Various pharmacological treatments to inhibit NiV proliferation have been tested in animal models. Ribavirin, m102.4 monoclonal antibody, and favipiravin have been explored as potential treatments. In the 1998–1999 NiV outbreaks in Malaysia, ribavirin was administered, resulting in a 36% reduction in mortality without serious side effects [10]. The m102.4 monoclonal antibody, which targets the ephrin-B2 and ephrin-B3 receptors of NiV, has shown effectiveness in neutralizing the virus in vitro and in vivo, providing passive therapeutic potential [1]. It has been experimentally used to protect animals from lethal NiV exposure [3, 53]. Favipiravir, a drug developed for influenza, has demonstrated efficacy in inhibiting NiV in vitro and in a Syrian hamster model, fully protecting animals from lethal infection [14]. Ongoing research aims to develop therapeutics and vaccines against NiV.

Research on antiviral drugs targeting Nipah virus (NiV) is ongoing, with ribavirin showing a 36% reduction in mortality in the 1998–1999 Malaysian outbreak, remdesivir ensuring 100% survival in infected African green monkeys, and favipiravir providing full protection in hamsters. Griffithsin (GRFT) and its synthetic variant 3mG inhibit viral entry at nanomolar levels, while nucleoside analogs such as R1479, GS-5734, and ALS-8112 exhibit anti-RNA synthesis properties, and peptide fusion inhibitors such as chloroquine block NiV F protein action, although further validation in natural hosts is required [30]. Vaccine development is critical owing to its widespread impact, with subunit vaccines using glycoproteins F or G eliciting protective immunity, HeVsG providing varying degrees of protection in different animals, and viral vector-based vaccines, including recombinant measles virus, MVA, VSV, rabies virus, AAV, ChAdOx1, NDV, and canarypox, showing strong immune responses, while virus-like particles (VLPs) and mRNA-based vaccines have demonstrated potent B-cell and T-cell responses. Monoclonal antibody (mAb) therapies, such as m102.4, h5B3.1, and Nip GIP35, offer effective post-exposure protection in non-human primates and ferrets, with promising neutralization at concentrations below 0.1 μg/mL, although concerns such as Antibody-Dependent Enhancement (ADE) require further study. These advancements in antivirals, vaccines, and monoclonal antibodies represent promising strategies for NiV treatment and prevention, although clinical validation remains essential [30].

Advancements in vaccine research have led to the development of live recombinant virus vectors, protein subunits, mRNA-based vaccines, and virus-like particle (VLP) approaches that hold promise for combating Nipah virus NiV infection [33]. The first NiV vaccine candidate was developed using a highly attenuated vaccinia virus strain (NYVAC) that encodes either F or G glycoproteins from the Malaysian NiV strain (NiV-M) [2]. Several other vaccine prototypes are underway that utilize diverse platforms to elicit protective immunity. Subunit-based vaccines, such as Equivac HeV, which utilizes the soluble Hendra virus (HeV) G glycoprotein, have shown cross-protection against NiV in ferrets [35]. Vector-based approaches, including recombinant vaccines, such as ChAdOx1 NiVB (adenovirus-based, tested in hamsters), rVSV-ΔG-NiVB (vesicular stomatitis virus-based, evaluated in monkeys), and rRABV/NIV (rabies virus vector-based, tested in mice), have shown promise in various animal models [33]. Virus-like particle (VLP)-based vaccines, including NiV-VLP vaccines expressing the G, F, and M proteins, have demonstrated efficacy in hamsters [46]. These under-trial strategies offer promising avenues for NiV prevention, with ongoing research focused on translating these findings to humans.

Research on species such as cynomolgus macaques, which remain asymptomatic despite being exposed to NiV, could offer valuable insights into protective immunity. Genomic sequencing of these species, as well as of African green monkeys and squirrel monkeys, which are more susceptible to NiV, could help identify human targets for future therapeutic interventions [36].

New approaches to various vaccine strategies

As of March 30, 2025, there are no licensed vaccines or treatments for Nipah virus (NiV), but vaccine candidates such as ChAdOx1 NipahB are in clinical trials. The University of Oxford is conducting the first-in-human trial of this vaccine with 51 participants supported by the CEPI. NiV, with a fatality rate of up to 75%, has caused outbreaks in South-East Asia, including Singapore, Malaysia, Bangladesh, and India, with the most recent outbreak in Kerala in September 2023 [34]. The sporadic

nature of NiV outbreaks makes traditional Phase-3 efficacy trials infeasible, as a study estimated that a cluster-randomized ring vaccination trial in Bangladesh would take 516 years to complete under the current incidence levels [25]. Alternative trial designs, such as controlled animal studies, surrogate immune markers, and alternative regulatory approval pathways, have been proposed. Regulatory agencies, such as the US FDA, EMA, and national authorities in Bangladesh and India, should consider emergency pathways similar to those used for Ebola during the 2014–2016 outbreak, which demonstrated the effectiveness of investigational stockpiles and ring vaccination trials [25]. Vaccines for other diseases such as influenza, smallpox, and COVID-19 have been approved using immune surrogate endpoints rather than conventional disease endpoints, a model that may be applied to NiV vaccine development. Given NiV's potential for increased transmissibility, the WHO, CEPI, and NIAID continue to support vaccine research and development.

Recent studies have explored novel vaccine designs using immunoinformatic and computational approaches. Shabbir et al. [37] developed a multi-epitope vaccine targeting NiV nucleoprotein to elicit strong immune responses. The vaccine, designed using linkers and adjuvants, exhibited high antigenicity (0.56), non-allergenicity, and non-toxicity. Docking analysis demonstrated strong binding to the ephrin B2 receptor (−920 kcal/mol), with immune simulations indicating high IgG and IgM levels and 88.3% global population coverage, supporting its potential for broad immunization. Similarly, Shahab et al. [38] employed reverse vaccinology to analyze the entire NiV proteome and identify antigenic B-cell and T-cell epitopes. The vaccine candidate demonstrated robust interactions with immune receptors TLR-2 and TLR-4, and computational immune response modeling suggested significant immune activation. However, both studies emphasized the need for further experimental validation before conducting clinical trials. These developments highlight promising avenues for NiV vaccine research; however, regulatory flexibility and continued investment are crucial for advancing these candidates toward licensure.

Future prospects

The adaptability of NiV results from its genetic evolution, host interactions, and environmental factors, making it a global priority. Future research should focus on sequencing more viral isolates to track mutations and better understand transmission dynamics. Investigating the environmental factors influencing outbreaks is essential for developing effective public health strategies. Strengthening global collaboration with WHO supporting funding and training will enhance surveillance and outbreak management. Development of vaccines and antiviral treatments with minimal side effects is crucial. A one-health approach that integrates wildlife conservation and public health measures is necessary to prevent future spillovers and improve vaccine efficacy across populations [31]. Future research should prioritize the development of broadly protective vaccines using multi-epitope and viral vector-based strategies. Given the challenges of large-scale trials, regulatory agencies should explore surrogate immune markers and control human infection models. Advances in computational immunology and AI-driven vaccine design will accelerate the candidate selection. In addition, global surveillance and early warning systems are crucial for timely outbreak responses. Strengthening international collaboration and public health policies will enhance pandemic preparedness. Investment in the development of antiviral drugs, including broad-spectrum inhibitors, can provide effective countermeasures. Finally, studying the potential of NiV for increased transmissibility is vital for assessing future pandemic risks.

Conclusion

The Nipah virus is a highly contagious and deadly pathogen that requires immediate attention. Preventive measures, such as avoiding contaminated food and implementing infection control practices, are crucial for curbing the spread of NiV. A multidisciplinary "One Health" approach involving collaboration between healthcare professionals, veterinarians, and ecologists is necessary to address the risks posed by NiV. The development of diagnostics, immunotherapies, vaccines, and antiviral drugs is essential for combating NiV. Non-Governmental Organizations (NGOs) can play a vital role in supporting these efforts through community outreach and education, supporting vaccination initiatives, conducting research, and advocating for NiV awareness. They can also provide medical aid and resources to affected populations. The high mortality rate of the virus and its potential for human-to-human transmission makes it critical to conduct research to effectively intervene in the infection cycle. Therefore, intensive research and collaborative approaches are needed.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12985-025-02728-4.

Supplementary Material 1.

Code availability
Not applicable.

Clinical trial number
Not applicable.

Declarations
This work is original and has not been published elsewhere, nor is it currently under consideration for publication elsewhere.

Authors' contributions
Conceptualization – AG, SC; Investigation – SM, SR, SC, JI, SG; Resources – AG, TKD, SC, MC; Supervision – AG, SC; Validation – AG, SC; Writing (original draft) – SM, SR; Writing (review & editing) – AG, SC.

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Data availability
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Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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