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Review

NIPAH Virus - "A Bane to Mankind"

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Zoonotic diseases are rare but the transmission of disease to humans may cause serious illness. Nipah virus (NiV) is a bat-borne zoonotic pathogen, which can cause severe encephalitis and respiratory distress. The transmission of Nipah virus from bats to humans was first reported in Malaysia in 1998. Different strains of NiV show different epidemiological and clinical features. Few of the strains are highly lethal and can spread to the community resulting in a global threat. However, the availability of effective management or prophylactic measures are only limited. Thus, it is essential to contain such outbreaks by implementing proper infection control and surveillance measures. Many serological and molecular diagnostic techniques have been developed for diagnosis of this infection. This review mainly focuses on the epidemiology, transmission of Nipah virus, pathogenesis and management of NiV infection. The review also throws light on the immune response of NiV in humans and the role of One Health approach in prevention and control of NiV infection.

Keywords: **Nipah virus, zoonotic disease, pathogenesis, immune response**

Introduction

Zoonotic diseases, despite being rare, can have devastating effects on humans. In addition to causing serious illness in humans, emerging zoonotic diseases have the potential to disrupt social well-being, entail substantial economic costs, and harbour the potential to evolve into a pandemic as seen in H1N1 influenza, HIV/AIDS pandemic, and the more recent COVID-19 [1]. The Nipah virus (NiV), is a zoonotic disease, endemic in Southeast Asia and the Western Pacific, has been linked to outbreaks of severe encephalitis and respiratory distress [2]. Though the number of NiV infections throughout the various outbreaks remain small, the severity of the disease results in a higher death rate. Bats, particularly the *Pteropus* species, serve as the primary reservoir for NiV, with transmission to humans occurring directly or through intermediate hosts like pigs, horses, dogs, and cats [3]. Recognizing its severity, the World Health Organization has classified NiV as a global health concern, emphasizing the need for research and vaccine development [4]. The Centre for Disease Control and Prevention categorizes NiV as category C pathogen and a potential bio- and agroterrorism agent, further underlining its significance in global health security [5].

Epidemiology

NiV first appeared in Malaysia in 1998, and the virus was named after Sungai Nipah, a hamlet in the state of Negeri Sembilan in Malaysia, where it was initially identified from a human index patient [6]. The transmission of NiV in different hosts varies geographically, influenced by factors like animal husbandry practices and dietary habits. NiV is most prevalent in areas with a significant population of *Pteropus* bats. The Malaysian NiV outbreak in 1998 resulted from a 'spill-over' incident,

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originating from the fruit bats. Initially misidentified as Japanese encephalitis (JE), the NiV isolated from cerebrospinal fluid of a patient in March 1999 [7]. The outbreak led to 283 cases and 109 fatalities, with additional cases reported in Singapore among abattoir workers with 11 cases and one fatality [8]. Close contact with pigs and their excreta was identified as a risk factor, leading to the culling of millions of infected pigs. Dogs were also found to be infected, but there was no evidence of human-to-human transmission in these outbreaks. The *Pteropus* bats were subsequently identified as the primary reservoir for NiV in Malaysia [9].

NiV epidemiology in Bangladesh was primarily seasonal outbreaks (December to May) occurring in central and north-western Bangladesh, known as the 'Nipah belt' [7]. Since 2001, bats have been the primary host, with pigs acting as intermediate hosts for spread of NiV. The most common mode of transmission was through consumption of NiV contaminated raw date palm sap during the harvest season [10]. While pigs exhibit high seroprevalence of NiV, they have not been linked to outbreaks. Person-to-person transmission was a significant mode of transmission in Faridpur, Bangladesh [11].

The two NiV outbreaks in India, recorded in villages of West Bengal (Siliguri in 2001 and Nadia in 2007) [12] occurred due to their close geographical proximity to the 'Nipah belt' in Bangladesh and in the state of Kerala in May 2008 [13]. These outbreaks were confirmed to be from bats and amplified by person-to-person transmission. Philippines experience NiV outbreak in 2014, reporting 82% fatality. Those patients had a history of close contact with horses or consumed horsemeat. Person-to-person transmission, especially nosocomial was also identified [14].

Phylogenetic and evolutionary analyses can help understand the epidemiology of NiV, thereby helping in understanding the origins of the virus and in devising preventive measures. Use of these analytical tools unveiled molecular similarity between NiV and Hendravirus (HeV), led to the introduction of a novel genus, *Henipavirus*, exclusively encompassing NiV and HeV [15]. Tracing genetic lineage of NiV through the areas of major outbreaks revealed the presence of the two major viral strains, NiV-M belonging to the Malaysian clade and NiV-B for the Bangladesh clade. Additionally, the Indian isolate, NiV-I was found to be a subtype of NiV-B [16]. NiV-M was implicated in the initial outbreaks in Malaysia/Singapore [17], while NiV-B caused recurring outbreaks between 2001 and 2015, in Bangladesh and northeast India [18, 19]. Nucleotide heterogeneity particularly between NiV-B and NiV-M, is more pronounced than nucleotide homology in Malaysia than in Bangladesh. Pigs in Malaysia harbour the two prominent strains of NiV, while in Bangladesh, the introduction of NiV from fruit bats to humans may account for the sequence heterogeneity [20]. This suggests variations in virus transmission dynamics between the two countries.

Non-human Hosts of NiV

NiV relies on both wild and domesticated animals as source and host for transmission and propagation. NiV spreads to humans through two main routes: via intermediate hosts like pigs and horses, or through food borne transmission, such as date palm sap tainted with fruit bat urine or saliva [21] (Fig. 1). Human outbreaks are often linked to the presence of diverse animal species.

Fruit bats, particularly in the *Pteropus* genus (*P. vampyrus*, *P. hypomelanus*, *P. lylei*, *P. giganteus*), are natural hosts of NiV, acting as reservoirs in Southeast Asia and sub-Saharan Africa [22]. Though NiV is asymptomatic in bats, sero-surveillance in various outbreaks revealed positive NiV-specific antibodies in blood and urine of multiple bat species, including *P. hypomelanus* and *P. vampyrus* [23]. The outbreaks in Malaysia was due to the presence of *P. hypomelanus*, *P. lylei*, and *P. vampyrus* and in India, NiV was first found in *P. giganteu* and then the insectivorous bat, *Megadermaspasma* [24]. In India, NiV and NiV-specific IgG antibodies were detected in *P. medius* bats in 2019, suggesting bats as the likely source of human infection. This was supported by gene sequence similarities between NiV samples obtained from bats and infected humans of various regions [25].

Pigs act as intermediate or amplifier host for NiV as they consume fruit contaminated by saliva, blood and urine of infected bats [26]. Swine infected with NiV exhibit a pronounced non-productive cough termed as "barking cough" with airway inflammation and encephalitis, commonly referred to as barking pig syndrome [27]. Serological surveys revealed identical gene sequences between viral isolates from pig and humans. In Malaysia

and Singapore, NiV infection was most prevalent in pig farmers, with 40% fatality rates was seen in abattoir workers [28, 29]. However, pigs as viral vectors in Bangladesh or India have not yet been demonstrated [30]. The presence of NiV has been documented in sheep and goats, but infection in bovine species, although permissive to NiV, has not yet been reported. While dogs and cats do not seem to be amplifying host of NiV, dogs are susceptible to NiV infection [31]. In the Philippines, NiV infections resulted from slaughtering and consuming horse meat [32]. Very few of the patients were small children, and the majority of the cases included men who worked with pigs [33]. The patients typically reported fever, headaches, and diminished consciousness as symptoms. The number of cases and deaths during the epidemic in Malaysia varied from 238 to 265 depending on the source, indicating a relatively high mortality rate [33].

Transmission of NiV

Food borne transmission of NiV occurs when *Pteropus* bats feed on fruit bearing trees, contaminating fruits and causing viral spill over to pigs and other farm animals. Ingesting fruit contaminated with bat saliva or inhaling aerosols containing droplets of contaminated urine or saliva can initiate the infection chain (Fig. 1). Studies suggest raw date palm juice as a significant source of virus, with a strong correlation between ingestion of sap by fruit bat and NiV. In Bangladesh, the ingestion of contaminated raw date palm sap is a common mode of NiV transmission, particularly during the date palm sap collecting season, aligning with the years of NiV epidemics [34].

Animal to human transmission is most notable where a coexisting ecosystem of bats, pigs, and humans creates an ideal environment for NiV transmission. Domestic and farm animals can contract the virus by consuming palm sap or partially eaten fruit contaminated with NiV containing faeces, urine, or saliva. Handling pigs in slaughterhouses and consuming infected pork meat pose severe risks to humans. During the Malaysian outbreak, the rapid spread of NiV was linked to direct contact with excretions and secretions of sick pigs, including urine, saliva, pharyngeal, and respiratory secretions. Necropsy of pigs revealed severe pulmonary symptoms, supporting the theory of aerosolized NiV transmission from pigs to humans as a significant mechanism. NiV antigen has been found in pig renal tubules, and an outbreak among Singaporean abattoir workers suggested a link between exposure to infected pig urine and NiV transmission [35].

A transmission of NiV between and within humans poses a significant public health concerns. Multiple outbreaks have been linked to human-to-human transmission, particularly in regions (mostly Southeast Asia)

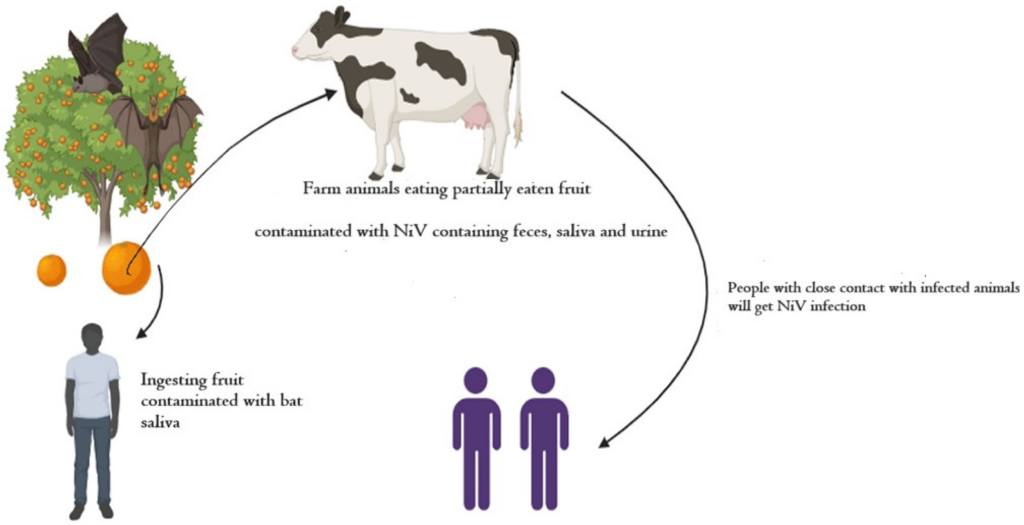

Fig. 1. Source and Transmission of NiV Infection. Bat transmit the virus indirectly through the contaminating the fruit with saliva. Through the infected farm animals NiV spread from bat to humans.

where close contact with infected individuals is a social norm. Respiratory secretions, notably saliva, plays a crucial role in person-to-person transmission of NiV [11]. Prolonged exposure to the secretions of infected individuals increases the risk of infection. Studies in Bangladesh and India indicate that caretakers of patients, healthcare professionals (nosocomial), and individuals in close contact with the afflicted contribute significantly to the spread of NiV [36]. More recently sexual transmission of NiV has been documented, with viral RNA detected in semen specimens even after clearance from blood and urine, suggesting a potential immunologically privileged niche in the testis [37].

Etiology and Replication Cycle of Nipah Virus (NiV)

NiV is a paramyxovirus belonging to the genus *Henipavirus*, family *Paramyxoviridae,* order *Mononegavirales* which includes both pathogenic and non-pathogenic viral species. NiV has an enveloped negative-sense, single-stranded RNA with 18.2 kb genome made of six genes arranged sequentially: nucleocapsid (N), phosphoprotein (P), matrix (M), fusion glycoprotein (F), attachment glycoprotein (G), and long polymerase (L) [37]. The genes, N, M, F and G encode for viral nucleocapsid (N) protein, viral matrix (M) protein, fusion protein and attachment glycoprotein, respectively (Fig. 2). The P gene produces the P protein and the other non-structural proteins V (49-aa) and W (43-aa) formed by frame shift of the G insertion site. V protein is formed by +1G and W protein by +2G shift of the reading frame.

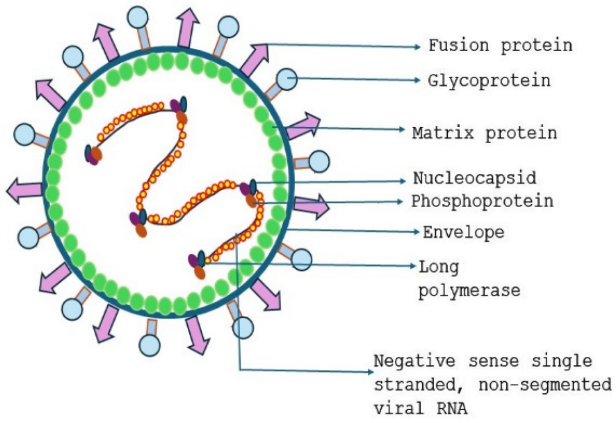

Fig. 2. Structure of Nipah Virus.

The rib nucleoprotein is formed by N, P, and L, while F and G proteins facilitate attachment and entry into the host cell. The N protein controls transcription and viral replication, and the M protein plays a significant role in assembling and releasing virions [15].

The replication cycle of NiV begins with the fusion of the virus to the host cell membrane. The attachment of the virus G protein is vastly, facilitating pH-independent entry into the host cell. Attachment and binding to the host cell begins when the globular head of the G protein interacts via the two types of receptors, Ephrin (EFN)-B2 or B3 [39]. Ephrins are Class B receptor tyrosine kinases, encoded by EFNB gene and is highly conserved across species [40]. EFNB2/B3 receptors are expressed on surface of endothelial cells of artery (not veins), epithelial cells of upper respiratory tract, alveolar pneumocytes, and in the central nervous system (CNS) [41]. The binding of G protein with the EFNB2 cell receptor induces allosteric changes in the protein, presenting the virus for entry through receptor-mediated mechanisms.

The binding of the G protein to the EFNB2/B3 receptor, activates F protein, which undergoes conformational changes, resulting in the fusion of the viral membrane with the host cell surface. F protein exists as an inactive precursor, F_0, on the plasma membrane. The F_0 are endocytosed and cleaved by the host cell protease, endosomal cathepsin L, to generate active pre-fusion proteins, F_1 and F_2, linked by a disulphide bond forming a heterodimer. After the internalization event, the F_1-F_2 heterodimers are transported back to the host cell surface, where they are either incorporated into newly budding virions or contribute to the formation of multinucleated syncytia between adjacent infected cells [42]. Upon entering the host cell, NiV genome undergoes transcription, translation, and replication processes. Initially, the viral RNA genome undergoes primary transcription at the 3' end, utilizing the viral RNA-dependent RNA polymerase to form messenger RNA (mRNA) [43]. The newly synthesized viral mRNA is capped and polyadenylated by the L protein for translation by the host cell machinery. The host cell then initiates viral replication, generating (+) sense antigenomes, which act as templates for the synthesis of (-) sense progeny genomes. Subsequently, viral components assemble on the plasma membrane to form new virions [44].

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Clinical Signs of NiV

The clinical signs of NiV in host animals are mostly similar to the clinical presentations of NiV in humans. In *Pteropus* bats, NiV infection is typically asymptomatic, however studies have detected the virus in biological sources like saliva, blood, and urine of bats [68]. In pigs, the severity of NiV infection varies with age. Suckling piglets can experience around 40% mortality with noticeable dyspnoea, while young pigs exhibit fevers, laboured breathing, and dry cough and adult pigs may show less severe respiratory and neurological symptoms [69].

Clinical manifestations of NiV infection in humans typically include fever along with encephalitis and/or respiratory complications [70]. The incubation period spans from 4 days to 2 months, with the majority of individuals (>90%) experiencing symptoms within 2 weeks of NiV exposure. Common signs comprise fever, headache, dizziness, and vomiting, progressing to severe encephalitis [71]. Neurological symptoms involve meningitis, diffuse encephalitis, and focal engagement of the medulla oblongata. A distinctive feature of NiV infection is the occurrence of relapses and delayed onset of encephalitis in survivors, extending months or even years beyond the initial infection [72]. Survivors may face neuropsychiatric sequelae, including depression, personality alterations, attention deficits, and verbal or visual memory deficits [73]. Geographical variations in NiV outbreaks result in significant differences in clinical features, with respiratory symptoms being more pronounced in outbreaks in Bangladesh and India, while Malaysian and Singaporean patients show a lower prevalence of respiratory symptoms [71, 72].

Pathogenesis of NiV

NiV, with its broad species tropism, can infect various cell types. NiV infections encompass diverse tissue and organ systems, like respiratory infection, endothelial infection leading to vasculitis, and terminal effects on the CNS. Symptoms of NiV begins with the entry of the virus by oronasal route followed by homing itself in the bronchiole epithelial cells, occasionally in the alveoli, and later in other respiratory tissues [45]. Individuals with respiratory symptoms have a higher likelihood of transmitting NiV, particularly in the NiV-B genotype, which facilitates human-to-human transmission. Histopathological examination of NiV-infected lungs reveals changes like necrotizing alveolitis, pulmonary edema, aspiration pneumonia, and the presence of multinucleated cells in alveolar regions [46].

The spread of virus from the respiratory epithelium to the endothelial cells of various organs, which serve as secondary sites for replication after initial viremia. The distribution of EFNB2/B3 in arterial endothelium provides a favourable conditions for broad dissemination of NiV through the bloodstream, leading to systemic vasculitis and to the brain, spleen, and kidneys [47]. Autopsy findings reveal extensive involvement of blood vessels in the CNS, lungs, heart, and kidneys, causing systemic vasculitis, necrosis, and extensive thrombosis. The CNS arteries exhibit syncytial or multinucleated large endothelial cells, and the damage to microvascular endothelial cells manifests as multifocal encephalitis [46].

In later stages, NiV induces encephalitis in infected individuals, with entry into the CNS occurring through two main processes: the haematogenous route (via the choroid plexus) and/or the anterograde route through olfactory nerves [46]. Additionally, reports suggest NiV may enter the CNS through circulating immune cells, particularly dendritic cells expressing CD169 marker [47]. The infection disrupts the blood-brain barrier, leading to the release of proinflammatory cytokines, IL-1β and TNF-α, causing neurological symptoms. CNS infection manifests as vasculitis, thrombosis, parenchymal necrosis, and viral inclusion bodies [48]. Both grey and white matter display vascular involvement, inflammation, and focal lesions, especially in the sub cortical and deep white matter of cerebral hemispheres [49]. Recent studies on pigs and hamsters indicate that NiV can enter the CNS via the olfactory nerve, infecting the olfactory epithelium and spreading to various regions [52].

Immune Response to NiV

Pteropus bats, as the primary host for NiV, exhibit resistance to viral pathogenesis attributed to their innate and adaptive immunity. The elevated body temperatures and high-energy metabolism in bats mimic fever, providing innate resistance to NiV [53]. Viral

pathology is absent in bats, allowing efficient viral replication and shedding. In *Pteropus* spp., the activation of the interferon (IFN) pathways against viral challenge varies largely. From the animal model for bat, *P. alecto,* used for studies on host-virus, it has been reported that bats have diverse IgH [54], an assemblage of Toll-like receptors (TLRs) [55], a smaller genomic locus for type I IFN and a stronger type III IFN response [56]. The adaptive humoral immunity in bats poses an enigmatic challenge, and investigations have revealed immune cells like B and T lymphocytes, and dendritic cells, macrophages, neutrophils, eosinophils, and basophils [57]. Despite the production of virus-neutralizing antibodies, live virus can still be detected in bat urine and saliva. The current knowledge about the immune response to NiV in bats is limited, relying on cell culture experiments and serum antibody detection.

Immune responses in humans are more advanced and employ both humoral and cell-mediated immunity. The immune response to NiV infection was effectively described in survivors from the 2018 NiV outbreak in India. Serum analysis revealed the prompt generation of NiV-specific IgG and IgM antibodies within a week of exposure, leading to the clearance of NiV from the blood. Elevated B lymphocyte counts correlated with the production of NiV-specific antibodies [37]. Similar humoral immune responses were observed in experimentally infected swine [58] and African green monkeys [59], where the animals developed neutralizing antibodies (IgM/IgG) and B cell activation.

Literature on cell-mediated immune responses to NiV in humans is limited, primarily due to constraints such as small sample sizes, insufficient coverage of disease progression, and a lack of samples from fatal cases. However, a study on survivors of the 2018 Kerala outbreak documented the T-cell response to NiV, highlighting the activation of $CD8^+$ T lymphocytes, which played a role in the clearance of NiV from the serum. Consequently there was an elevation of $Ki67^+$, a subset of CD8+ T cells, causing increase in granzyme B, and PD-1 [37]. Experimental research on swine and African green monkey models provided insights into cell-mediated immune responses, including the upregulation of CD25 on memory cells and T_h cells in swine [58], and an increase in $CD8^+$ T-cell numbers in African green monkeys [60]. These findings suggest that cell-mediated immune responses, particularly involving $CD8^+$ T cells, play a crucial role in combating NiV infection.

Cytokines play a crucial role in the immune response against NiV, contributing significantly to antiviral activity. During NiV infection, various inflammatory cytokines are triggered at different stages and sites in the host, potentially exacerbating clinical symptoms and increasing vascular permeability, which facilitates viral dissemination [60]. The NiV RNA activates cytoplasmic RNA helicases, preventing downstream signalling and activation of the IFNβ promoter in the IFN-I system [61]. NiV-infected endothelial cells produce IFNβ, along with chemokines (such as CXCL10 or IP-10), interleukin-6 (IL-6), ISG56, and OAS1 [62]. CXCL10 attracts activated T lymphocytes, and IL-6 functions as an inflammatory molecule stimulating acute-phase proteins. The expression of CXCL10 mRNA closely correlates with NiV replication, detected in the brain of NiV-infected golden hamsters and brain epithelial cells during the Malaysia NiV outbreak, suggesting its role in NiV-associated encephalitis .Lethal NiV Infection Induces Rapid Overexpression of CXCL10 [63].

NiV causes the release of inflammatory cytokines, such as IL-1α, IL-6, IL-8, granulocyte colony-stimulating factor, granulocyte-macrophage colony-stimulating factor, and monocyte chemoattractant protein-1 (MCP-1), from the infected respiratory epithelium, contributing to Acute respiratory distress syndrome [50]. The secreted cytokines perform functions like; IL-6 plays a role in dendritic cell maturation [64], IL-8 facilitates granulocyte chemotaxis [64], and MCP-1 helps regulate the blood-brain barrier [66]. These cytokines, along with CXCL10, stimulates the production of monocytes and T cell migration to the infection site [67]. The appearance of TNF-α and IL-1β in the brain coincides with the initial signs of NiV infection, and their pro-inflammatory effects compromise the blood-brain barrier integrity, contributing to neurological impairments observed in NiV-infected patients [68].

Diagnosis of NiV

Different methods have been employed for the diagnosis of NiV infection. Early-stage diagnosis is feasible through RT-PCR tests on various samples, including throat, nasal passage, urine, cerebrospinal fluid, and blood. RT-

PCR for NiV was first used in 2004, and specifically targeted in amplifying the N gene sequence [75]. Enzyme-linked immunosorbent assay (ELISA) is a simple technique to identify NiV, and involves detection antibodies IgG/IgM [76], and a variant technique of sandwich ELISA using rabbit polyclonal antibodies against the NiV G protein [77]. The WHO recommends PCR as the most sensitive diagnostic method, with NiV-specific IgM ELISA as an alternative serological approach. However, ELISA, while reliable, exhibits lower sensitivity and specificity compared to molecular detection. Additional diagnostic methods compriseof nucleic acid amplification, sequencing, immunofluorescence assay, histopathology, virus isolation, viral neutralization test, and high-throughput techniques for whole-genome sequencing [78, 79].

Treatment of NiV

The primary approach to treating NiV infection involves providing supportive care, which includes ensuring rest, hydration, and addressing the symptoms of acute encephalitis syndrome. The fundamental treatment strategy involves maintaining an open airway, preventing venous thrombosis, and restoring balance in fluid and electrolytes [80]. Several substances have been tested in the pursuit of a drug that can hinder the proliferation of NiV. Though ribavirin, which is effective against respiratory syncytial virus, was administered to 140 patients during the Malaysian outbreak of 1998, the efficacy of ribavirin is a matter of debate. Chong *et al.,* reported 40% decrease in mortality [81], whereas Goh *et al.*, found no changes [72]. During the 2018 NiV outbreak in Kerala, ribavirin was administered to six patients orally, and only two of them survived [82]. The antiviral drug acyclovir was administered in Singapore, but it did not result in positive outcomes for the patients [8]. Additionally, the antimalarial drug chloroquine exhibited effectiveness in inhibiting NiV in cell cultures, although this outcome could not be validated in animal models [83]. Favourable results were observed with the administration of the drug Favipiravir (T-705) and the monoclonal antibodies m102.4 in animal trials [84, 85]. The monoclonal antibody m102.4, which targets EFNB2 and B3 has shown to be effective in new ferret model of acute NiV infection [86]. Researchers are assessing the *in vitro* antiviral activity of GRFT (Griffithsin) and its synthetic trimeric tandemer (3mG) against NiV and other viruses. An initial *in vivo* evaluation of oxidation-resistant GRFT exhibited significant protection against a lethal NiV challenge in golden Syrian hamsters [87].

Prevention of NiV

The morbidity and mortality faced by healthcare workers (HCWs) in the care of patients with NiV necessitate clear guidelines based on existing evidence and available resources [11]. Drawing from the successful containment of Ebola and SARS, the importance of standard precautions, hand hygiene, and personal protective equipment (PPE) are essential components of a comprehensive infection prevention and control strategy [88]. All hospitals are required to adhere to standard infection control precautions, with additional measures such as droplet precautions that relies on isolation (one-patient isolation rooms or cohorting), contact and airborne precautions in the event of NiV infection. Additionally, proper patient isolation, infection control precautions, and triage procedures are crucial, and hospitals in at-risk areas need to be well-prepared for Nipah cases. The importance of regional action plans, policies, and strategies for NiV prevention and control in South and South East Asia is also emphasized [35]. Implementation of endorsed action plans and public health awareness through various media, including social platforms, television, radio, and printed materials as part of public health announcement is crucial [80]. Specific preventive measures for farm workers and villagers are highlighted, including avoiding direct contact with animals and refraining from consuming potentially contaminated date palm products [68]. More emphasis on hand hygiene like washing hands with soap/water and/or using alcohol-based hand sanitizer is important. The utilization of appropriate PPE during patient examinations is recommended to prevent infections among HCWs, with a focus on proper PPE removal procedures to mitigate risks associated with NiV exposure [89].

Future Prospects in NiV

NiV is recognized as an emerging pathogen, causing zoonotic outbreaks with high mortality rates. Following

the initial documented NiV outbreak in humans, the virus has persisted in causing repeated outbreaks in many Southeast Asian countries, emphasizing the ongoing risk to human and animal health. Bats, the natural reservoirs, are implicated in viral transmission to humans and animals, posing a global threat due to the widespread distribution of bats. Addressing this challenge necessitates a comprehensive approach involving preventive and therapeutic measures. Recent efforts have been directed toward studying host-reservoir immunology, although a definitive understanding of the host-pathogen interaction in the natural host is still lacking. Essential tools, including host-specific cell lines and high-throughput sequencing, are required to advance our comprehension of these interactions. On the opposite side of the transmission cycle, comprehending the protective factors in dead-end hosts, such as humans, is critical for devising effective preventive and therapeutic approaches against NiV infection. Positive outcomes from vaccine and antibody treatment experiments in animal models underscore the significance of neutralizing antibodies for protection. Investigating the exact mechanisms of protection in these studies may yield valuable insights into the disease process. Identifying aspects of the immune response that are deficient or counterproductive in human NiV infection could open avenues for targeted interventions to modulate the immune response, potentially enhancing survival rates.

One Health Approach in Controlling Nipah Virus

One health approach is a way in changing the environmental factors in controlling the infectious disease which affects not only the humans but also the non-humans. Many international agencies like Food and Agricultural Organisation, World Organisation for Animal Health and World Health Organisation has well acknowledged that a key component of disease control and prevention efforts is the One Health concept [90]. The transmission of NiV occurs more than one species, one health approach is utmost important with the involvement of scientist from various sectors to see the best result [91].

Current Research in NiV Virus

The virus was just added to the WHO's list of emerging pathogens of priority. Currently there is no vaccination or approved treatment exists for NiV. Many scientific laboratories are focusing on the potential vaccinations being researched and developed (Table 1). Most of them focus on the G and F proteins found on the virus's surface, which are essential for it to penetrate human cells and proliferate throughout the body. The researchers at the Vaccine Research Institute of the ANRS MIE/ Inserm (VRI) concentrated on the critical function that antigen-presenting cells (APCs) play in the establishment of protective responses in order to design their new vaccine. Specific portions of the surface proteins of the Bangladesh strain of the NiV-B virus are carried by the potential vaccine, known as CD40.NiV [92]. United Kingdom started the first vaccination trial against Nipah Virus. Vaccine named ChAdOx1 Nipah B was developed by the Scientist in the Oxford University [93].

Conclusion

In conclusion, NiV stands as an emerging zoonotic pathogen with significant implications for global health. Despite its relatively low frequency of outbreaks, the

Table 1. Vaccines to combat NiV in clinical trials.

S. No	Vaccine	Platform	Clinical trials
1	ChAdOx1-developed by University of Oxford	Viral vector based vaccine	Phase I [93]
2	Auro Vaccines + PATH	Protein based vaccine	Phase I [93]
3	PHV	Viral vector based vaccine	Phase I [94]
4	mRNA-1215 developed by Moderna	mRNA based vaccine	Phase I [95]
5	CD40.NiV	Protein based vaccine	Pre clinical trials [92]
6	HeV-sG-V	Glycoprotein vaccine	Phase I [96]
7	M102.4	Monoclonal antibody	Phase I [96]

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severity of NiV infections, including high mortality rates and potential for person-to-person transmission, underscores the need for comprehensive research, preventive measures, and therapeutic interventions. The virus, primarily transmitted by the natural reservoirs, *Pteropus* bats, has been responsible for outbreaks in Southeast Asia. Bats and pigs play pivotal roles as hosts and intermediaries, respectively, while the consumption of contaminated food, such as date palm sap, poses a significant risk to humans. The geographical variability in NiV strains and transmission dynamics between countries, particularly Malaysia and Bangladesh, emphasizes the complexity of the disease.Understanding the epidemiology, sources, and transmission pathways of NiV is crucial for effective prevention and control strategies. The life cycle, pathogenesis, and immune responses of NiV in both natural hosts (bats) and humans have been areas of active research. While bats demonstrate innate resistance to NiV, the human immune response involves humoral and cell-mediated components. Cytokines, such as IL-6 and TNF-α, contribute to the immune response but can also exacerbate clinical symptoms. Looking ahead, the continued collaboration between researchers, healthcare professionals, and international organizations is imperative to unravel the complexities of NiV and develop effective strategies for prevention, diagnosis, and treatment. The One Health approach, considering the interconnectedness of human, animal, and environmental health, will be vital in mitigating the ongoing and future threats posed by NiV.

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Author Contributions

Dr.Jaiganeshan involved in the data collection, manuscript preparation and analysis of data. Dr.Lakshmi.K involved in the designing, supervising of the work and editing the final manuscript. All authors have made a substantial, direct, and intellectual contribution to the manuscript and approved it for publication.

Conflict of Interest

The authors have no financial conflicts of interest to declare.

References

1. Carroll D, Daszak P, Wolfe ND, Gao GF, Morel CM, Morzaria S. 2018. The global virome project. *Science* **359**: 872-874.
2. Devnath P, Wajed S, Chandra Das R, Kar S, Islam I, Masud HMA Al. 2022. The pathogenesis of Nipah virus: A review. *Microb. Pathog.* **170**: 105693.
3. Mackenzie JS, Chua KB, Daniels PW, Eaton BT, Field HE, Hall RA. 2001. Emerging viral diseases of Southeast Asia and the Western pacific. *Emerg. Infect. Dis.* **7**: 497-504.
4. https://www.who.int/teams/blueprint/nipah-henipaviruses.
5. Lam S-K. 2003. Nipah virus - a potential agent of bioterrorism? *Antiviral Res.* **57**: 113-119.
6. Singh RK, Dhama K, Chakraborty S, Tiwari R, Natesan S, Khandia R. 2019. Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies - a comprehensive review. *Vet. Q* **39**: 26-55.
7. Luby SP, Gurley ES. 2012. Epidemiology of henipavirus disease in humans. *Curr. Top. Microbiol. Immunol.* **359**: 25-40.
8. Paton NI, Leo YS, Zaki SR, Auchus AP, Lee KE, Ling AE. 1999. Outbreak of Nipah-virus infection among abattoir workers in Singapore. *Lancet* **354**: 1253-1256.
9. Rahman SA, Hassan SS, Olival KJ, Mohamed M, Chang L-Y, Hassan L. 2010. Characterization of Nipah virus from naturally infected *Pteropus vampyrus* bats, Malaysia. *Emerg. Infect. Dis.* **16**: 1990-1993.
10. Luby SP, Rahman M, Hossain MJ, Blum LS, Husain MM, Gurley E. 2006. Foodborne transmission of Nipah virus, Bangladesh. *Emerg. Infect. Dis.* **12**: 1888-1894.
11. Gurley ES, Montgomery JM, Hossain MJ, Bell M, Azad AK, Islam MR. 2007. Person-to-person transmission of Nipah virus in a Bangladeshi community. *Emerg. Infect. Dis.* **13**: 1031-1037.
12. Kulkarni DD, Tosh C, Venkatesh G, Senthil Kumar D. 2013. Nipah virus infection: current scenario. *Indian J. Virol.* **24**: 398-408.
13. Ajith Kumar AK, Anoop Kumar AS. 2018. Deadly Nipah outbreak in Kerala: Lessons learned for the future. *Indian J. Crit. Care Med.* **22**: 475-476.
14. Chatterjee P. 2018. Nipah virus outbreak in India. *Lancet* **391**: 2200.
15. Harcourt BH, Tamin A, Ksiazek TG, Rollin PE, Anderson LJ, Bellini WJ, *et al.* 2000. Molecular characterization of Nipah virus, a newly emergent paramyxovirus. *Virology* **271**: 334-349.
16. Liew YJM, Ibrahim PAS, Ong HM, Chong CN, Tan CT, Schee JP, *et al.* 2022. The immunobiology of Nipah virus. *Microorganisms* **10**: 1162.
17. Chua KB, Goh KJ, Wong KT, Kamarulzaman A, Tan PS, Ksiazek TG, *et al.* 1999. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. *Lancet* **354**: 1257-1259.
18. Arankalle VA, Bandyopadhyay BT, Ramdasi AY, Jadi R, Patil DR, Rahman M. 2011. Genomic characterization of Nipah virus, West Bengal, India. *Emerg. Infect. Dis.* **17**: 907-909.
19. Lo MK, Lowe L, Hummel KB, Sazzad HMS, Gurley ES, Hossain MJ, *et al.* 2012. Characterization of Nipah virus from outbreaks in

Bangladesh, 2008-2010. *Emerg. Infect. Dis.* **18**: 248-255.
20. Halpin K, Hyatt AD, Plowright RK, Epstein JH, Daszak P, Field HE. 2007. Emerging viruses: coming in on a wrinkled wing and a prayer. *Clin. Infect. Dis.* **44**: 711-717.
21. Chua KB. 2003. Nipah virus outbreak in Malaysia. *J. Clin. Virol*. **26**: 265-275.
22. Sharma V, Kaushik S, Kumar R, Yadav JP, Kaushik S. 2019. Emerging trends of Nipah virus: A review. *Rev. Med. Virol.* **29**: e2010.
23. Yadav PD, Raut CG, Shete AM, Mishra AC, Towner JS, Nichol ST, *et al.* 2012. Detection of Nipah virus RNA in fruit bat (Pteropus giganteus) from India. *Am. J. Trop. Med. Hyg.* **7**: 576-578.
24. Plowright RK, Becker DJ, Crowley DE, Washburne AD, Huang T, Nameer PO, *et al.* 2019. Prioritizing surveillance of Nipah virus in India. *PLoS Negl. Trop. Dis.* **13**: 1-17.
25. Sudeep AB, Yadav PD, Gokhale MD, Balasubramanian R, Gupta N, Shete A. 2021. Detection of Nipah virus in *Pteropus medius* in 2019 outbreak from Ernakulam district, Kerala, India. *BMC Infect. Dis.* **21**:162.
26. Thakur N, Bailey D. 2019. Advances in diagnostics, vaccines and therapeutics for Nipah virus. *Microbes Infect.* **21**: 278-286.
27. Middleton DJ, Westbury HA, Morrissy CJ, van der Heide BM, Russell GM, Braun MA, *et al*. 2002. Experimental Nipah virus infection in pigs and cats. *J. Comp. Pathol.* **126**: 124-136.
28. Parashar UD, Sunn LM, Ong F, Mounts AW, Arif MT, Ksiazek TG, *et al*. 2000. Case-control study of risk factors for human infection with a new zoonotic paramyxovirus, Nipah virus, during a 1998-1999 outbreak of severe encephalitis in Malaysia. *J. Infect. Dis.* **181**: 1755-1759.
29. AbuBakar S, Chang L-Y, Ali ARM, Sharifah SH, Yusoff K, Zamrod Z. 2004. Isolation and molecular identification of Nipah virus from pigs. *Emerg. Infect. Dis*. **10**: 2228-2230.
30. Mourya D, Yadav P, Rout M, Pattnaik B, Shete A, Patil D. 2019. Absence of Nipah virus antibodies in pigs in Mizoram State, North East India. *Indian J. Med. Res.* **149**: 677-679.
31. Nikolay B, Salje H, Hossain MJ, Khan AKMD, Sazzad HMS, Rahman M, *et al.* 2019. Transmission of Nipah virus - 14 years of investigations in Bangladesh. *N. Engl. J. Med.* **380**: 1804-1814.
32. Ching PKG, de los Reyes VC, Sucaldito MN, Tayag E, Columna-Vingno AB, Malbas FFJ, *et al.* 2015. Outbreak of henipavirus infection, Philippines, 2014. *Emerg. Infect. Dis.* **21**: 328-331.
33. Skowron K, Bauza-Kaszewska J, Grudlewska-Buda K, Wiktorczyk-Kapischke N, Zacharski M, Bernaciak Z, *et al.* 2022. Nipah virus-another threat from the world of zoonotic viruses. *Front. Microbiol.* **12**: 811157.
34. Aditi, Shariff M. 2019. Nipah virus infection: A review. *Epidemiol. Infect.* **147**: e95.
35. Bruno L, Nappo MA, Ferrari L, Di Lecce R, Guarnieri C, Cantoni AM, *et al.* 2023. Nipah virus disease: Epidemiological, clinical, diagnostic and legislative aspects of this unpredictable emerging zoonosis. *Animals* **13**: 159.
36. Chadha MS, Comer JA, Lowe L, Rota PA, Rollin PE, Bellini WJ, *et al.* 2006. Nipah virus-associated encephalitis outbreak, Siliguri, India. *Emerg. Infect. Dis*. **12**: 235-240.
37. Arunkumar G, Abdulmajeed J, Santhosha D, Aswathyraj S, Robin S, Jayaram A, *et al.* 2019. Persistence of Nipah virus RNA in semen of survivor. *Clin. Infect. Dis.* **69**: 377-378.
38. Sun B, Jia L, Liang B, Chen Q, Liu D. 2018. Phylogeography, transmission, and viral proteins of Nipah virus. *Virol. Sin*. **33**: 385-393.
39. Steffen DL, Xu K, Nikolov DB, Broder CC. 2012. Henipavirus mediated membrane fusion, virus entry and targeted therapeutics. *Viruses* **4**: 280-308.
40. Bonaparte MI, Dimitrov AS, Bossart KN, Crameri G, Mungall BA, Bishop KA, *et al.* 2005. Ephrin-B2 ligand is a functional receptor for Hendra virus and Nipah virus. *Proc. Natl. Acad. Sci. USA* **102**: 10652-10657.
41. Liebl DJ, Morris CJ, Henkemeyer M, Parada LF. 2003. mRNA expression of ephrins and Eph receptor tyrosine kinases in the neonatal and adult mouse central nervous system. *J. Neurosci. Res.* **71**: 7-22.
42. Aguilar HC, Aspericueta V, Robinson LR, Aanensen KE, Lee B. 2010. A quantitative and kinetic fusion protein-triggering assay can discern distinct steps in the nipah virus membrane fusion cascade. *J. Virol.* **84**: 8033-8041.
43. Lamb RA. 2007. Paramyxoviridae: the viruses and their replication. Bernard N fields, david N knipe PMH, fields Virol. Fifth Edit, Lippincott, Williams, and Wilkins; pp. 1449-1496.
44. Lyles DS. 2013. Assembly and budding of negative-strand RNA viruses. *Adv. Virus Res.* **85**: 57-90.
45. Clayton BA, Middleton D, Arkinstall R, Frazer L, Wang L-F, Marsh GA. 2016. The nature of exposure drives transmission of Nipah viruses from Malaysia and Bangladesh in ferrets. *PLoS Negl. Trop. Dis.* **10**: e0004775.
46. Wong KT, Shieh W-J, Kumar S, Norain K, Abdullah W, Guarner J, *et al.* 2002. Nipah virus infection: pathology and pathogenesis of an emerging paramyxoviral zoonosis. *Am. J. Pathol.* **161**: 2153-2167.
47. Geisbert TW, Daddario-DiCaprio KM, Hickey AC, Smith MA, Chan Y-P, *et al*. 2010. Development of an acute and highly pathogenic nonhuman primate model of Nipah virus infection. *PLoS One* **5**: e10690.
48. Weingartl H, Czub S, Copps J, Berhane Y, Middleton D, Marszal P, *et al*. 2005. Invasion of the central nervous system in a porcine host by nipah virus. *J. Virol.* **79**: 7528-7534.
49. Tiong V, Shu M-H, Wong WF, AbuBakar S, Chang L-Y. 2018. Nipah virus infection of immature dendritic cells increases its transendothelial migration across human brain microvascular endothelial cells. *Front. Microbiol*. **9**: 2747.
50. Rockx B, Brining D, Kramer J, Callison J, Ebihara H, Mansfield K, *et al*. 2011. Clinical outcome of henipavirus infection in hamsters is determined by the route and dose of infection. *J. Virol.* **85**: 7658-7671.
51. Liu J, Coffin KM, Johnston SC, Babka AM, Bell TM, Long SY, *et al.* 2019. Nipah virus persists in the brains of nonhuman primate survivors. *JCI Insight* **4**: e129629.
52. Munster VJ, Prescott JB, Bushmaker T, Long D, Rosenke R, Thomas T, *et al*. 2012. Rapid Nipah virus entry into the central

nervous system of hamsters via the olfactory route. *Sci. Rep.* **2**: 736.
53. Brook CE, Dobson AP. 2015. Bats as "special" reservoirs for emerging zoonotic pathogens. *Trends Microbiol*. **23**: 172-180.
54. Baker ML, Tachedjian M, Wang L-F. 2010. Immunoglobulin heavy chain diversity in Pteropid bats: evidence for a diverse and highly specific antigen binding repertoire. *Immunogenetics* **62**: 173-184.
55. Cowled C, Baker M, Tachedjian M, Zhou P, Bulach D, Wang L-F. 2011. Molecular characterisation of Toll-like receptors in the black flying fox *Pteropus alecto*. *Dev. Comp. Immunol.* **35**: 7-18.
56. Jones MEB, Amman BR, Sealy TK, Uebelhoer LS, Schuh AJ, Flietstra T, *et al.* 2019. Clinical, histopathologic, and immunohistochemical characterization of experimental marburg virus infection in a natural reservoir host, the Egyptian rousette bat (*Rousettus aegyptiacus*). *Viruses* **11**: 214.
57. Turmelle AS, Ellison JA, Mendonça MT, McCracken GF. 2010. Histological assessment of cellular immune response to the phytohemagglutinin skin test in Brazilian free-tailed bats (*Tadarida brasiliensis*). *J. Comp. Physiol. B, Biochem. Syst. Environ. Physiol.* **180**: 1155-1164.
58. Berhane Y, Weingartl HM, Lopez J, Neufeld J, Czub S, Embury-Hyatt C, *et al.* 2008. Bacterial infections in pigs experimentally infected with Nipah virus. *Transbound Emerg. Dis.* **55**: 165-174.
59. Lara A, Cong Y, Jahrling PB, Mednikov M, Postnikova E, Yu S, *et al.* 2019. Peripheral immune response in the African green monkey model following Nipah-Malaysia virus exposure by intermediate-size particle aerosol. *PLoS Negl. Trop. Dis.* **13**: e0007454.
60. Cong Y, Lentz MR, Lara A, Alexander I, Bartos C, Bohannon JK, *et al*. 2017. Loss in lung volume and changes in the immune response demonstrate disease progression in African green monkeys infected by small-particle aerosol and intratracheal exposure to Nipah virus. *PLoS Negl. Trop. Dis.* **11**: e0005532.
61. Habjan M, Andersson I, Klingström J, Schümann M, Martin A, Zimmermann P, *et al.* 2008. Processing of genome 5′ termini as a strategy of negative-strand RNA viruses to avoid RIG-I-dependent interferon induction. *PLoS One* **3**: e2032.
62. Lo MK, Miller D, Aljofan M, Mungall BA, Rollin PE, Bellini WJ, *et al*. 2010. Characterization of the antiviral and inflammatory responses against Nipah virus in endothelial cells and neurons. *Virology* **404**: 78-88.
63. Mathieu C, Guillaume V, Sabine A, Ong KC, Wong KT, Legras-Lachuer C. 2012. Lethal Nipah virus infection induces rapid overexpression of CXCL10. *PLoS One* **7**: e32157.
64. Gupta M, Lo MK, Spiropoulou CF. 2013. Activation and cell death in human dendritic cells infected with Nipah virus. *Virology* **441**: 49-56.
65. Prasad AN, Woolsey C, Geisbert JB, Agans KN, Borisevich V, Deer DJ, *et al.* 2020. Resistance of cynomolgus monkeys to Nipah and Hendra virus disease is associated with cell-mediated and humoral immunity. *J. Infect. Dis*. **221**: S436-447.
66. Stamatovic SM, Shakui P, Keep RF, Moore BB, Kunkel SL, Van Rooijen N. 2005. Monocyte chemoattractant protein-1 regulation of blood-brain barrier permeability. *J. Cereb Blood Flow Metab.* **25**: 593-606.
67. Escaffre O, Borisevich V, Vergara LA, Wen JW, Long D, Rockx B. 2016. Characterization of Nipah virus infection in a model of human airway epithelial cells cultured at an air-liquid interface. *J. Gen. Virol*. **97**: 1077-1086.
68. Ang BSP, Lim TCC, Wang L. 2018. Nipah virus infection. *J. Clin. Microbiol.* **56**. https://doi.org/10.1128/jcm.01875-17.
69. Wacharapluesadee S, Hemachudha T. 2007. Duplex nested RT-PCR for detection of Nipah virus RNA from urine specimens of bats. *J. Virol. Methods* **141**: 97-101.
70. Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2022 (OIE Terrestrial Manual 2022). World Organ Anim Heal. https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-manual-online-access/.
71. Clayton BA, Middleton D, Bergfeld J, Haining J, Arkinstall R, Wang L, *et al*. 2012. Transmission routes for nipah virus from Malaysia and Bangladesh. *Emerg. Infect. Dis.* **18**: 1983-1993.
72. Goh KJ, Tan CT, Chew NK, Tan PS, Kamarulzaman A, Sarji SA, *et al.* 2000. Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. *N. Engl. J. Med.* **342**: 1229-1235.
73. Abdullah S, Chang LY, Rahmat K, Goh KJ, Tan CT. 2012. Late-onset Nipah virus encephalitis 11 years after the initial outbreak: A case report. *Neurol. Asia* **17**: 71-74.
74. Ng B-Y, Lim CCT, Yeoh A, Lee WL. 2004. Neuropsychiatric sequelae of Nipah virus encephalitis. *J. Neuropsychiatry Clin. Neurosci*. **16**: 500-504.
75. Guillaume V, Lefeuvre A, Faure C, Marianneau P, Buckland R, Lam SK, *et al.* 2004. Specific detection of Nipah virus using real-time RT-PCR (TaqMan). *J. Virol. Methods* **120**: 229-237.
76. Mohd Nor MN, Gan CH, Ong BL. 2000. Nipah virus infection of pigs in peninsular Malaysia. *Rev. Sci. Tech*. **19**: 160-165.
77. Kaku Y, Noguchi A, Marsh GA, Barr JA, Okutani A, Hotta K, *et al*. 2012. Antigen capture ELISA system for henipaviruses using polyclonal antibodies obtained by DNA immunization. *Arch. Virol*. **157**: 1605-1609.
78. Mazzola LT, Kelly-Cirino C. 2019. Diagnostics for Nipah virus: a zoonotic pathogen endemic to Southeast Asia. *BMJ Glob Health* **4**: e001118.
79. Ma L, Chen Z, Guan W, Chen Q, Liu D. 2019. Rapid and specific detection of all known Nipah virus strains sequences with reverse transcription-loop-mediated isothermal amplification. *Front. Microbiol.* **10**: 418.
80. Ambat AS, Zubair SM, Prasad N, Pundir P, Rajwar E, Patil DS, *et al.* 2019. Nipah virus: A review on epidemiological characteristics and outbreaks to inform public health decision making. *J. Infect. Public Health* **12**: 634-639.
81. Chong HT, Kamarulzaman A, Tan CT, Goh KJ, Thayaparan T, Kunjapan SR, *et al.* 2001. Treatment of acute Nipah encephalitis with ribavirin. *Ann. Neurol.* **49**: 810-813.
82. Banerjee S, Niyas VKM, Soneja M, Shibeesh AP, Basheer M, Sadanandan R, *et al.* 2019. First experience of ribavirin postexposure prophylaxis for Nipah virus, tried during the 2018 outbreak in Kerala, India. *J. Infect*. **78**: 491-503.

83. Freiberg AN, Worthy MN, Lee B, Holbrook MR. 2010. Combined chloroquine and ribavirin treatment does not prevent death in a hamster model of Nipah and Hendra virus infection. *J. Gen. Virol.* **91**: 765-772.
84. Sayed A, Bottu A, Qaisar M, Mane MP, Acharya Y. 2019. Nipah virus: a narrative review of viral characteristics and epidemiological determinants. *Public Health* **173**: 97-104.
85. Devnath P, Masud HMAA. 20210 Nipah virus: a potential pandemic agent in the context of the current severe acute respiratory syndrome coronavirus 2 pandemic. *New Microb. New Infect.* **41**: 100873.
86. Bossart KN, Zhu Z, Middleton D, Klippel J, Crameri G, Bingham J, *et al.* 2009. A neutralizing human monoclonal antibody protects against lethal disease in a new ferret model of acute nipah virus infection. *PLoS Pathog*. **5**: e1000642.
87. Lo MK, Spengler JR, Krumpe LRH, Welch SR, Chattopadhyay A, Harmon JR, *et al.* 2020. Griffithsin inhibits Nipah virus entry and fusion and can protect syrian golden hamsters from lethal Nipah virus challenge. *J. Infect. Dis.* **221**: S480-492.
88. Siegel JD, Rhinehart E, Jackson M, Chiarello L. 2007 Guideline for isolation precautions: Preventing transmission of infectious agents in health care settings. *Am. J. Infect. Control* **35**: S65-164.
89. Weber DJ, Rutala WA, Schaffner W. 2010. Lessons learned: protection of healthcare workers from infectious disease risks. *Crit. Care Med.* **38**: S306-314.
90. Rabinowitz PM, Kock R, Kachani M, Kunkel R, Thomas J, Gilbert J, *et al.* 2013. Toward proof of concept of a one health approach to disease prediction and control. *Emerg. Infect. Dis.* **219**: e13026512.
91. Singhai M, Jain R, Jain S, Bala M, Singh S, Goyal R. 2021. Nipah virus disease: recent perspective and one health approach. *Annal. Glob. Health* **87**: 102.
92. Pastor Y, Reynard O, Iampietro M, Surenaud M, Picard F, El Jahrani N, *et al.* 2024. A vaccine targeting antigen-presenting cells through CD40 induces protective immunity against Nipah disease. *Cell Rep. Med.* **19**: 5.
93. First-in-human vaccine trial for deadly Nipah virus launched https://www.ox.ac.uk/news/2024-01-11-first-human-vaccine-trial-deadly-nipah-virus-launched. Published on 11.01.2024.
94. https://static.cepi.net/downloads/2024-04/CEPI%20active%20portfolio%20overview%20website_Last%20Updated%204%20Apr%202024.pdf. Accessed on August 7, 2024.
95. https://s29.q4cdn.com/435878511/files/doc_presentations/programdetail/other/Nipah-(11.04.21).pdf. Accessed on August 7, 2024.
96. Rodrigue V, Gravagna K, Yao J, Nafade V, Basta NE. 2024. Current progress towards prevention of Nipah and Hendra disease in humans: A scoping review of vaccine and monoclonal antibody candidates being evaluated in clinical trials. *Trop. Med. Int. Health* **29**: 354-3264.

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