

## Review Article

# THERAPEUTIC ADVANCEMENT IN TREATMENT AND PREVENTION OF NIPAH VIRAL INFECTION: A Review

---

### Abstract:

Nipah virus (NiV) infection poses a significant threat to public health, with outbreaks resulting in high mortality rates. This review highlights advancements in treatments, vaccination strategies, and preventive measures against NiV. Antiviral therapies such as Ribavirin, Favipiravir, Acyclovir, Remdesivir, and Balapiravir show varying degrees of efficacy in vitro and in vivo models. Monoclonal antibodies like m102.4, h5B3.1, and nAH1.3 exhibit potent neutralizing activity against NiV, although their efficacy in human subjects warrants further investigation. Chloroquine and fusion inhibitory peptides demonstrate promising antiviral properties in vitro but require validation in animal models. Vaccination approaches including recombinant measles virus, subunit vaccines, vector vaccines, and mRNA-1215 vaccine show encouraging results in preclinical and clinical trials. Prevention strategies encompass early outbreak detection through populational surveillance systems, exposure-based screening, and educational interventions to minimize human transmission risks, emphasizing the importance of avoiding raw date palm sap during outbreak seasons and employing physical barrier strategies to prevent bat-to-human transmission.

**Keywords:** *Nipah Virus (NiV), Antiviral Therapies, Monoclonal Antibodies, Vaccine Development, Preventive Measures*

### 1. Introduction:

Nipah Virus (NiV) is a high mortality zoonotic emergent, WHO priority pathogen, classified as Biosafety Level 4, due to its outbreak propensity in relation with the current lack of effective therapeutic or vaccinal agents approved for human use<sup>(1,2)</sup>. Nipah virus is a paramyxovirus belonging to the Henipavirus genus, the Paramyxovirinae subfamily, the Paramyxoviridae family, and the Mononegavirales order. NiV is a negative sense, single-stranded, enveloped RNA virus<sup>(3)</sup>. Viral Isolations of multiple origin demonstrate two viral strains, NiV-M (Malaysia) and NiV-B (Bangladesh), features of which explain the variation of lethality, infectivity, and pathogenesis observed in human cases during outbreaks<sup>(4,5)</sup>. All human cases reported during the Malaysia-Singapore outbreak belong to NiV-M variant and the outbreaks reported in Bangladesh and India belong to NiV-B

variant, which underlines the multiple viral emergences from the natural reservoir *Pteropus* species (Flying foxes in India and Bangladesh) to humans<sup>(6)</sup>.

### 1.1 Transmission:

During the Malaysia-Singapore outbreak, only pig-to-human transmission was documented, whereas interhuman transmission has been a common finding during the outbreaks located in Bangladesh and India. These differences might relate to respiratory involvement and the subsequent capacity of viral dissemination, viral strain properties or genotypes, patient basal health status, differences in health care attention, and other unknown variables<sup>(9)</sup>. NiV transmission from *Pteropus* spp. to humans requires an interaction interface which allows viral emergence from its natural reservoir. The most important one is fresh palm sap, as well as consumption of derived products, which accounts for the vast majority of outbreaks in Bangladesh<sup>(8)</sup>.

### 1.2 Incubation:

The median incubation period of the secondary cases who had a single exposure to Nipah case was nine days (range 6–11 days) but exposure to onset of illness varies from 6-16 days [18, 13, 22]. The median incubation period following single intake of raw date palm sap to onset of illness is 7 days (range: 2-12 days) in Bangladesh<sup>(11)</sup>.

### 1.3 Pathophysiology:

A pleomorphic extracellular bilayer defines the outer viral surface in which the attachment (G) and fusion (F) proteins are inserted. The inner surface is shaped by matrix proteins (M) constituting the viral capsid, which contains a single RNA strand attached to nucleocapsid viral proteins (N), phosphoproteins (P), and the large RNA polymerase enzyme (L). The virus reaches the respiratory tract following aerosol transmission and respiratory droplets. After situating in upper and lower respiratory epithelium, virus particles penetrate epithelial cells by a membrane fusion process. The tetrameric G attachment glycoprotein head region interacts with cellular surface Ephrin B2/B3 receptors; simultaneously, the C-terminal portion of G glycoprotein activates the trimeric F fusion glycoprotein. The F protein contains two hydrophobic domains which form a six-helical bundle able to penetrate the host cell membrane, thus initiating membrane fusion and posterior viral replication using host cell machinery. The expression of F and G viral glycoproteins in basolateral host cell membranes allows local dissemination by promoting membrane cellular fusion with adjacent epithelial cells and formation of characteristic cellular syncytia. Systemic dissemination takes place by viral budding and release which determines extension to mucosal-associated lymphoid tissue (MALT) and leucocyte attachment, leading the virus to reach the blood stream<sup>(7)</sup>.

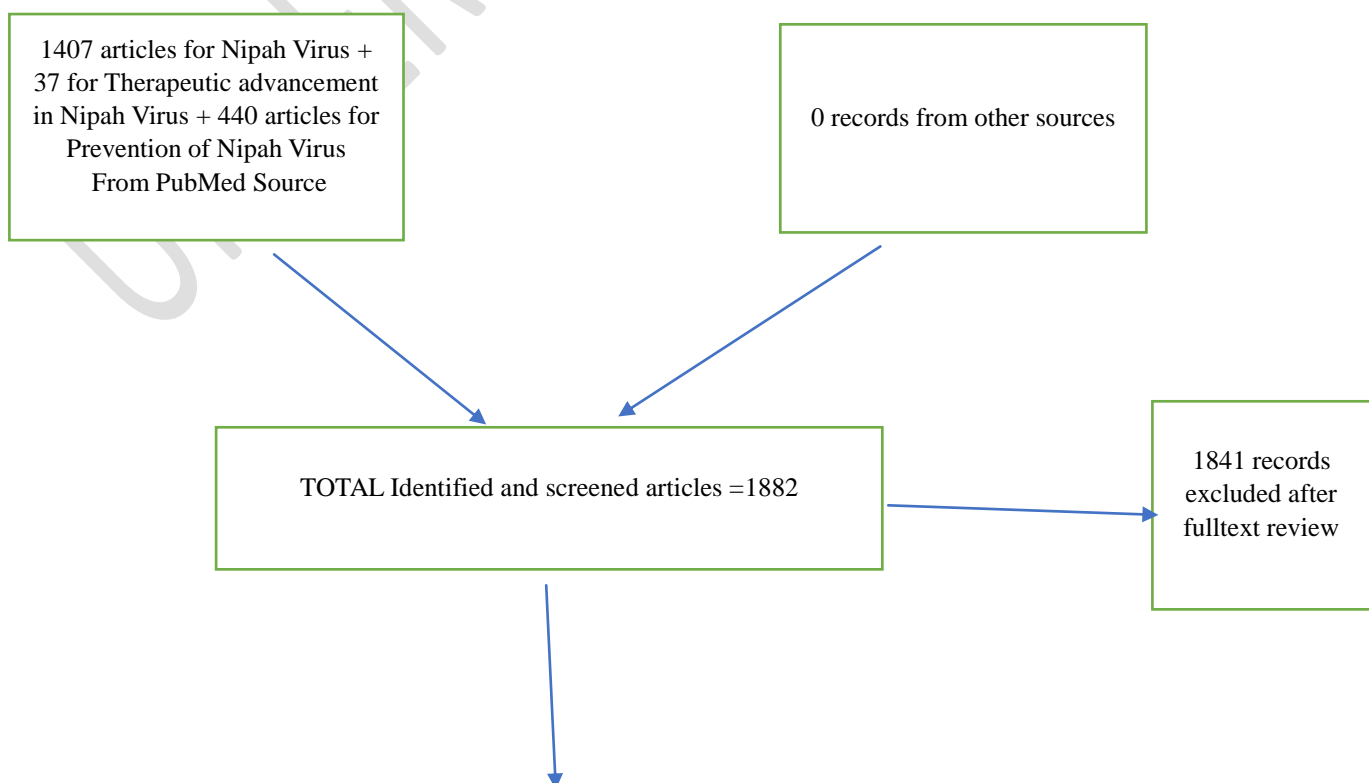
As NiV and the *Pteropus* spp. have most likely co-evolved for centuries, it is assumed that NiV has developed specific evasion mechanisms against *Pteropus* immune response. Therefore, the high interspecies immunity conservation observed in mammals may partially explain the wide infectious range of the virus. NiV blocks innate and adaptive immune responses by the inhibition of synthesis and release of cytokines, mainly IFN type 1  $\alpha/\beta$ , as well as CCL4, CCL5, and TNF- $\alpha$ . Among all P gene-derived products, the major inhibitory capacity remains on the W protein, which blocks IFN type 1  $\alpha/\beta$  gene expression from host cell nuclei.

### 1.4 Clinical Presentations:

The acute phase of Nipah virus infection manifests as a sudden-onset, rapidly progressive encephalitis, often accompanied by respiratory complications such as atypical pneumonia and disseminated vasculitis. Following an incubation period typically lasting 7–11 days, individuals may experience flu-like symptoms including moderate to high-grade fever, altered cognition, shortness of breath, and cough. Subsequent neurologic and respiratory deterioration ensues, leading to conditions such as encephalitis and acute respiratory distress syndrome (ARDS). This multisystemic failure culminates in eventual death, typically occurring within an average of six days from the onset of symptoms, primarily due to brainstem involvement. Estimates suggest a mortality rate of approximately 75%, with asymptomatic cases being rare. Furthermore, survivors of Nipah virus infection often face long-term neurological deficits, with around 22% experiencing residual neurological impairment. It's worth noting a notable discrepancy in the clinical presentation between the Malaysia-Singapore outbreak and subsequent outbreaks in Bangladesh and India. The former exhibited a notable absence of respiratory involvement, whereas respiratory conditions became a common feature in the latter outbreaks. This description outlines the grave clinical consequences of Nipah virus infection, highlighting the urgent need for effective preventive measures and therapeutics to combat this highly virulent pathogen<sup>(10,11)</sup>.

## 2. Methodology

This review Identified all the available articles in the electronic databasePubMed by using the search terms “Nipah Virus”, “ Therapeutic Advancement in Nipah Virus” , “ Prevention of Nipah Virus” which were available till March 2024 in a retrospective manner. A total of 1882 articles were identified i.e. 1407 articles for Nipah Virus, 37 for Therapeutic advancement in Nipah Virus and 440 articles for Prevention of Nipah Virus. Out of the identified 1882 articles, 1713 were excluded as they did not depict the study’s focus, 128 were overlapping results and only 36 articles were included for the study.The Cochrane Collaboration’s tool was applied to assess the risk of bias in each study based on the Cochrane Handbook.



41 Articles included in the review

Fig 1. Flow chart showing study protocol

UNDER PEER REVIEW

### 3. Results and Discussion:

Table 1 compares the various available treatment and Prevention strategies which have been published and followed as a measure to control the outspread of Nipah virus.

**Table 1. Summary of the treatment and Prevention modalities available for Nipah Virus**

Therapeutic Advancements	Description
<b>Anti-viral Therapy</b>	<ol style="list-style-type: none"> <li><b>Ribavirin:</b> Used during the NiV outbreak in 1998, showed a 36% reduction in mortality. Its efficacy in reducing mortality remains debatable.</li> <li><b>Favipiravir:</b> Demonstrated antiviral activity against NiV in in vivo models, showing a 100% survival rate.</li> <li><b>Acyclovir:</b> Used empirically during the March 1999 NiV outbreak in Singapore, with eight out of nine patients surviving, though its efficacy is uncertain.</li> <li><b>Remdesivir:</b> Showed a 67% survival rate in African green monkeys when administered early during Nipah virus infection.</li> <li><b>Balapiravir:</b> Pending in vivo experimentation but demonstrated efficacy in vitro against NiV.</li> </ol>
<b>Monoclonal Antibodies</b>	<ol style="list-style-type: none"> <li><b>m102.4:</b> A human monoclonal antibody with extensive neutralizing activity against NiV.</li> <li><b>h5B3.1:</b> A humanized monoclonal antibody considered a potential candidate for post-exposure treatment/prophylaxis.</li> <li><b>nAH1.3:</b> Another broadly neutralizing antibody with potential for combination therapy. Additional monoclonal antibodies are under development, showing high potential for HNV neutralization.</li> </ol>
<b>Chloroquine</b>	Despite being highly effective in vitro, chloroquine has shown ineffectiveness in in vivo NiV infection models.
<b>Fusion Inhibitory Peptides</b>	<ol style="list-style-type: none"> <li><b>Cholesterol-tagged fusion-inhibitory peptides:</b> Demonstrated effectiveness in blocking viral penetration in animal models.</li> <li><b>Inhaled fusion-inhibitory lipopeptides:</b> Showed relative mortality risk reduction in animal models.</li> </ol>
<b>Vaccination</b>	<ol style="list-style-type: none"> <li><b>Recombinant VSV-vectored vaccination:</b> Exhibited good efficacy in hamster models.</li> <li><b>Subunit vaccines:</b> Showed complete protection in animal models.</li> <li><b>Vector vaccines:</b> Showed adequate serological response and protection in animal models.</li> <li><b>mRNA-1215 vaccine:</b> Under evaluation in Phase 1 clinical trial, shows promise for human usage.</li> <li><b>Passive immunization:</b> Polyclonal serum remains a potential candidate for this aim.</li> </ol>
<b>Prevention</b>	<ol style="list-style-type: none"> <li><b>Early Outbreak Detection and Containment:</b> Utilization of populational surveillance systems and exposure-based screening.</li> <li><b>Human Transmission Prevention:</b> Warn against drinking raw date palm sap, implement educational interventions, and physical barrier strategies for bat-to-human transmission prevention.</li> </ol>

#### 3.1 Advancement in Treatments:

##### 3.1.1 Anti-viral therapy:

**Ribavirin:** The open-label trial led by Chong HT et al. documented a 36% decrease in mortality rates with Ribavirin administration, accompanied by no reported adverse effects. Ribavirin emerged as the primary pharmaceutical intervention during the 1998 NiV outbreak, leveraging its wide-ranging antiviral efficacy against both DNA and RNA viruses(12). However, findings from a NiV-infected hamster model revealed that Ribavirin merely delayed mortality, suggesting that the observed decline in human mortality during the same outbreak could be attributed to improved patient care and empirical treatments rather than Ribavirin's sole action.(15) A subsequent study of the 1998 outbreak, encompassing 94 patients with epidemiologically and clinically confirmed NiV infections, indicated Ribavirin utilization in 78% of cases but failed to associate its use with a substantial reduction in mortality rates(18).

**Favipiravir:** Favipiravir, acting as a ribonucleotide analog and specifically targeting the viral RNA polymerase enzyme, exhibits broad-spectrum antiviral effects against RNA viruses by hindering their replication and transcription processes(13). Research by Dawes BE et al. illustrated that administering the drug at a dosage of 300 mg/kg/day twice daily orally in in vivo simulation models using hamsters resulted in no observed morbidity and a 100% survival rate(14).

**Acyclovir:** In the March 1999 NiV outbreak in Singapore, nine abattoir workers diagnosed with encephalitis and subsequently testing positive for NiV IgM were treated empirically with ceftriaxone and acyclovir, which is another guanosine analogue. Of these individuals, eight survived, although it's uncertain whether acyclovir usage contributed to their survival (18). There is no published research on acyclovir's effectiveness against NiV either in vitro or through additional in vivo trials..

**Remdesivir:** In 2023, De Wit E et al. conducted a study indicating that African green monkeys treated with Remdesivir at a dosage of 10mg/kg three days after Nipah virus inoculation showed a 67% survival rate. The study suggests that administering Remdesivir early in Nipah virus infection is crucial for its effectiveness, similar to its current use in COVID-19 patients. It proposes that Remdesivir may be most beneficial for Nipah virus patients in the early stages of the disease. Additionally, to enhance treatment efficacy, considering a higher dose of Remdesivir could be warranted(16).

**Balapiravir:** The nucleoside analogue, R1479 (balapiravir), has shown promising in vitro effectiveness against NiV, and currently awaits in vivo testing. It demonstrated antiviral efficacy against both NiV and HeV, with EC50 values of 4 µM and 2.25 µM, respectively (17).

Table 2 compares the various pharmacokinetic profile of the antiviral therapy proposed for usage towards Nipah Virus infection.

**Table 2 Comparative pharmacokinetics of various antivirals used for treatment of Nipah virus**

Parameter	Acyclovir	Ribavirin	Balapiravir	Remdesivir
<b>Route of Administration</b>	Oral, IV, Topical	Oral, IV	Oral	IV
<b>Bioavailability</b>	~15% - 30% (Oral)	~45% (Oral)	Unknown	~100% (IV)
<b>Protein Binding</b>	9% - 33%	20% - 40%	Not Available	87% - 90%
<b>Metabolism</b>	Limited hepatic metabolism (acyclovir is primarily excreted unchanged in the urine)	Metabolized by multiple pathways, primarily by phosphorylation by host cell enzymes	Not Available	Intracellular metabolism by host cell enzymes
<b>Half-life</b>	2.5 - 3.3 hours (Adults)	~25 - 30 hours	Not Available	1 hour (Plasma), ~24 hours (Tissue)
<b>Excretion</b>	Urine (as unchanged drug)	Urine (as unchanged drug and metabolites)	Not Available	Urine (as parent compound and metabolites)
<b>Special Considerations</b>	Dose adjustment may be necessary in renal impairment.	Dose adjustment required in renal impairment and anemia may occur.	Not Available	Dose adjustment may be necessary in hepatic or renal impairment.

### 3.1.2 Monoclonal Antibodies:

**m102.4**: Through screening of G-soluble glycoprotein form antibody libraries, a potent human monoclonal antibody has been developed to target the G viral glycoprotein–Ephrin B2/B3 interaction surface. Affinity maturation ensued with light chain reconstruction and random mutation of heavy chain variable regions (22,27). From 2010 to 2017, this monoclonal antibody, referred to as m102.4, was compassionately administered to individuals at significant risk of Hendra virus (HeV) or Nipah virus (NiV) exposure in Australia, the USA, and India. Notably, these individuals displayed no signs of infection or adverse health effects post-administration of the monoclonal antibody. The use of m102.4 in humans, without clinical trials or regulatory approval such as FDA endorsement, underscores the urgent need for therapeutics and countermeasures against highly pathogenic henipaviruses, known for their high fatality rates ranging from 50% to 100% (28). In vitro, m102.4 exhibits extensive neutralizing activity against all tested strains of NiV and HeV. Additionally, its in vivo efficacy against lethal doses of NiV has been confirmed in African Green Monkey and ferret experimental models, even when administered therapeutically after clinical signs onset and virus detection. Notably, the monoclonal antibody retains adequate stability in vivo, with biological activity lasting up to eight days post-infusion in animal models. Despite its compassionate use in humans since 2010 for post-exposure treatment against NiV and HeV in the USA, India, and Australia, the true efficacy of m102.4 in human subjects remains uncertain (28).

**h5B3.1**: Developed is a humanized monoclonal antibody that specifically targets the prefusion conformation of the F viral glycoprotein. Engineered to impede virus attachment to host cell membranes and prevent viral penetration, it achieves this by binding to quaternary F glycoprotein epitopes. This antibody is under investigation as a promising option for post-exposure treatment and prophylaxis against viral infections. However, its effectiveness and safety profile await validation through in vivo studies (28).

**nAH1.3**: An extensively neutralizing antibody has been discovered, which interrupts the F fusion-triggering mechanism similar to m102.4, demonstrating comparable potency. These antibodies focus on unique antigenic sites that do not compete with each other. The combination of these antibodies could present a synergistic treatment strategy, potentially improving therapeutic effectiveness against Nipah virus infection (29).

Several additional monoclonal antibodies have been developed, targeting various epitopes, showing promising potential for neutralizing the highly pathogenic Nipah virus (HNV) by blocking its attachment to host cells. These antibodies include h1F5, h12B2, Nip GIP35, Nip GIP1.7, HENV26, HENV32, 4H3, 2D3, 1H8, 1F2, 1F3, 4B8, 1A9, 2B12, and 4F6. However, their safety and efficacy profiles require in vivo evaluation in the near future to determine their clinical usefulness and potential for future clinical application (30).

**Table 3. Various available Monoclonal Antibody therapy**

Monoclonal Antibody	Target	Mechanism
m102.4	G viral glycoprotein–Ephrin B2/B3 interaction	Blocks interaction between G glycoprotein and Ephrin B2/B3 receptors
h5B3.1	Prefusion conformation of F viral glycoprotein	Prevents virus-host cell membrane attachment and viral penetration
nAH1.3	F fusion-triggering mechanism	Interferes with the fusion-triggering mechanism of the F glycoprotein

### 3.1.3 Chloroquine:

In vitro studies demonstrated significant efficacy of the antimalarial drug chloroquine, both alone and when combined with ribavirin. However, when tested in in vivo NiV infection models involving hamsters, ferrets, and AGMs, chloroquine was found to be ineffective (19,20).

### 3.1.4 Fusion Inhibitory Peptides

***Cholesterol-tagged fusion-inhibitory peptides:*** Formulated to obstruct F glycoprotein conformational alterations crucial for viral pore-mediated penetration of host cells, this design incorporates a cholesterol tag for enhanced antiviral potency by guiding peptides to the target host cell membrane. In Golden Hamster experimental models, simultaneous administration with viral inoculation resulted in an 80% survival rate against lethal viral doses, indicating heightened penetration and significant drug concentration in the CNS, lung, and vascular endothelium. However, delaying infusion by 48 hours led to a notable decrease in survival rate to 40% (21).

***Inhaled fusion-inhibitory lipopeptides:*** One advantage of the inhaled administration route is its ability to deliver the drug directly to the respiratory system, effectively targeting the primary viral entry pathway. In vivo testing has been performed in Golden Hamster and African Green Monkey models, revealing a 33% reduction in relative mortality risk for the African Green Monkey model (22,23). Nanoparticle formulation stands as a promising potential therapy option for the future; however, as of now, no in vivo or in vitro experiments have been carried out (24).

## 3.2 Vaccination:

Table 4 highlights the advantages and drawbacks of the various vaccines available for Nipah virus.

Various viral vectors, including the vesicular stomatitis virus glycoprotein (VSV-G), canarypox virus, and rhabdovirus, have been investigated for experimental vaccine development. Notably, a recombinant measles virus (rMV) vaccine has shown promise for human use. In a hamster model, vaccination with recombinant VSV vectors was reported to demonstrate significant efficacy (25).

**Subunit vaccines:** Highly specific epitopes or viral peptides offer a cost-effective means for vaccine production. Bioinformatics tools predict that the primary epitopes capable of eliciting an adequate immune response include fractions of the F and G glycoproteins, making them prime candidates (31). Experimentation on African Green Monkey models has demonstrated complete protection and the generation of high IgG levels against NiV with a subunit vaccine derived from the oligomeric soluble form of G recombinant HeV glycoprotein (sGHeV). The observed heightened immunogenicity and remarkable efficacy support further assessment and potential authorization for human use in the future (32,33).

**Vector vaccines:** An attenuated virus capable of expressing recombinant G/F NiV glycoproteins has shown encouraging outcomes in in vivo trials involving pig and Golden Hamster animal models, eliciting sufficient serological responses with various viral vectors (including canarypox virus, vesicular stomatitis virus, and Venezuelan equine encephalitis virus). Additionally, virus-like particles produced from mammalian cells,

which express F, G, and M viral proteins, have displayed the capacity to provoke a robust neutralizing response and offer complete protection against lethal NiV doses in Golden Hamster models (33).

**mRNA-1215 vaccine:** NIAID and Moderna have collaborated to develop a candidate mRNA vaccine currently undergoing Phase 1 clinical assessment. This vaccine encodes the prefusion state of the F protein, which is covalently linked to the G protein monomer (pre-F/G) from the Malaysian strain of NiV (34).

**Table 4 Advancement in Vaccination for Nipah Virus**

Vaccine Type	Description	Development Stage	Advantages	Drawbacks
Recombinant Measles Virus (rMV) Vaccine	Utilizes a recombinant measles virus as a vector for Nipah antigens	Preclinical	Strong immunogenicity; potential for mass vaccination campaigns	Safety and efficacy in humans need to be established
Subunit Vaccines	Utilizes epitopes or viral peptides of Nipah antigens	Preclinical	Highly specific immune response; easy to produce; potentially low-cost	Requires identification of optimal antigens; efficacy in humans needs to be confirmed
Vector Vaccines	Attenuated virus expressing Nipah antigens	Preclinical	Induces serological response; potential for mass vaccination	Safety and efficacy in humans need to be established
mRNA-1215-Vaccine	Utilizes mRNA encoding Nipah antigens	Phase 1 Clinical Trials	Rapid development; potential for customized vaccines	Safety and efficacy in larger populations need to be confirmed
Passive Immunization	Administers polyclonal serum against Nipah antigens	Experimental	Immediate immunity; potential for post-exposure prophylaxis	Logistical challenges in administration and production

Passive immunization: a polyclonal serum against the G and F proteins remains as a potential candidate for this aim<sup>(33)</sup>.

### 3.3 Prevention

#### 3.3.1 early outbreak detection and containment.

**Populational surveillance systems:** Various strategies have been employed in India and Bangladesh, including Nipah belt-focused hospital surveillance coupled with intensified efforts during Nipah season, establishment of a 24-hour hotline for reporting adverse health events, and monitoring of mass media information (11,35). From 2007 to 2012, mass media monitoring was conducted through the National Media-Based Public Surveillance System, proving to be a highly effective, cost-efficient, and sustainable method for outbreak detection. This approach is particularly suitable for low-income countries with limited health infrastructure, such as Bangladesh, as it involves extensive monitoring of major media sources to promptly identify and investigate potential NiV outbreaks (11,36).

**Exposure-based screening:** In Bangladesh during 2012–2013, the utilization of concise hospital admission questionnaires demonstrated remarkable effectiveness and efficiency

in early detection of NiV-encephalitis cases and prevention of interhuman transmission. Specifically, inquiring about sap consumption and history of contact with febrile patients exhibiting altered cognition within the preceding 30 days since symptom onset proved to be a valuable screening tool for NiV, particularly during Nipah season (with a recorded negative predictive value of 99% during wintertime). Furthermore, the implementation of screening questionnaires enables a more optimal allocation of resources for NiV transmission prevention in hospital settings, where resources are often limited (36).

### 3.3.2 Human Transmission Prevention

The Bangladeshi government strongly warns against drinking raw date palm sap during outbreak seasons unless it has been protected by wearing bamboo skirts during collecting or by boiling it for 10 minutes<sup>(26)</sup>.

**Populational/community educational intervention:** Tailoring a multilevel information campaign to address specific risk factors within particular populations, such as discouraging fresh sap consumption in rural regions and mitigating direct contact transmission in hospital environments, enhances the efficacy of educational efforts in preventing infectious diseases (11). In 2009, extensive messaging was disseminated in rural areas of Bangladesh to discourage sap consumption. The "only safe sap" campaign emerged as the most impactful approach, notably improving disease comprehension and transmission awareness. This message adopts a harm reduction strategy, recognizing abstinence as the ideal outcome while promoting alternatives that minimize risk (38).

**Physical barrier strategies for bat-to-human transmission prevention:** During the date palm sap harvesting season, which aligns with the Nipah outbreak period in Bangladesh, the consumption of contaminated sap is the main route for the emergence of Nipah virus (NiV) (39). Local harvesters, known as "gachhis," collect and sell fresh sap early in the morning, and consumers often consume it on the same day. Unfortunately, in such situations, there is little decrease in the viable viral load in contaminated sap, highlighting the urgent necessity for interventions to prevent sap contamination from *Pteropus* spp., the reservoir of NiV(39).

Traditionally, gachhis have utilized several techniques to safeguard sap from degradation due to bat urine and excrements. These methods encompass employing tree branches to shield the sap circulation area, treating bark with lime, and installing bamboo skirts. Evidence from infrared cameras unequivocally demonstrates that only bamboo skirts, locally referred to as "banas," successfully prevent direct contact between bats and sap flow (40). Camera evidence supports the frequent visits of *Pteropus* spp. to date palm trees, leading to sap contamination through direct contact and feeding(40).

While additional testing is necessary to assess the scalability of the bana method, it remains a promising preventive measure. Preventing zoonotic transmission is recognized as the most efficient and cost-effective strategy for controlling human outbreaks. Moreover, it is a low-cost intervention that is simple to implement and embraced by gachhis, thus preserving the traditional practice of harvesting and consuming fresh sap (41).

#### **4. Conclusion:**

The advancements in treatments, vaccination, and preventive measures against NiV offer hope in combating this deadly virus. While antiviral therapies and monoclonal antibodies show promise, further clinical studies are needed to ascertain their efficacy and safety in humans. Vaccination strategies demonstrate potential for mass immunization campaigns, with ongoing clinical trials assessing their safety and effectiveness. Preventive measures focusing on early outbreak detection, community education, and physical barriers to bat-to-human transmission are crucial for mitigating NiV outbreaks. Continued research and collaboration are essential to develop comprehensive strategies for the prevention and control of NiV infection, ultimately safeguarding public health worldwide.

#### **Declarations:**

**Ethics approval and consent to participate: Not applicable**

**Data access statement: Not applicable**

**Consent for publication: Not applicable**

**Availability of data and materials:** The data and materials used in this text were obtained from previously published studies and reports. References are provided within the text.

#### **5. Reference:**

1. Angeletti S., Lo Presti A., Cella E., Ciccozzi M. Molecular epidemiology and phylogeny of Nipah virus infection: A mini review. *Asian Pac. J. Trop. Med.* 2016;9:630–634. doi: 10.1016/j.apjtm.2016.05.012
2. Aditi, Shariff M. Nipah virus infection: A review. *Epidemiol Infect.* 2019 Jan;147:e95.
3. Singh RK, Dhama K, Chakraborty S, Tiwari R, Natesan S, Khandia R, Munjal A, Vora KS, Latheef SK, Karthik K, Singh Malik Y, Singh R, Chaicumpa W, Mourya DT. Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies - a comprehensive review. *Vet Q.* 2019 Dec;39(1):26-55.
4. Nikolay B., Salje H., Hossain M.J., Khan A.K.M.D., Sazzad H.M.S., Rahman M., Daszak P., Ströher U., Pulliam J.R.C., Kilpatrick A.M., et al. Transmission of Nipah Virus—14 Years of Investigations in Bangladesh. *N. Engl. J. Med.* 2019;380:1804–1814. doi: 10.1056/NEJMoa1805376.
5. Hossain M.J., Gurley E.S., Montgomery J.M., Bell M., Carroll D.S., Hsu V.P., Formenty P., Croisier A., Bertherat E., Faiz M.A., et al. Clinical presentation of nipah virus infection in Bangladesh. *Clin. Infect. Dis.* 2008;46:977–984. doi: 10.1086/529147.

6. World Health Organization National Guideline for Management, Prevention and Control of Nipah Virus Infection including Encephalitis. 2011. [(accessed on 30 December 2023)]
7. Kerry R.G., Malik S., Redda Y.T., Sahoo S., Patra J.K., Majhi S. Nano-based approach to combat emerging viral (NIPAH virus)infection.Nanomedicine.2019;18:196–220.doi: 10.1016/j.nano.2019.03.004.
8. Gurley E.S., Hegde S.T., Hossain K., Sazzad H.M.S., Hossain M.J., Rahman M., Sharker M.A.Y., Salje H., Islam M.S., Epstein J.H., et al. Convergence of Humans, Bats, Trees, and Culture in Nipah Virus Transmission, Bangladesh. *Emerg. Infect. Dis.* 2017;23:1446–1453. doi: 10.3201/eid2309.161922.
9. Epstein J.H., Field H.E., Luby S., Pulliam J.R.C., Daszak P. Nipah Virus: Impact, Origins, and Causes of Emergence. *Curr. Infect. Dis. Rep.* 2006;8:59–65. doi: 10.1007/s11908-006-0036-2.
10. Hossain M.J., Gurley E.S., Montgomery J.M., Bell M., Carroll D.S., Hsu V.P., Formenty P., Croisier A., Bertherat E., Faiz M.A., et al. Clinical presentation of nipah virus infection in Bangladesh. *Clin. Infect. Dis.* 2008;46:977–984. doi: 10.1086/529147.
11. World Health Organization National Guideline for Management, Prevention and Control of Nipah Virus Infection including Encephalitis. 2011. [(accessed on 30 December 2023)]. Available online: [https://www.who.int/docs/default-source/searo/bangladesh/pdf-reports/year-2007-2012/national-guideline-for-management-prevention-and-control-of-nipah-virus-infection-including-encephalitis.pdf?sfvrsn=a5801092\\_2](https://www.who.int/docs/default-source/searo/bangladesh/pdf-reports/year-2007-2012/national-guideline-for-management-prevention-and-control-of-nipah-virus-infection-including-encephalitis.pdf?sfvrsn=a5801092_2)
12. Chong HT, Kamarulzaman A, Tan CT, Goh KJ, Thayaparan T, Kunjapan SR, Chew NK, Chua KB, Lam SK. Treatment of acute Nipah encephalitis with ribavirin. *Ann Neurol.* 2001 Jun;49(6):810-3. doi: 10.1002/ana.1062. PMID: 11409437.
13. Pérez-García, A. et al. A Randomized, Controlled Study on the Safety and Efficacy of Maraviroc and/or Favipiravir vs Currently Used Therapy in Severe COVID-19 Adults. “COMVIVIR” Trial. (2020).
14. Dawes B.E., Kalveram B., Ikegami T., Juelich T., Smith J.K., Zhang L., Park A., Lee B., Komeno T., Furuta Y., et al. Favipiravir (T-705) protects against Nipah virus infection in the hamster model. *Sci. Rep.* 2018;8:7604–7615. doi: 10.1038/s41598-018-25780-3.
15. Thakur N, Bailey D. Advances in diagnostics, vaccines and therapeutics for Nipah virus. *Microbes Infect.* 2019 Aug-Sep;21(7):278-286. doi: 10.1016/j.micinf.2019.02.002. Epub 2019 Feb 26. PMID: 30817995.
16. de Wit E, Williamson BN, Feldmann F, Goldin K, Lo MK, Okumura A, Lovaglio J, Bunyan E, Porter DP, Cihlar T, Saturday G, Spiropoulou CF, Feldmann H. Late remdesivir treatment initiation partially protects African green monkeys from lethal Nipah virus infection. *Antiviral Res.* 2023 Aug;216:105658. doi: 10.1016/j.antiviral.2023.105658. Epub 2023 Jun 23. PMID: 37356729; PMCID: PMC10529221.
17. Goh K.J., Tan C.T., Chew N.K., Tan P.S.K., Kamarulzaman A., Sarji S.A., Wong K.T., Abdullah B.J.J., Chua K.B., Lam S.K. Clinical Features of Nipah Virus Encephalitis among Pig Farmers in Malaysia. *N. Engl. J. Med.* 2000;342:1229–1235. doi: 10.1056/NEJM200004273421701.
18. Paton N.I., Leo Y.S., Zaki S.R., Auchus A.P., Lee K.E., Ling A.E., Chew S.K., Ang B., Rollin P.E., Umaphathi T., et al. Outbreak of Nipah-Virus Infection among Abattoir

- Workers in Singapore. *Lancet*. 1999;354:1253–1256. doi: 10.1016/S0140-6736(99)04379-2.
19. Pallister J, Middleton D, Cramer G, Yamada M, Klein R, Hancock TJ, et al. Chloroquine administration does not prevent Nipah virus infection and disease in ferrets. *J Virol* 2009;83:11979e82.
  20. Freiberg AN, Worthy MN, Lee B, Holbrook MR. Combined chloroquine and ribavirin treatment does not prevent death in a hamster model of Nipah and Hendra virus infection. *J Gen Virol* 2010;91:765e72.
  21. Porotto M., Rockx B., Yokoyama C.C., Talekar A., Devito I., Palermo L.M., Liu J., Cortese R., Lu M., Feldmann H., et al. Inhibition of Nipah virus infection in vivo: Targeting an early stage of paramyxovirus fusion activation during viral entry. *PLoS Pathog*. 2010;6:e1001168. doi:10.1371/journal.ppat.1001168.
  22. Lo M.K., Feldmann F., Gary J.M., Jordan R., Bannister R., Cronin J., Patel N.R., Klena J.D., Nichol S.T., Cihlar T., et al. Remdesivir (GS-5734) protects African green monkeys from Nipah virus challenge. *Sci. Transl. Med.* 2019;11:eaau9242. doi: 10.1126/scitranslmed.aau9242.
  23. Mathieu C., Porotto M., Figueira T.N., Horvat B., Moscona A. Fusion Inhibitory Lipopeptides Engineered for Prophylaxis of Nipah Virus in Primates. *J. Infect. Dis.* 2018;218:218–227. doi:10.1093/infdis/jiy152
  24. Kerry R.G., Malik S., Redda Y.T., Sahoo S., Patra J.K., Majhi S. Nano-based approach to combat emerging viral (NIPAH virus) infection. *Nanomedicine*. 2019;18:196–220. doi: 10.1016/j.nano.2019.03.004.
  25. Singh RK, Dhama K, Chakraborty S, et al. Nipah virus: epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies - a comprehensive review. *Vet Q*. 2019;39:26-55.
  26. Dhillon J, Banerjee A. Controlling Nipah virus encephalitis in Bangladesh: Policy options. *Pol J Public Health*. 2015;36:270-282
  27. Zhu Z., Bossart K.N., Bishop K.A., Cramer G., Dimitrov A.S., McEachern J.A., Feng Y., Middleton D., Wang L.F., Broder C.C., et al. Exceptionally potent cross-reactive neutralization of Nipah and Hendra viruses by a human monoclonal antibody. *J. Infect. Dis.* 2008;197:846–853. doi: 10.1086/528801.
  28. Dang HV, Chan YP, Park YJ, Snijder J, Da Silva SC, Vu B, Yan L, Feng YR, Rockx B, Geisbert TW, Mire CE, Broder CC, Veesler D. An antibody against the F glycoprotein inhibits Nipah and Hendra virus infections. *Nat Struct Mol Biol*. 2019 Oct;26(10):980-987. doi: 10.1038/s41594-019-0308-9. Epub 2019 Sep 30. PMID: 31570878; PMCID: PMC6858553.
  29. Wang Z., Amaya M., Addetia A., Dang H.V., Reggiano G., Yan L., Hickey A.C., DiMaio F., Broder C.C., Veesler D. Architecture and antigenicity of the Nipah virus attachment glycoprotein. *Science*. 2022;375:1373–1378. doi: 10.1126/science.abm5561.
  30. Mishra G., Prajapat V., Nayak D. Advancements in Nipah virus treatment: Analysis of current progress in vaccines, antivirals, and therapeutics. *Immunology*. 2023. *online ahead of print*
  31. Kamthania M., Sharma D.K. Screening and structure-based modeling of T-cell epitopes of Nipah virus proteome: An immunoinformatic approach for designing peptide-based vaccine. *3 Biotech*. 2015;5:877–882. doi: 10.1007/s13205-015-0303-8.
  32. Bossart K.N., Rockx B., Feldmann F., Brining D., Scott D., LaCasse R., Geisbert J.B., Feng Y.R., Chan Y.P., Hickey A.C., et al. A Hendra virus G glycoprotein subunit vaccine protects African green monkeys from Nipah virus challenge. *Sci. Transl. Med.* 2012;4:146ra107. doi: 10.1126/scitranslmed.3004241

33. Thakur N., Bailey D. Advances in diagnostics, vaccines and therapeutics for Nipah virus. *Microbes Infect.* 2019;21:278–286. doi: 10.1016/j.micinf.2019.02.002.
34. Rzymiski P., Szuster-Ciesielska A., Dzieciatkowski T., Gwenzi W., Fal A. mRNA vaccines: The future of prevention of viral infections? *J. Med. Virol.* 2023;95:e28572. doi: 10.1002/jmv.28572
35. Ao T.T., Rahman M., Haque F., Chakraborty A., Hossain M.J., Haider S., Alamgir A.S., Sobel J., Luby S.P., Gurley E.S. Low-Cost National Media-Based Surveillance System for Public Health Events, Bangladesh. *Emerg. Infect. Dis.* 2016;22:720–722. doi: 10.3201/eid2204.150330.
36. Sazzad H.M., Luby S.P., Ströher U., Daszak P., Sultana S., Afroj S., Rahman M., Gurley E.S. Exposure-based screening for Nipah virus encephalitis, Bangladesh. *Emerg. Infect. Dis.* 2015;21:349–351. doi: 10.3201/eid2102.141129
37. Luby S.P., Gurley E.S., Hossain M.J. Transmission of human infection with Nipah virus. *Clin. Infect. Dis.* 2009;49:1743–1748. doi: 10.1086/647951
38. Nahar N., Paul R.C., Sultana R., Sumon S.A., Banik K.C., Abedin J., Asaduzzaman M., Garcia F., Zimicki S., Rahman M., et al. A Controlled Trial to Reduce the Risk of Human Nipah Virus Exposure in Bangladesh. *Ecohealth.* 2017;14:501–517. doi: 10.1007/s10393-017-1267-4.
39. Khan M.S., Hossain J., Gurley E.S., Nahar N., Sultana R., Luby S.P. Use of infrared camera to understand bats' access to date palm sap: Implications for preventing Nipah virus transmission. *Ecohealth.* 2010;7:517–525. doi:10.1007/s10393-010-0366-2.
40. Nahar N., Sultana R., Gurley E.S., Hossain M.J., Luby S.P. Date palm sap collection: Exploring opportunities to prevent Nipah transmission. *Ecohealth.* 2010;7:196–203. doi: 10.1007/s10393-010-0320-3.
41. Weatherman S., Feldmann H., de Wit E. Transmission of henipaviruses. *Curr. Opin. Virol.* 2018;28:7–11. doi: 10.1016/j.coviro.2017.09.004.