





## NARRATIVE REVIEW OPEN ACCESS

# Risk Evaluation and Mitigation Strategies for Potential Outbreaks of Nipah Virus Infection: Evidenced by the Recent Incidences in Southeast Asian Countries

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## ABSTRACT

**Background:** The importance of studying Nipah virus (NiV) stems from its high fatality rates and potential for causing widespread outbreaks. Recent incidences in Southeast Asian countries highlight the urgent need for effective risk evaluation and mitigation strategies.

**Justification:** Studying NiV in Southeast Asia is crucial due to the geographic and epidemiological significance that makes this region predominantly susceptible to the virus.

**Objectives:** This study aims to identify the risk factors of NiV, evaluate current mitigation strategies, and suggest improvements against this virus.

**Methods:** This review incorporates articles from the PubMed database related to available NiV treatments, vaccines, mitigation strategies, transmission data, and mortality to comprise an extensive analysis of pertinent information.

**Findings:** NiV warrants international attention, due to the high mortality rate and the rising number of human-to-human transmission vectors. NiV is difficult to diagnose early on in the infection due to its generic symptoms, and the two strains of NiV (B and M), pose significant challenges to healthcare institutions. Vaccines, such as the VSV-stored, virus-like particle-based, and mRNA-based NiV show promising results in both animal and human studies. Synthetic medicines, like Ribavirin, and favipiravir showed promising results in NiV-infected patients. Therapeutic infectious particles increased survival from 10% to roughly 70%–80% in animals. Phytochemicals, like serpentine and neoandrographolide are alternatives to NiV-G ligands. Griffithsin, an algae derivative has also shown efficacy in treating NiV infections. Artificial intelligence determines the NiV infection with an accuracy of 88.3%.

**Conclusions:** The strategies to control NiV must be one of a One Health approach, incorporating environmental and social factors. Extensive research on vaccines that showed promising results in animals needs to be tested for humans on a large scale. The major mitigation strategy available is the public awareness during the outbreak about NiV transmission vectors, quarantine protocol, and food hygiene.

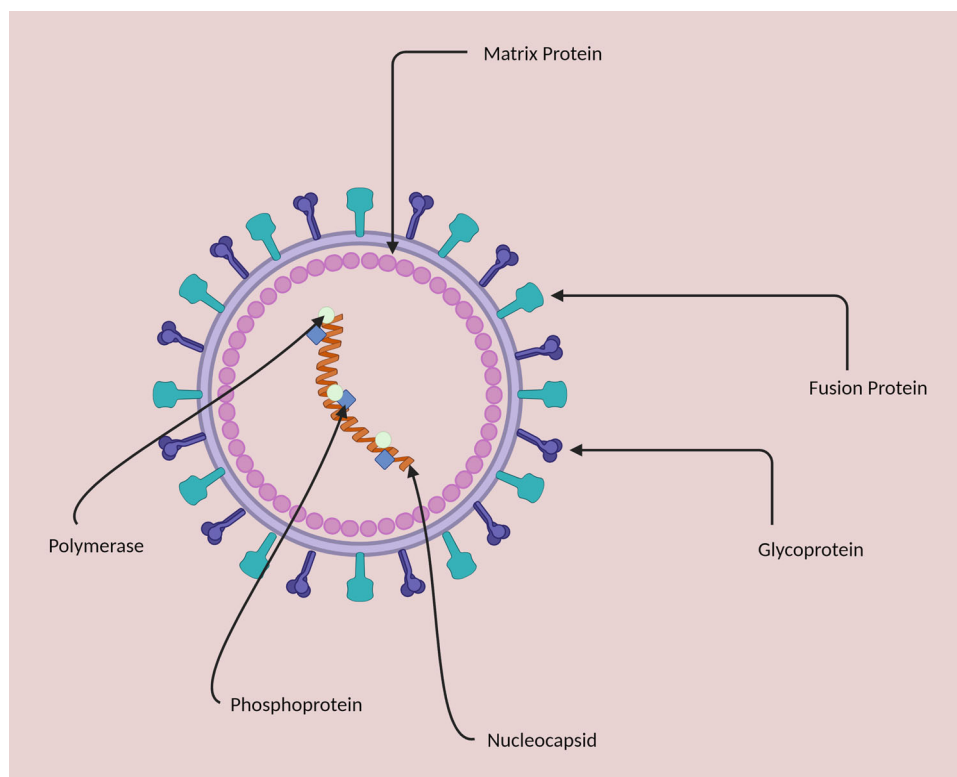
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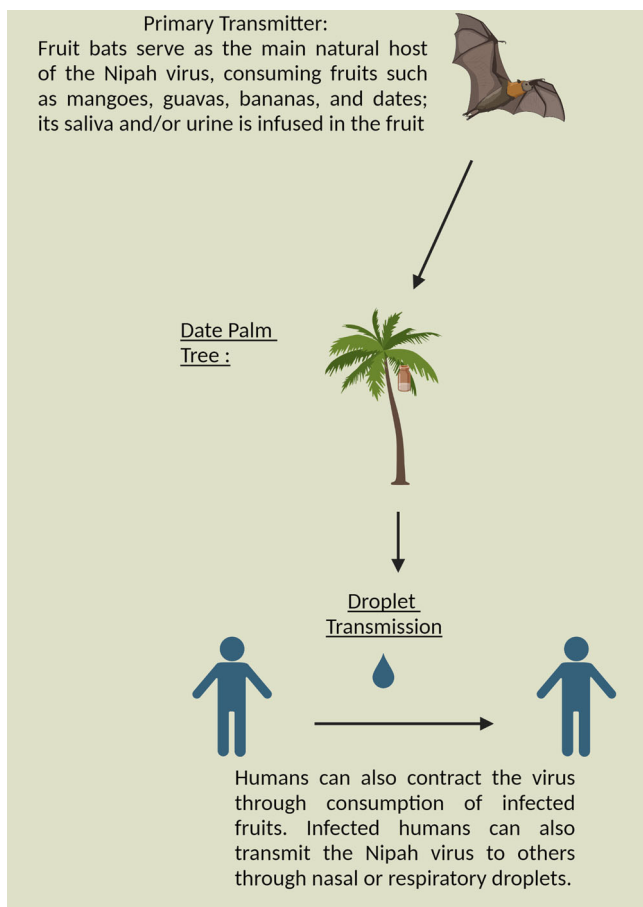
## 1 | Background

As tensions from the COVID-19 pandemic are beginning to settle, our world is about to be met with another threat known as the (NiV), which is a type of zoonotic virus, belonging to the genus *Henipavirus* of the family *Paramyxoviridae* and subfamily *Orthoparamyxoviridae* [1]. It is 15% larger than typical *Paramyxoviruses* [2, 3], and it has a unique 3′–5′ ladder structure that induces transcription and replication of new viral RNA, thus leading to a faster mutation rate than most viruses [3, 4]. There are two isolated strains of NiV, B, and M, denoted NiV-B and NiV-M respectively [5]. NiV-B was originally isolated from Bangladesh, and is found to be associated with respiratory symptoms at a much higher rate than NiV-M along with being more transmissible human-to-human [5]. NiV-M is a milder strain and was originally isolated from the outbreaks in Malaysia and Singapore [5]. The genetic difference between NiV-B and M is 8.2%, with the NiV-B genome being six nucleotides longer in the intron region of the F protein gene [5]. The V gene in NiV-B, which is related to the deception of the host immune system, shows the only variation between the two genomes, possibly the cause of its increased virulence [5]. NiV is a spherically shaped virus, much like other orthoparamyxoviridae [6]. Compared to the pleomorphic nature of the *Henipavirus* genus, NiV is a non-segmented, single-stranded RNA virus, which contains 6 genes related to nucleocapsid (N), phosphoprotein (P), matrix (M), fusion glycoprotein (F), attachment glycoprotein (G), and long polymerase encoding [6]. To infect other cells, it alters the G and F proteins and binds to the viral receptor-binding protein (RBP) which neutralize the antibody. The F protein then enters the host cell, the viral membrane attaches to the host cell membrane, the

M and N proteins are altered, and the viral genome is ejected into the host cell (Figure 1) [2]. There are severe virological threats related to NiV beyond SARS-CoV-2. The NiV can easily transmitted by direct contact with infected animals, such as bats or pigs, or their bodily secretions, bat blood, saliva, and urine [7]. The NiV produces various infections in humans, causing the inflammation of the central nervous system (fatal encephalitis), affecting a range of clinical presentations, like fever, headache, cough, and sore throat, from asymptomatic infections (subclinical) to acute respiratory infections [7]. In severe cases, encephalitis and seizures occur, progressing to coma within 24–48 h [7]. Long-term neurological complications, like seizures, encephalopathy, cerebral atrophy, and personality disorders, have been reported in survivors [7–9]. Similar to how the SARS-Cov-2 virus mirrors some cases of seasonal influenza virus, (respiratory syncytial virus or other viral respiratory infections), NiV has been improperly diagnosed due to the nonspecific early symptoms as Japanese encephalitis based on its symptoms, making it difficult for medical professionals to accurately recognize it without performing laboratory testing [10, 11]. In addition, there are currently no drugs and vaccines specific to NiV. The World Health Organization (WHO) identified NiV as a “virus of concern” and mandated research to be done for potential treatments and effective preventive measures, including vaccines [7]. The identification of NiV in the urine and saliva of Malaysian Island flying foxes (*Pteropus hypomelanus* and *Pteropus vampyrus*), serves as the main natural reservoir of the disease [12]. The transmission of NiV from bats to pigs resulted in the first outbreak in 1998–1999 amongst pigs in Malaysia [12, 13]. Southeast Asian countries such as the Philippines and Thailand have also been affected by the NiV through initial transmission



**FIGURE 1** | Structure of the Nipah virus. The Nipah virus is composed of six proteins: the matrix protein (M), the fusion protein (F), the glycoprotein (G), the nucleocapsid (N), the phosphoprotein (P), and RNA polymerase (L).



**FIGURE 2** | Transmission routes of the Nipah virus. The Nipah virus is most commonly transmitted by the *Pteropus* fruit bat, in which humans will consume infected date palm sap, and thus spread it to others through secretions.

from infected fruit bats in the area or via human-to-human contact, with Bangladesh and India being the most prominent [7, 14–17]. Transmission of the disease is possible through the consumption of fruits or fruit products contaminated with the animal's secretions of bodily fluids [1]. Urine or saliva can be infused into the date sap of the date palm trees (*Phoenix dactylifera*) (Figure 2) [18]. Domestic animals foraging on and consuming contaminated dates can then become a host of NiV [19]. NiV has a concerning  $R_0$ , which has been measured from the 1918, 1957, 1968, and 2009 outbreaks to have median  $R_0$ 's of 1.80, 1.65, 1.80, and 1.46 respectively [20]. For reference, an  $R_0$  of greater than 1 indicates that the virus increases in infectivity when an individual in a population is infected. The disease can spread amongst humans through nasal or respiratory droplets excreted by coughing and sneezing, urine, or blood transmissions, as stated by the Centers for Disease Control (transmission section), when in close contact with an individual with Nipah encephalitis [1]. Study showed, regarding cases in Bangladesh, 51% of patients developed the illness after close contact with another NiV patient [21]. NiV symptoms are categorized in an infection range from mild to severe, with death occurring in 40%–70% of documented cases between 1998 and 2018 in Bangladesh [1]. As of 2017, there have been more than 600 cases of NiV with fatality rates ranging up to 100% for some outbreaks [18]. However, it needs to be mentioned that a true picture of the

fatality cases is missing which might be because of the limited symptoms, limited data, and limited diagnostic services in remote areas and low-to-middle-income countries. Similar to the beginnings of the COVID-19 virus outbreak, people who lack first-hand knowledge show very low awareness of the matter, and we must be proactive as the NiV virus shows high pathogenicity and severity [22]. With the newest case emerging in September 2021 resulting in death [23], no NiV vaccine available, and lingering controversy over COVID-19 policies, the NiV threat must be recognized. Many policymakers are unaware of the risk NiV poses on their communities and likewise are ignorant of the best methods to control outbreaks and vectors of transmission. The rationale of this study is to discuss the threats of NiV infection in public health comprehensively and to inform policymakers on the best methods currently available to control the spread of this emergent infectious disease.

## 2 | Methods

### 2.1 | Study Design

In this review article, a wide-ranging literature (Scopus indexed and Web of Science) search related to the NiV outbreak in Southeast Asia, and its transmission, treatment, and Public safety strategies of NiV was executed in the PubMed database and extracted suitable information from appropriate ones. Articles written only in English was chosen for this review. Articles not indexed in Pubmed, Medline, Google Scholar, and authentic cites were omitted from our selections.

### 2.2 | Prevalence and Current Spread of NiV

The prevalence of NiV infection has substantially increased throughout the globe after the first outbreak occurred in Malaysia. The initial spread, known as a spillover event is seen when people come in contact with the infected person who has in close association with an infected animal or its body fluids (such as saliva or urine). Overall, the disease burden of this virus has resulted in 265 cases in Malaysia (1998–1999), 11 cases in Singapore (1999), 209 total cases in Bangladesh (2001, 2003–2007, 2008–2012), and 90 total cases in India (2001, 2007, 2018), leading to a total of 333 deaths since 1998 [24]. While little to no cases have been reported in other continents, there is an increased risk for outbreaks due to the high population and favorable growth environment of the *Pteropus* genus in Indonesia, Southeast Asia, Pakistan, southern China, the Philippines, and northern Australia (Figure 3) [24].

The major mode of transmission of NiV was different between the affected countries [22]. The NiV was first documented in Sungai Nipah in Malaysia, for which it got its name, and the outbreaks were linked to infected pigs in M in 1998–1999 [12, 13]. In the Philippines, the NiV outbreaks have associated the horses and In India and Bangladesh, outbreaks were related to the consumption of date palm sap [14, 25]. The virus spread into Singapore and infected humans through the handling of infected pigs, and to combat the spread, mass slaughtering of the pigs took place [26]. This resulted in 276 cases of encephalitis at a 40% fatality rate



**FIGURE 3** | Areas of the world with Nipah virus outbreaks. Outbreaks have been most frequently reported in India, Malaysia, and Bangladesh (red). Other countries in the surrounding areas have experienced few outbreaks (yellow). Areas of concern include those that the *Pteropus* fruit bat habituates and could potentially infect those that live there (gray).

[26]. The virus was then reported in Bangladesh in 2001, where it spread by means of food and droplet vectors. Outbreaks occurred frequently from 2001 to 2012, with 209 cases reported and a 77% fatality rate. During this time, two outbreaks in 2001 and 2007 were documented in West Bengal, India with a fatality rate of 70%. In South-East Asia, the virus reported a 74.5% fatality rate between 2001 and 2012 [15]. The virus was quiet for some time, however in 2018 in Kerala, India there were 18 cases reported with 17 fatalities [16]. This might be due to the deforestation and habitat loss or the NiV's increased ability to spread between people easily [27]. Recent cases of NiV have arisen since February of 2023 in Bangladesh with 11 confirmed cases and 8 being fatal [28]. Earlier the symptoms were the primary determining factors for NiV assessment because of the lack of the optimum diagnosis tools, however, at present house-laboratory-based serological, nucleic acid amplification, and qRT-PCR techniques were developed for the diagnosis of this virus.

### 2.3 | A Threat to the Global Public Health

NiV is a real and present threat to public health because of the rising number of alarming vectors for transmission, difficulties in early diagnosis from other viral infections, development of new strains and mutation-driven biological changes, an alarming fatality rate (40%–75% in Bangladesh, reported by WHO) and a transmission rate of 33% (82 cases caused by person-to-person transmission out of total 248 NiV infected cases from April 2001 to April 2014 in Bangladesh) [29].

The human-to-human transmission vector, however, is the most concerning as a threat on a global scale, at least at this

moment. since there is a high probability that a singular person could infect many, especially in densely populated areas like India or Bangladesh. This is usually a case in poor-resource settings, but in high-income countries, appropriate quarantine would be easier to impose, limiting contact with bodily fluids and secretions. A study showed that a singular infected patient in Kerala, India could infect 22 others with only 2 surviving [16], and another showed that the 9 NiV patients in Bangladesh (2001–2007) could infect 62 others [20]. Although these outbreaks of NiV have been relatively localized, the distribution of *Pteropus* fruit bats is extensive, ranging from sub-Saharan Africa to North Australia [7]. As these bats migrate, they could infect a population of *Pteropus* which has no immunity to this virus [30]. The immense range of *Pteropus* could prove to be what turns local outbreaks in Southeast Asia, into a pandemic ranging into half of Africa. Along with the *Pteropus* bat and pigs, contact with the other intermediate symptomatic host animals including horses, cats, dogs, and sheep can infect the human [31].

NiV is difficult to diagnose also due to its generic symptoms, such as headache, fever, and vomiting [29]. The first stages of infection present like a simple influenza infection [32]. NiV produces influenza-like symptoms that rapidly progress into acute respiratory syndrome, encephalitis, and then rapidly progress to coma within 24–48 h [1, 7]. This presents a difficult diagnosis for physicians, if they delay treatment their patient could have long-lasting neurologic damage, while a false diagnosis wastes hospital resources [33]. Delay in isolating, improper quarantine or unable to keep an infected patient in quarantine would pose a danger not only to the general public but also to the hospital staff as well.

The virus' potential of developing new strains and mutations is also worth noting. There are currently two strains, the Bangladesh strain (NiV-BD) and the Malaysian strain (NiV-MY), and the symptoms and the strength of the virus depend on which strain is present in the infected individual [34]. These two strains are approximately 92% identical in nucleotide sequence. The greatest heterogeneity between NiV-BD and NiV-MY lies in the untranslated regions (UTRs) of the P gene which expedites an open reading frame shift enabling the translation of the accessory proteins, required for viral gene transcriptional translational efficiency [17, 34]. This may cause differential replicative ability of NiV at sites of transmission and is well demonstrated for mutations for other paramyxoviruses [35–37]. In vitro study showed that the NiV-BD and NiV-MY strains have different viral replicative kinetics and induction of innate immune factors [38]. The NiV-MY strain produced more rapid and severe cytopathology and replicated to higher titers over time compared to NiV-BD, in hamster kidney cells [7]. Another study conducted in the ferret model showed that with the same degree of viral load in anatomical sites, the level of replication of NiV-BD is higher than the NiV-MY and showed a higher rate of respiratory tract shedding during clinical disease [39, 40]. In most cases, patients infected by the NiV-BD presented severe respiratory symptoms while few patients infected with NiV-MY reported respiratory distress [39]. The NiV-BD strain has a higher CFR (75%) and shorter incubation period compared to NiV-MY (CFR: 40% in Malaysia and Singapore) [17, 33, 41]. In addition, a small proportion of patients from NiV-BD outbreaks presented with myoclonus, while significant segmental myoclonus (involuntary contraction of muscles supplied in the brainstem or the spine) has been found in patients affected by the NiV-MY strain [40, 42, 43]. With each NiV-related infection, mutation-driven biological changes can occur, and the greatest threat would be associated with increased transmissibility between humans and/or gaining new routes of transmission and/or changes to the incubation period. This could be associated with lower mortality (as is a case sometimes with viruses, e.g., Omicron SARS-CoV-2 lineage), but it could lead to high mortality anyway.

## 2.4 | Disease Burden and Therapeutic Measures

NiV infection can be asymptomatic, and transmissible before the symptomatic phase [5]. The incubation period for NiV has an average range from 4 to 14 days [7]. The incubation period ranged from 4 days to 2 months during the Malaysian outbreak, whereas it was 10 days in Bangladesh [41] and 6–14 days in Kerala with a median of 9.5 days [16]. The initial symptoms developed in the infected people as fever, headaches, myalgia (muscle pain), vomiting, cough, sore throat, and breathing difficulties, which could be followed by dizziness, drowsiness, and altered consciousness [5]. The severity of infection usually begins with vasculitis within many organs and can lead to vasculitis-induced thrombosis, ischemia, and parenchymal necrosis mostly within the Central Nervous System [44]. This leads to acute or on-set lethal encephalitis. NiV has also been shown to cause a relapse of encephalitis months to years after recovery [44].

Currently, there are no licensed antivirals specifically for any strain of NiV [5]. The main treatment that has been used thus far for NiV has been ribavirin [40, 45, 46]. Although, there is not

enough clinical evidence to prove its efficacy, it has been shown to reduce mortality at a rate of 36% and less neurological problems in survivors [46]. Another antiviral that is promising in vitro inhibition activity against NiV is Favipiravir. Favipiravir is already licensed in Japan for influenza viruses and has shown a 100% survival rate with NiV [47]. A promising treatment that has been shown effective in mice is the use of therapeutic infectious particles (TIPs). One study had shown that the use of active TIPs in NiV-infected mice had increased survival rates from 10% to roughly 70%–80% [48].

## 2.5 | Short- and Long-Term Preventive Measures

Since there are unavailability of effective medications against NiV infections, several effective preventative measures, like educational efforts, non-pharmaceutical methods, surveillance programs, and vaccine development are the best options to follow strictly.

### 2.5.1 | Educational and Public Awareness Efforts

Educating the people through massive advertisements or educational messages about NiV, its possible transmissions, and the necessary steps to handle is important to reduce the exposure of this virus through increasing awareness. Educational advertisements are to be locally distributed in various ways before and during the viral season [7, 49]. Several cost-effective methods were initiated to reduce the behavior of human exposure to date palm sap such as televised public service announcements, and posters in various locations during the 2012–2014 sap harvesting season [50]. A study conducted throughout 30 districts across Bangladesh showed that after watching the TV announcement, a reduction of exposure to NiV was found to decrease from 12% to 11% [50]. Posters indicating “no raw sap” consumption in restricted areas reduced NiV exposure from 31% to 21% and indications of “only safe sap” areas showed a 2% decrease from 12% to 10% [50]. Another means of intervention, using *banas* (a type of barrier typically made from bamboo, used to prevent bats from accessing date palm sap) as both an indication for “only safe sap” consumption while also a barrier to prevent bats from contaminating the sap with NiV could reduce the possibility of NiV infections.

In general, public health educational messages about the transmission methods, the spread, and the symptoms of the virus are lacking within the local population, and in efforts to decrease the infection rate and the spread of the virus, there have been suggestions for additions to the current policy recommendations. The first addition would be to enhance the knowledge of the population by implementing NiV education into the school curriculum. Providing education to the younger generation could help with the mistrust that the elderly and local population have with the medical system. The same education would be provided to the traditional healers whom the locals trust, and this would allow a more open and accepted talk between patients and their families [37]. In addition, to reach the more rural areas of Bangladesh methods via radio announcements or newspaper articles could be utilized. The

announcements could include a short synopsis of the harm, how to avoid the sap, and what to do if you have been exposed.

### 2.5.2 | Nonpharmacological Preventive Measures

There are currently no strict policies, but there are a few recommendations in place by the government. In the short term, the best plan of action regarding the NiV is to continually monitor and control any spread that may occur. It is highly encouraged not to consume raw date palm sap (a sweet drink harvested and consumed in Southeast Asia, during winter season) during the peak outbreak season of May to November. If consumed, the sap should be boiled for 10 min. A more cost-effective method would be protecting the plant with a bamboo skirt (A low tech method prevents fruit bats from accessing the date palms sap) [7]. Identifying the infected animals in the affected area, isolating them immediately, and/or killing them if needed are good preventative options to reduce NiV infections. Apart from the non-pharmaceutical, disinfectant might be used to reduce the NiV to undetectable levels in the air. Study showed that spraying aerosol with 10% Sodium Hypochlorite and 80% ethanol will help to eradicate NiV in the small particles of aerosol [51].

### 2.5.3 | Surveillance Programs

Another addition to the policy regimen could be various surveillance techniques, including geographic hotspots of bat habitats, date harvesting locations, and common NiV affected areas. The government began a surveillance program in hospitals along the Nipah outbreak belt for early detection [7, 49]. The surveillance programs include regular testing for health-care workers, screenings for patients presenting with symptoms followed by a strict quarantine process, and contact tracing [5].

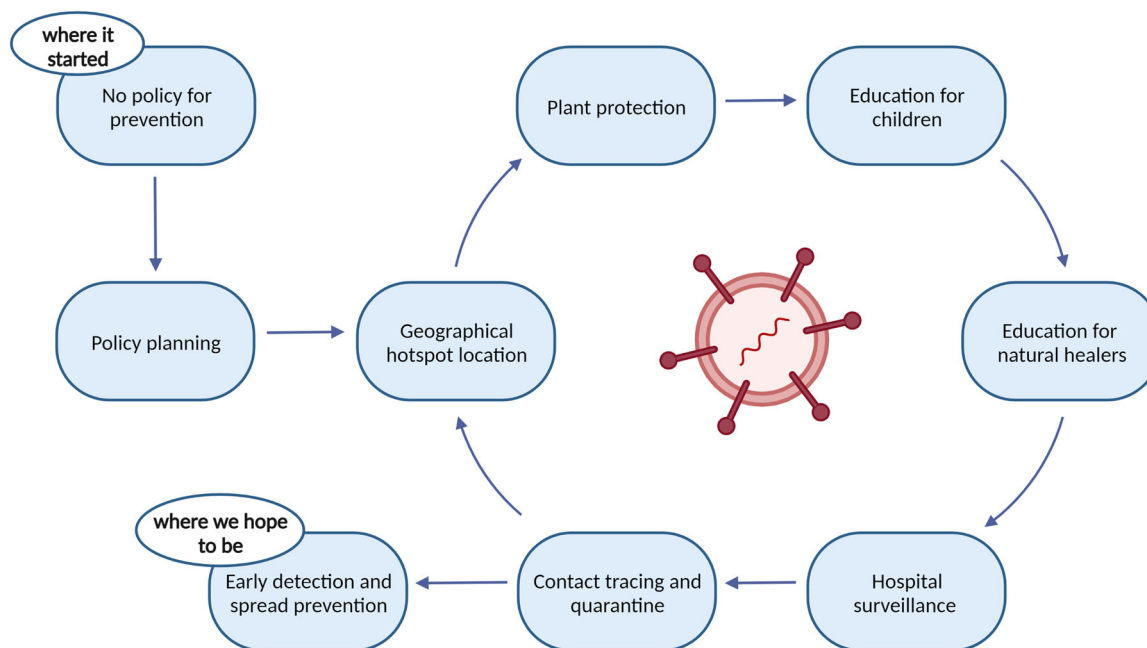
The mapping of the bat habitat and harvesting locations could help to identify the high-risk areas, and modifications such as bamboo skirts could then be put in place to protect the plants. The surveillance of the population would trace current outbreak locations, and, if a pattern is discovered, the data collected can help prevent future outbreaks. Lastly, in addition to surveillance would be infection control and quarantine efforts. The addition of infectious disease control would target clinical settings and would be used to implement contact tracing and quarantine areas for those infected patients (Figure 4) [49].

### 2.5.4 | Vaccine Development

Mutations of NiV strains are a great challenge for the researcher to develop an effective vaccine. There is currently vaccine research occurring and some studies are quite promising. A recombinant vectored vaccine being tested in African Green Monkeys. The study reported a 100% survival rate when vaccinated 7 days before the infection [52]. Another developing vaccine based on virus-like particles reported a 100% survival rate in the hamster model. This study showed both one-dose and three-dose series produced substantial immunity against NiV [52]. The National Institute of Health launched a clinical trial of NiV Vaccine (mRNA 1215) on humans, based on the mRNA technology, which was manufactured by Moderna, Inc., Cambridge, Massachusetts, and was developed in collaboration with The National Institute of Allergy and Infectious Diseases [53].

## 2.6 | Role of Medicinal Plants in Treating NiV Infections

The considerable adverse effects and pharmacokinetic challenges pertinent antivirals (i.e., ribavirin) possess leads many clinicians



**FIGURE 4** | The policies for controlling the spread of the Nipah virus. Include surveillance of the outbreak areas, protecting the areas and hospitals it has been found in, educating both the children and hospital staff, and contact tracing and quarantine measures for those infected. With these policies put into place, the virus will be able to be detected early and thus prevented from spreading any further.

and researchers to look into natural compounds that may possess a milder adverse effect profile. A series of studies identified two phytochemicals, serpentine and neoandrographolide as the most promising alternatives, which target the NiV-G ligand [54]. The researchers, rather than focus on one viral enzyme, looked for a compound that indiscriminately targeted many viral ligands. This led to the isolation of RASE0125 (17-O-Acetylnortetraphyllicine) and CARS 0358 which inhibit NiV ligands F, G, and N with unique mechanisms between the two [55]. An algae derivative, griffithsin (GRFT) has shown efficacy in Syrian Golden Hamsters and in vitro [55]. A combination of natural compounds used in traditional Chinese medicine has shown a significant effect in the curing and treating of NiV.

## 2.7 | Use of Artificial Intelligence (AI) Tools in NiV Outbreaks

AI's current use in surveillance, prevention, and control of NiV is mainly predictive, taking in many variables and factors to observe, categorize, collect, and interpret data from a variety of sources. This utility is not limited to public health, but can also be used in the diagnosis of NiV from molecular assays, leading to a more rapid introduction of therapy and quarantine. AI can also be used to interpret physiologic data, which can be useful in the diagnosis of zoonotic diseases leading to faster prevention and treatment measures [56]. Using ML techniques, Kannan et. al have developed a predictive model for the early diagnosis of NiV [57]. This model uses various factors, both clinical and analytical along with a method called the restricted Boltzmann machine, to determine NiV infection with an accuracy of 88.3% [57].

## 2.8 | "One Health" Approach in Controlling NiV Outbreaks

Due to the zoonotic nature of the NiV, the response must be a combination of responses to the environment, people, and animal factors as they relate to this infection [58]. The most successful approach that combines these necessary factors would be the one health approach, which has been shown to be effective in controlling NiV outbreaks. For example, in the 2019 outbreak, the one health approach stopped the spread of the NiV infection as well, there were no mortalities from the NiV during this outbreak [58]. The One Health approach has limited utility though, as it does not stop the emergence of new diseases alone.

## 3 | Discussions

NiV poses a major public health risk due to the large number of human-to-human transmission vectors, the generic symptoms related to early infections, as well as there being two strains of this virus [16, 21, 32, 33]. Studies showed that there are various mutation-related differences between the two NiV strains (NiV-BD and NiV-MY), the most relevant being different incubation periods and increased rate of transmission human-to-human [35–37]. It

is of utmost importance to educate the Southeast Asian population about the risk and mitigation strategies if we want to reduce the transmission of NiV [59]. Some means through which this could be done is using local stations and new outlets to disseminate information and educate public leaders such as teachers, healthcare workers, and local officials. It is likewise important to present information from social media platforms, working internationally with NGOs so that the greatest number of people can be reached with mitigation and quarantine protocols. Due to the population density of the endemic areas of NiV, strong guidelines, and control strategies, working in tandem with a One Health approach would be the only effective means of limiting NiV spread [60]. Part of the control strategies would be the implementation of nonpharmacological treatment, vaccine development and implementation, and effective antiviral regimens. These measures have shown to be effective in the limitation of and decrease in mortality of NiV infection [7, 49, 52]. Other nations must follow India's example, as the Indian Council of Medical Research and Integrated Disease Surveillance Program has started collaborating with the National Centre for Disease Control in India to find ways to limit the animal vector of NiV transmission [61].

## 3.1 | Limitations

The current study and surveillance of the NiV are limited in Southeast Asian countries. There is growing concern about the potential global impact of NiV and a collaborative data network is needed to gather information on this virus in other continents that may mitigate the risk.

## 4 | Conclusion

The control and prevention of NiV in Southeast Asian countries would be possible by strictly following the guidelines and control strategies utilizing the One Health approach. Extensive research on vaccines that showed promising results in animals needs to be tested for humans on a large scale to prevent the aggression of NiV infections. Several public health measures, like quarantining the animal premises if an outbreak is suspected, establishing surveillance to prevent early warning for veterinary and human public health authorities, and routinely examining the samples taken from people and animals suspected NiV infections by trained staff are crucial to reduce the risk of NiV infections.

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### Author Contributions

**Md. Ashrafur Rahman:** conceptualization, supervision, writing-review and editing. **Yeasna Shanjana:** conceptualization, supervision, writing-review and editing. **Sydney Cronmiller:** conceptualization, data curation, writing-original draft. **Donovan Zong:** conceptualization, data curation, writing-original draft. **Rob Davis:** conceptualization, data curation, writing-original draft. **Julianne Ernest:** conceptualization, data curation, writing-original draft. **Jonah Nguyen:** validation, writing-review and editing. **Amanda Rawa:** validation, writing-review and editing. **Marie Roke Thomas:** validation, writing-review and editing. **Md.**

**Rabiul Islam:** conceptualization, supervision, writing–review and editing.

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### Ethics Statement

The authors have nothing to report.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The authors have nothing to report.

### References

- Centers for Disease Control and Prevention, What is the Nipah Virus? (2020), <https://www.cdc.gov/vhf/nipah/about/index.html>.
- L. F. Wang, M. Yu, E. Hansson, et al., “The Exceptionally Large Genome of Hendra Virus: Support for Creation of a New Genus Within the Family Paramyxoviridae,” *Journal of Virology* 74, no. 21 (2000): 9972–9979, <https://doi.org/10.1128/jvi.74.21.9972-9979.2000>.
- B. H. Harcourt, A. Tamin, K. Halpin, et al., “Molecular Characterization of the Polymerase Gene and Genomic Termini of Nipah Virus,” *Virology* 287, no. 1 (2001): 192–201, <https://doi.org/10.1006/viro.2001.1026>.
- B. H. Harcourt, A. Tamin, T. G. Ksiazek, et al., “Molecular Characterization of Nipah Virus, a Newly Emergent Paramyxovirus,” *Virology* 271, no. 2 (2000): 334–349, <https://doi.org/10.1006/viro.2000.0340>.
- N. Hauser, A. C. Gushiken, S. Narayanan, S. Kottilil, and J. V. Chua, “Evolution of Nipah Virus Infection: Past, Present, and Future Considerations,” *Tropical Medicine and Infectious Disease* 6, no. 1 (2021): 24, <https://doi.org/10.3390/tropicalmed6010024>.
- A. D. Hyatt, S. R. Zaki, C. S. Goldsmith, T. G. Wise, and S. G. Hengstberger, “Ultrastructure of Hendra Virus and Nipah Virus Within Cultured Cells and Host Animals,” *Microbes and Infection* 3, no. 4 (2001): 297–306, [https://doi.org/10.1016/s1286-4579\(01\)01383-1](https://doi.org/10.1016/s1286-4579(01)01383-1).
- World Health Organization. Nipah Virus. (2018), <https://www.who.int/news-room/fact-sheets/detail/nipah-virus>.
- C. C. Broder, K. Xu, D. B. Nikolov, et al., “A Treatment for and Vaccine Against the Deadly Hendra and Nipah Viruses,” *Antiviral Research* 100, no. 1 (2013): 8–13, <https://doi.org/10.1016/j.antiviral.2013.06.012>.
- J. J. Sejvar, J. Hossain, S. K. Saha, et al., “Long-Term Neurological and Functional Outcome in Nipah Virus Infection,” *Annals of Neurology* 62, no. 3 (2007): 235–242, <https://doi.org/10.1002/ana.21178>.
- Centers for Disease Control and Prevention. Diagnosis, (2020), <https://www.cdc.gov/vhf/nipah/about/index.html>.
- Z. Yin, H. Wang, J. Yang, et al., “Japanese Encephalitis Disease Burden and Clinical Features of Japanese Encephalitis in Four Cities in the People’s Republic of China,” *The American Society of Tropical Medicine and Hygiene* 83, no. 4 (2010): 766–773, <https://doi.org/10.4269/ajtmh.2010.09-0748>.
- K. B. Chua, “Nipah Virus Outbreak in Malaysia,” *Journal of Clinical Virology* 26, no. 3 (2003): 265–275, [https://doi.org/10.1016/s1386-6532\(02\)00268-8](https://doi.org/10.1016/s1386-6532(02)00268-8).
- S. K. Lam and K. B. Chua, “Nipah Virus Encephalitis Outbreak in Malaysia,” *Clinical Infectious Diseases* 34, no. Suppl 2 (2002): S48–S51, <https://doi.org/10.1086/338818>.
- P. K. G. Ching, V. C. de los Reyes, M. N. Sucaldito, et al., “Outbreak of Henipavirus Infection, Philippines, 2014,” *Emerging Infectious Diseases* 21, no. 2 (2015): 328–331, <https://doi.org/10.3201/eid2102.141433>.
- S. Wacharapluesadee, B. Lumlertdacha, K. Boongird, et al., “Bat Nipah Virus, Thailand,” *Emerging Infectious Diseases* 11, no. 12 (2005): 1949–1951, <https://doi.org/10.3201/eid1112.050613>.
- G. Arunkumar, R. Chandni, D. T. Mourya, et al., “Outbreak Investigation of Nipah Virus Disease in Kerala, India, 2018,” *The Journal of Infectious Diseases* 219, no. 12 (2019): 1867–1878, <https://doi.org/10.1093/infdis/jiy612>.
- M. K. Lo, L. Lowe, K. B. Hummel, et al., “Characterization of Nipah Virus From Outbreaks in Bangladesh, 2008–2010,” *Emerging Infectious Diseases* 18, no. 2 (2012): 248–255, <https://doi.org/10.3201/eid1802.111492>.
- B. A. Clayton, “Nipah Virus: Transmission of a Zoonotic Paramyxovirus,” *Current Opinion in Virology* 22 (2017): 97–104, <https://doi.org/10.1016/j.coviro.2016.12.003>.
- V. P. Hsu, M. J. Hossain, U. D. Parashar, et al., “Nipah Virus Encephalitis Reemergence, Bangladesh,” *Emerging Infectious Diseases* 10, no. 12 (2004): 2082–2087, <https://doi.org/10.3201/eid1012.040701>.
- P. Devnath and H. M. A. A. Masud, “Nipah Virus: A Potential Pandemic Agent in the Context of the Current Severe Acute Respiratory Syndrome Coronavirus 2 Pandemic,” *New Microbes and New Infections* 41 (2021): 100873, <https://doi.org/10.1016/j.nmni.2021.100873>.
- S. P. Luby, M. J. Hossain, E. S. Gurley, et al., “Recurrent Zoonotic Transmission of Nipah Virus Into Humans, Bangladesh, 2001–2007,” *Emerging Infectious Diseases* 15, no. 8 (2009): 1229–1235, <https://doi.org/10.3201/eid1508.081237>.
- M. Gaudino, N. Aurine, C. Dumont, et al., “High Pathogenicity of Nipah Virus From *Pteropus lylei* Fruit Bats, Cambodia,” *Emerging Infectious Diseases* 26, no. 1 (2020): 104–113, <https://doi.org/10.3201/eid2601.191284>.
- WHO Disease Outbreak news Nipah Virus Infection- India, (2023), <https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON490>.
- A. S. Ambat, S. M. Zubair, N. Prasad, et al., “Nipah Virus: A Review on Epidemiological Characteristics and Outbreaks to Inform Public Health Decision Making,” *Journal of Infection and Public Health* 12, no. 5 (2019): 634–639, <https://doi.org/10.1016/j.jiph.2019.02.013>.
- B. Sun, L. Jia, B. Liang, Q. Chen, and D. Liu, “Phylogeography, Transmission, and Viral Proteins of Nipah Virus,” *Virologica Sinica* 33, no. 5 (2018): 385–393, <https://doi.org/10.1007/s12250-018-0050-1>.
- P. A. Tambyah, J. H. Tan, B. K. C. Ong, K. H. Ho, and K. P. Chan, “First Case of Nipah Virus Encephalitis in Singapore,” *Internal Medicine Journal* 31, no. 2 (2001): 132–133.
- Gavi, VacinesWork. “What is Nipah Virus, and Why is it Spreading Again?” Accessed October 24, 2023, <https://www.gavi.org/vaccineswork/what-nipah-virus-and-why-it-spreading-again>.
- Centers for Disease Control and Prevention., “Update: Outbreak of Nipah Virus-Malaysia and Singapore, 1999,” *MMWR. Morbidity and Mortality Weekly Report* 48, no. 16 (1999): 335–337.
- World Health Organization, Nipah Virus Infection-Bangladesh, (2023), <https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON442> (Accessed October 24, 2023).
- B. Nikolay, H. Salje, M. J. Hossain, et al., “Transmission of Nipah Virus - 14 Years of Investigations in Bangladesh,” *New England Journal of Medicine* 380, no. 19 (2019): 1804–1814, <https://doi.org/10.1056/NEJMoa1805376>.
- J. H. Epstein, S. J. Anthony, A. Islam, et al., “Nipah Virus Dynamics in Bats and Implications for Spillover to Humans,” *Proceedings of the National Academy of Sciences* 117, no. 46 (2020): 29190–29201, <https://doi.org/10.1073/pnas.2000429117>.



32. J. S. Mackenzie, K. B. Chua, P. W. Daniels, et al., "Emerging Viral Diseases of Southeast Asia and the Western Pacific," *Emerging Infectious Diseases* 7, no. 3 Suppl (2001): 497–504, <https://doi.org/10.3201/eid0707.017703>.
33. N. Thakur and D. Bailey, "Advances in Diagnostics, Vaccines and Therapeutics for Nipah Virus," *Microbes and Infection* 21, no. 7 (2019): 278–286, <https://doi.org/10.1016/j.micinf.2019.02.002>.
34. C. E. Mire, B. A. Satterfield, J. B. Geisbert, et al., "Pathogenic Differences Between Nipah Virus Bangladesh and Malaysia Strains in Primates: Implications for Antibody Therapy," *Scientific Reports* 6 (2016): 30916, <https://doi.org/10.1038/srep30916>.
35. B. H. Harcourt, L. Lowe, A. Tamin, et al., "Genetic Characterization of Nipah Virus, Bangladesh, 2004," *Emerging Infectious Diseases* 11, no. 10 (2005): 1594–1597, <https://doi.org/10.3201/eid1110.050513>.
36. D. E. Anderson, A. Castan, M. Bisailon, and V. von Messling, "Elements in the Canine Distemper Virus M 3' UTR Contribute to Control of Replication Efficiency and Virulence," *PLoS One* 7, no. 2 (2012): e31561, <https://doi.org/10.1371/journal.pone.0031561>.
37. M. Takeda, S. Ohno, F. Seki, Y. Nakatsu, M. Tahara, and Y. Yanagi, "Long Untranslated Regions of the Measles Virus M and F Genes Control Virus Replication and Cytopathogenicity," *Journal of Virology* 79, no. 22 (2005): 14346–14354, <https://doi.org/10.1128/JVI.79.22.14346-14354.2005>.
38. Y. Yan, S. N. Rout, S. H. Kim, and S. K. Samal, "Role of Untranslated Regions of the Hemagglutinin-Neuraminidase Gene in Replication and Pathogenicity of Newcastle Disease Virus," *Journal of Virology* 83, no. 11 (2009): 5943–5946, <https://doi.org/10.1128/JVI.00188-09>.
39. B. L. DeBuyscher, E. de Wit, V. J. Munster, D. Scott, H. Feldmann, and J. Prescott, "Comparison of the Pathogenicity of Nipah Virus Isolates From Bangladesh and Malaysia in the Syrian Hamster," *PLoS Neglected Tropical Diseases* 7, no. 1 (2013): e2024, <https://doi.org/10.1371/journal.pntd.0002024>.
40. B. A. Clayton, D. Middleton, R. Arkinstall, L. Frazer, L. F. Wang, and G. A. Marsh, "The Nature of Exposure Drives Transmission of Nipah Viruses From Malaysia and Bangladesh in Ferrets," *PLoS Neglected Tropical Diseases* 10, no. 6 (2016): e0004775, <https://doi.org/10.1371/journal.pntd.0004775>.
41. K. J. Goh, C. T. Tan, N. K. Chew, et al., "Clinical Features of Nipah Virus Encephalitis Among Pig Farmers in Malaysia," *New England Journal of Medicine* 342, no. 17 (2000): 1229–1235, <https://doi.org/10.1056/NEJM200004273421701>.
42. K. B. Chua, K. J. Goh, K. T. Wong, et al., "Fatal Encephalitis Due to Nipah Virus Among Pig-Farmers in Malaysia," *The Lancet* 354, no. 9186 (1999): 1257–1259, [https://doi.org/10.1016/S0140-6736\(99\)04299-3](https://doi.org/10.1016/S0140-6736(99)04299-3).
43. H. T. Chong, S. R. Kunjapan, T. Thayaparan, et al., "Nipah Encephalitis Outbreak in Malaysia, Clinical Features in Patients From Seremban," *Canadian Journal of Neurological Sciences/Journal Canadien des Sciences Neurologiques* 29, no. 1 (2002): 83–87, <https://doi.org/10.1017/s0317167100001785>.
44. H. T. Chong, M. J. Hossain, and C. T. Tan, "Differences in Epidemiologic and Clinical Features of Nipah Virus Encephalitis Between the Malaysian and Bangladesh Outbreaks," *Neurol Asia* 13 (2008): 23–26.
45. C. T. Tan, K. J. Goh, K. T. Wong, et al., "Relapsed and Late-Onset Nipah Encephalitis," *Annals of Neurology* 51, no. 6 (2002): 703–708, <https://doi.org/10.1002/ana.10212>.
46. H. T. Chong, A. Kamarulzaman, C. T. Tan, et al., "Treatment of Acute Nipah Encephalitis With Ribavirin," *Annals of Neurology* 49, no. 6 (2001): 810–813, <https://doi.org/10.1002/ana.1062>.
47. K. Johnson, M. Vu, and A. N. Freiberg, "Recent Advances in Combating Nipah Virus," *Faculty Reviews* 10 (2021): 74, <https://doi.org/10.12703/r/10-74>.
48. R. Lipin, A. K. Dhanabalan, K. Gunasekaran, and R. V. Solomon, "Piperazine-Substituted Derivatives of Favipiravir for Nipah Virus Inhibition: What Do in Silico Studies Unravel," *SN Applied Sciences* 3, no. 1 (2021): 110, <https://doi.org/10.1007/s42452-020-04051-9>.
49. S. R. Welch, J. R. Spengler, J. R. Harmon, et al., "Defective Interfering Viral Particle Treatment Reduces Clinical Signs and Protects Hamsters From Lethal Nipah Virus Disease," *mBio* 13, no. 2 (2022): e0329421, <https://doi.org/10.1128/mbio.03294-21>.
50. J. Dhillon and A. Banerjee, "Controlling Nipah Virus Encephalitis in Bangladesh: Policy Options," *Journal of Public Health Policy* 36, no. 3 (2015): 270–282, <https://doi.org/10.1057/jphp.2015.13>.
51. N. Nahar, M. Asaduzzaman, R. Sultana, et al., "A Large-Scale Behavior Change Intervention to Prevent Nipah Transmission in Bangladesh: Components and Costs," *BMC Research Notes* 10, no. 1 (2017): 225, <https://doi.org/10.1186/s13104-017-2549-1>.
52. S. J. Smither, L. S. Eastaugh, L. M. O'Brien, A. L. Phelps, and M. S. Lever, "Aerosol Survival, Disinfection and Formalin Inactivation of Nipah Virus," *Viruses* 14, no. 9 (2022): 2057, <https://doi.org/10.3390/v14092057>.
53. S. L. Foster, C. Woolsey, V. Borisevich, et al., "A Recombinant VSV-Vectored Vaccine Rapidly Protects Nonhuman Primates Against Lethal Nipah Virus Disease," *Proceedings of the National Academy of Sciences* 119, no. 12 (2022): e2200065119, <https://doi.org/10.1073/pnas.2200065119>.
54. P. Rzymiski, A. Szuster-Ciesielska, T. Dzieciatkowski, W. Gwenz, and A. Fal, "mRNA Vaccines: The Future of Prevention of Viral Infections?," *Journal of Medical Virology* 95, no. 2 (2023): e28572, <https://doi.org/10.1002/jmv.28572>.
55. V. Randhawa, S. Pathania, and M. Kumar, "Computational Identification of Potential Multitarget Inhibitors of Nipah Virus by Molecular Docking and Molecular Dynamics," *Microorganisms* 10, no. 6 (2022): 1181, <https://doi.org/10.3390/microorganisms10061181>.
56. M. K. Lo, J. R. Spengler, L. R. H. Krumpel, et al., "Griffithsin Inhibits Nipah Virus Entry and Fusion and Can Protect Syrian Golden Hamsters From Lethal Nipah Virus Challenge," *The Journal of Infectious Diseases* 221, no. Suppl\_4 (2020): S480–S492, <https://doi.org/10.1093/infdis/jiz630>.
57. A. I. Saleh and A. H. Rabie, "Human Monkeypox Diagnose (HMD) Strategy Based on Data Mining and Artificial Intelligence Techniques," *Computers in Biology and Medicine* 152 (2023): 106383.
58. M. Kannan and C. Priya, "An Early Detection Of NIPAH Infectious Disease Based On Integrated Medical Features For Human Using Ensemble RBM Techniques," *Journal of Pharmaceutical Negative Results* 13, no. 9 (2022): 2344–2364.
59. M. Singhai, R. Jain, S. Jain, M. Bala, S. Singh, and R. Goyal, "Nipah Virus Disease: Recent Perspective and One Health Approach," *Annals of Global Health* 87, no. 1 (2021): 102, <https://doi.org/10.5334/aogh.3431>.
60. J. Joshi, Y. Shah, K. Pandey, et al., "Possible High Risk of Transmission of the Nipah Virus in South and South East Asia: A Review," *Tropical Medicine and Health* 51, no. 1 (2023): 44, <https://doi.org/10.1186/s41182-023-00535-7>.
61. V. Sharma, S. Kaushik, R. Kumar, J. P. Yadav, and S. Kaushik, "Emerging Trends of Nipah Virus: A Review," *Reviews in Medical Virology* 29, no. 1 (2019): e2010, <https://doi.org/10.1002/rmv.2010>.