Transmission Dynamics, Demographic Patterns, And Strategies For Effective Control And Management of Nipah Virus

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Abstract- *Nipah virus (NiV) infection, first identified in Malaysia in 1998, is a zoonotic disease caused by a pathogen from the Paramyxoviridae family (Singh et al., 2019). Subsequent outbreaks have been documented in Singapore, Bangladesh, and India, highlighting its regional significance (Sharma et al., 2019). The infection poses a severe threat to human health by targeting the respiratory and nervous systems, leading to high mortality rates (Banerjee et al., 2019). As an RNA virus, its transmission occurs through several routes, including from bats to humans, pigs to humans, and through human-to-human contact (Gurley et al., 2007). Fruit bats of the Pteropus genus, such as Pteropus hypomelanus and Pteropus vampyrus, are identified as the primary natural reservoir for the virus (Chua et al., 2000). A critical challenge in managing NiV is the absence of a specific vaccine or approved antiviral treatment, a situation that has persisted from its discovery in 1999 through to the present year of 2022 (Satterfield et al., 2016). Different strains of the virus exhibit distinct clinical and epidemiological features, complicating public health responses (Clayton et al., 2016). The cornerstone of outbreak containment lies in rapid diagnostic procedures and the stringent implementation of infection control measures (Mazzola & Kelly-Cirino, 2019). To this end, a multitude of serological and molecular diagnostic techniques have been developed for effective diagnosis and surveillance (Yadav et al., 2021). Managing the disease becomes particularly difficult when it emerges in new geographical areas where awareness and infrastructure may be lacking (Plowright et al., 2019). The high case fatality rate, estimated to be between 75% and 95%, coupled with the potential for the virus to spread to new regions, underscores the urgent and critical need for developing effective control and management strategies (Shariff, 2019). It is noted that the NiV-B (Bangladesh) strain appears to be more lethal compared to the strains from Malaysia (NiV-M), India (NiV-I), and Singapore (NiV-S) (Harcourt et al., 2005). Presently, the global research community is actively pursuing vaccine development, with several candidates undergoing pre-clinical trials in animal models such as pigs, horses, and monkeys (Thakur & Bailey, 2019). This article seeks to comprehensively examine the barriers and current progress in the development of medicines and vaccines for this particular and highly pathogenic virus.*

I. INTRODUCTION

The Nipah virus (NiV) is classified within the henipavirus genus of the Paramyxoviridae family (Chua et al., 2000). It is counted among a group of highly potent viral diseases, including COVID-19, SARS, Ebola, influenza, and Marburg virus disease, all of which present substantial risks to global public health (Skowron et al., 2022). The virus was initially discovered as the causative agent of an outbreak of febrile encephalitis affecting both livestock and humans (Chua, 2003). Its identification in 1998 and 1999 during a severe outbreak of porcine encephalitis in Malaysia marked its emergence as a novel human pathogen (Chua et al., 2000).

The increasing frequency of emerging infectious diseases is often driven by the close interconnection between environments, domestic animals, humans, and wildlife, which facilitates the spillover of pathogens into human populations (Daszak et al., 2013). Human-driven factors such as deforestation, global travel, agricultural expansion, and wildlife trade intensify interactions at the human-animal interface, thereby creating increased opportunities for pathogen exchange and the emergence of new diseases (Epstein et al., 2006).

Recognizing its severe potential, the World Health Organization (WHO) has listed Nipah virus as a priority pathogen necessitating urgent research and development efforts to combat its outbreak potential (Shariff, 2019). Epidemiological data indicate that by recent counts, NiV has

infected nearly 640 individuals across South and Southeast Asia (Mahedi et al., 2023). Although the absolute number of cases is relatively low compared to other infectious diseases, the associated mortality rate is exceptionally high, varying across outbreaks. The natural route of transmission can occur through the inhalation of infectious droplets or aerosols (Devnath et al., 2022). The virus was first isolated and identified by Dr. Law Bing Chua in 1999 in Malaysia in the aftermath of an outbreak among pig farmers, and it derives its name from the village of Kampung Sungai Nipah, the location of its discovery (Ambat et al., 2019). A more recent outbreak was confirmed in India in 2021, demonstrating its continued threat (Nazmunnahar et al., 2023). Due to its virulence and high mortality, agencies including the National Institute of Allergy and Infectious Diseases (NIAID) and the Centers for Disease Control and Prevention (CDC) have classified NiV as a Category C potential bioterrorism agent, indicating it is a pathogen that could be engineered for mass dissemination (Skowron et al., 2022).

The clinical presentation of NiV infection typically includes fever, cough, labored breathing, and headache, with encephalitis and seizures representing common and serious neurological complications (Singh et al., 2019). In contrast to vector-borne diseases like malaria, the initial human infections in Malaysia were predominantly observed in adults who had direct physical contact with infected pigs (Chua, 2003). Transmission to humans can occur via several pathways: direct contact with infected animals (such as pigs or bats), consumption of contaminated food products, and through close contact with infected human secretions (Gurley et al., 2007; de Wit et al., 2014). The virus demonstrates a tropism for human kidney and lung cells, where it replicates efficiently and causes significant respiratory distress, and it is believed to propagate within the host through a cell-to-cell mechanism, facilitating its spread (Banerjee et al., 2019).

The Virus

Nipah virus possesses subtle but significant structural differences when compared to typical paramyxoviruses (Wong et al., 2002). It is an enveloped virus characterized by a negative-sense, single-stranded RNA genome packaged within a helical nucleocapsid (Chua et al., 2000). The viral particle is composed of six primary structural proteins: the Matrix (M) protein, the Glycoprotein (G), the Phosphoprotein (P), the Fusion (F) protein, the Nucleocapsid (N) protein, and the large RNA Polymerase (L) protein (Soman Pillai et al., 2020). A critical complex within the virus is the ribonucleoprotein, formed by the association of the P, N, and L proteins with the viral RNA genome. This indescribable complex is responsible for regulating the essential processes of viral RNA synthesis and transcription (Singh et al., 2019).

Epidemiology

Nipah virus was first recognized in Malaysia in 1998 in individuals who had close contact with swine populations (Ksiazek et al., 2011). Shortly thereafter, in March 1999, an outbreak was recorded among 11 abattoir workers in Singapore, with an average age of 44 years (Chew et al., 2000). Since its initial emergence, documented outbreaks of NiV have occurred in Malaysia, Singapore, Bangladesh, and India. Furthermore, the virus has been identified and isolated from flying fox (fruit bat) populations in these countries, as well as in Cambodia and Thailand, confirming the wide geographic distribution of the reservoir host (Soman Pillai et al., 2020).

Cumulative data until June 2018 from affected countries including India, Singapore, and Bangladesh reported 643 laboratory-confirmed human cases, resulting in at least 380 deaths, which corresponds to a high fatality rate of 59% (Sharma et al., 2019). The initial cases reported from the state of Perak in Malaysia in September 1998 presented with a constellation of symptoms including headaches, fever, and altered consciousness (Luby, 2013). Epidemiological investigations determined that many human infections were linked to direct contact with sick pigs, particularly those exhibiting respiratory symptoms or through exposure to porcine urine (Parashar et al., 2000, as cited in Singh et al., 2019). Pteropid bats, which are endemic to tropical and subtropical regions across Australia, Asia, and East Africa, have been conclusively established as the reservoir host associated with NiV outbreaks reported in various parts of the world (Soman Pillai et al., 2020). This is consistent with the broader pattern of zoonotic diseases, as approximately 75% of all emerging infectious diseases and about 60% of known human pathogens are zoonotic in origin, underscoring the critical importance of the human-animal-ecosystem interface (Ksiazek et al., 2011).

1. Malaysia

The virus is believed to have originated in the state of Perak before spreading southward to the states of Negeri Sembilan and Selangor (Chua, 2003). During disease surveillance activities carried out by the Malaysian Ministry of Health from September 1998 to December 1999, a total of 283 cases of viral encephalitis were reported, culminating in 109 fatalities (Chua, 2003). Research involving the collection of blood samples from volunteered human participants, as well as from pigs in selected farms across Peninsular Malaysia, was

conducted following the acquisition of necessary ethical approvals (Chang et al., 2020). The state of Negeri Sembilan reported the highest burden, with 281 cases and 109 associated mortalities (Chua, 2003). The outbreak also involved other species; dogs were found to be commonly infected on affected farms, and the death of dogs was identified as one of the risk factors during the Malaysian outbreak (Shariff, 2019).

2. Bangladesh

Outbreaks of NiV have raised significant public health concerns in numerous Bangladeshi villages. One such outbreak period was documented from January 1 to 13, 2003, in the villages of East Chalksia and Biljoania (Hsu et al., 2004). Bangladesh, which shares a border with India on three sides, has reported several cases of NiV infections, with its first recorded cases occurring concurrently with India in 2001 (Hsu et al., 2004). A distinctive feature of NiV epidemiology in Bangladesh is that the fatal human infection is primarily transmitted through person-to-person contact, a pattern different from the Malaysian outbreak (Gurley et al., 2007). Surveillance data, as reported by the Bangladesh Institute of Epidemiology, Disease Control and Research, indicated that as of February 6, 2023, the country had already registered 10 cases of Nipah virus for the year, with 7 of those cases proving fatal (Nazmunnahar et al., 2023; Rahman et al., 2021).

3. India

Nipah virus represents a potential threat to global health security. India experienced its first recorded outbreaks in 2001 and 2007, both occurring in the state of West Bengal (Arankalle et al., 2011). A major outbreak in 2018 in the state of Kerala involved a 27-year-old man who presented with encephalitis at a private hospital in Kozhikode District. His family members developed symptoms such as headache, vomiting, and fever, and his brother succumbed to the same illness after a 12-day period (Arunkumar et al., 2019). This outbreak resulted in 21 deaths out of 28 infected individuals (Plowright et al., 2019). Another outbreak in West Bengal, occurring between April 9 and 28, 2007, in the village of Belechuapara, Nadia district, led to five persons becoming ill and dying within a short period (Arankalle et al., 2011). The urban center of Siliguri was also the site of a significant outbreak, which affected hospitalized patients, their family contacts, and medical staff across four hospitals. Japanese encephalitis, which is endemic to the region, was initially suspected, but the epidemiological characteristics pointed to a different etiology, which was later confirmed to be NiV (Chadha et al., 2006).

4. Singapore

During the period of March 10–19, 1999, an outbreak occurred among 11 workers in a single Singaporean abattoir, resulting in cases of Nipah-virus-associated encephalitis or pneumonia and one fatality (Chew et al., 2000). A case-control study identified that all 13 case-patients, compared to 63% of control subjects, reported contact with live pigs, establishing this as the most important risk factor (Chew et al., 2000). In response, Singapore implemented a ban on swine importation from affected Malaysian states on March 3, 1999, followed by a complete ban on Malaysian pig imports and the closure of abattoirs on March 19, 1999, which effectively contained the outbreak (Chew et al., 2000). A subsequent serological survey found that 1.5% of tested individuals who had been exposed to the virus had antibodies indicative of NiV infection, and notably, over half of these seropositive individuals (54.5%) were clinically well and reported no history of significant pulmonary or serological disease (Chan et al., 2002).

5. Philippines

An outbreak of Nipah virus was reported in the Philippines in the year 2014, involving over seventeen human cases (Arguin et al., 2002). The clinical presentation of human cases is typically characterized by an abrupt onset of non-specific symptoms such as fever, headache, dizziness, and vomiting (Satterfield et al., 2016). These can rapidly progress to neurological signs, including reduced levels of consciousness, segmental myoclonus, areflexia, hypotonia, and abnormal doll's eye reflex, which usually develop within a week of fever onset (Alam, 2022). Tachycardia has also been observed as part of the clinical picture in some patients (Alam, 2022).

Demographic Outbreak of Nipah Virus

The understanding of human Nipah virus infection was very limited prior to the major outbreak that occurred in Malaysia in 1999 (Mahedi et al., 2023). Surveillance data from Bangladesh, covering the period from April 2001 to December 2021, reported a total of 322 Nipah virus cases, which included 241 (75%) probable cases (Satter et al., 2023). The Malaysian outbreak served as a critical alert to the global public health community, drawing attention to the unique pathogenicity and dissemination potential of this novel paramyxovirus (Daszak et al., 2013). Emerging infectious diseases like NiV are widely recognized as major threats to global public health security (Wong et al., 2002). The discovery of this new human pathogen was made possible through a multidisciplinary investigation that seamlessly integrated epidemiology, microbiology, molecular biology, and pathology (Chua et al., 2000). The Henipavirusgenus,

within the family Paramyxoviridae, includes both Nipah virus and Hendra virus, and it is now well-established that fruit bats (genus Pteropus) serve as the natural reservoir hosts for these viruses (Chua et al., 2000).

Transmission of Nipah Virus

Nipah virus was first identified as the pathogen responsible for large outbreaks of encephalitis in Malaysia and Singapore that spanned from October 1998 to June 1999 (Goh et al., 2000). The most common symptoms observed in Malaysia were fever (in 97% of patients), headache (61%), and reduced consciousness (55%), with a reported case-fatality rate of 40% (Goh et al., 2000). Epidemiological studies found that the vast majority of case-patients either lived on pig farms (95% in Malaysia) or were employed in abattoirs (100% in Singapore) (Chua et al., 2000). Subsequent serologic and reverse transcription–PCR (RT-PCR) testing of pteropid fruit bats in Malaysia and Cambodia confirmed Nipah virus infection in these animals, providing strong evidence that they act as the reservoir hosts (Chua et al., 2000). The transmission dynamics during the Southeast Asian outbreaks appeared to be bimodal, involving bats and pigs. In Malaysia and Singapore, close contact with pigs was the primary risk factor for human infection, while studies of healthcare workers suggested that the risk for nosocomial transmission in that context was relatively low (Gurley et al., 2007).

In contrast, the transmission pattern observed in Bangladesh is notably different. There, no intermediate animal host like pigs has been consistently identified in relation to the outbreaks (Gurley et al., 2007). Since 2001, outbreaks of Nipah virus have occurred almost every year in Bangladesh and are characterized by higher case-fatality rates (Hsu et al., 2004). Epidemiological data strongly suggest that in Bangladesh, the virus is transmitted directly from its natural reservoir, fruit bats, to humans. This primarily occurs through the consumption of raw date palm sap that has been contaminated with bat excreta, with subsequent human-to-human transmission playing a significant role in amplifying outbreaks (Luby et al., 2009, as cited in Gurley et al., 2007). The first recognized human cases of Nipah virus infection in Bangladesh occurred in 2001, when 13 people developed Nipah virus encephalitis, nine of whom died (Hsu et al., 2004).

The outbreak in Singapore among abattoir workers in March 1999 led to swift public health interventions. A ban on swine importation from Malaysian states experiencing the outbreak was imposed on March 3, 1999, followed by a comprehensive ban on all pig imports from Malaysia and the closure of abattoirs on March 19, 1999 (Chew et al., 2000). The first reported outbreak of Nipah virus in South India occurred in 2001, with another outbreak following in 2007 (Arankalle et al., 2011). The 2018 outbreak in Kerala, India, demonstrated multiple transmission routes, with evidence of both animal-to-human (potentially from bats or pigs) and human-to-human transmission, the latter occurring through close contact with infected patients (Arunkumar et al., 2019).

Clinical Features of Nipah Virus

Numerous studies have been conducted to characterize the clinical features of patients with Nipah virus encephalitis who were admitted to various hospitals in Kuala Lumpur, Malaysia, Singapore, and more recently, Kerala, India (Goh et al., 2000; Arunkumar et al., 2019). The case definition for these studies was typically based on a combination of neuroimaging findings, thorough clinical evaluations, cerebrospinal fluid (CSF) analysis, and relevant epidemiological data (Goh et al., 2000). The primary and most commonly observed symptoms across outbreaks were headache, fever, dizziness, and vomiting (Goh et al., 2000). In one specific study conducted between February and June 1999, a total of 94 patients were diagnosed with Nipah virus infection. The average age of these patients was 37 years, and the male-to-female ratio was disproportionately high at 4.5 to 1. A striking 93 out of the 94 patients reported having had direct contact with pigs within the two weeks preceding the onset of their illness (Goh et al., 2000). A significant proportion of the patients (52%) experienced decreased consciousness and notable brainstem dysfunction, indicating severe neurological involvement (Goh et al., 2000).

The incubation period for NiV infection is known to vary widely, ranging from 4 to 21 days (Shariff, 2019). Several distinctive clinical signs have been documented, including segmental myoclonus, areflexia, hypotonia, hypertension, and tachycardia. These signs are highly suggestive of pathological involvement of the brainstem and the upper cervical spinal cord (Epstein et al., 2006). Laboratory analysis of cerebrospinal fluid revealed abnormalities in the majority of patients (75%), though these findings were often non-specific (Lim et al., 2003). Serological testing confirmed the presence of antibodies against Hendra virus (which cross-react with NiV) in the blood serum or cerebrospinal fluid of 92% of the patients (76 out of 83) (Lam & Chua, 2002). A common finding among the 33 patients who died was severe and widespread brainstem involvement (Lam & Chua, 2002). The clinical course can also be complicated by neurological relapse, which has been observed in some patients following an initially mild presentation of the disease (Lim et al., 2003). Outcomes vary

significantly; while 53% of patients in one cohort made a full recovery, a substantial minority (15%) were left with persistent and often debilitating neurological deficits (Hsu et al., 2004).

Pathogenesis of Nipah Virus

Hendra virus (HeV) and Nipah virus (NiV) are two emerging zoonotic pathogens capable of causing severe respiratory disease and inflammation of the brain (encephalitis) in humans (Escaffre et al., 2013). These viruses possess the ability to infect a broad range of species, and in the case of Nipah virus, well-documented instances of human-to-human transmission have occurred (Gurley et al., 2007). Although the precise route of entry in human infections is not completely defined, studies conducted on animal models suggest that the respiratory tract may serve as a primary portal of entry for the virus (Escaffre et al., 2013).

Knowledge of the pathogenesis of Hendra and Nipah viruses has been largely derived from detailed histopathological studies of affected tissues (Hooper et al., 2001). A hallmark of infection with both viruses is the formation of syncytial cells within the endothelial lining of blood vessels. This pathology primarily targets the vasculature and/or the nervous system, culminating in clinical manifestations of pneumonia or encephalitis (Hooper et al., 2001). In pigs, Nipah virus also demonstrates a tropism for the respiratory epithelium, which contributes to the high contagiosity observed in infected swine populations (Hooper et al., 2001).

Gross pathological findings during autopsies are often non-specific and can be challenging to identify, particularly within the central nervous system (CNS) (Wong et al., 2002). In a limited number of cases, however, small, distinct, and sometimes hemorrhagic necrotic lesions have been discovered upon examination (Wong et al., 2002). Histopathological examination consistently reveals widespread damage to blood vessels and surrounding tissues across multiple organ systems (Wong et al., 2002). The severe and often overwhelming involvement of the central nervous system is the primary reason why symptomatic patients typically present with signs and symptoms of acute encephalitis. This clinical picture results from a complex interplay of ischemia, microinfarction due to vascular damage, and direct neuronal infection by the virus, all of which contribute to the profound neurological manifestations seen in severe cases (Wong et al., 2002).

Diagnosis

The early and accurate diagnosis of NiV infection is critical for initiating appropriate patient care and implementing public health containment measures. This relies on a suite of laboratory tests, including nucleic acid amplification tests (NAAT), enzyme-linked immunosorbent assays (ELISA) for the detection of IgG, IgM, or viral antigens, immunofluorescence assays, histopathological examination, and traditional virus isolation and neutralization techniques (Mazzola & Kelly-Cirino, 2019). Diagnostic samples can be collected from symptomatic individuals or during post-mortem examinations. For serological diagnosis, it is recommended to collect convalescent serum samples 10 to 14 days after the onset of infection to allow for antibody development (Shariff, 2019). In India, the National Centre for Disease Control (NCDC) recommends the collection of throat swabs (placed in viral transport medium), urine, blood, and cerebrospinal fluid (CSF) for diagnostic purposes (Singh et al., 2019). Ensuring the safe collection and transport of these samples is paramount; they should be packaged using a triple-container system and maintained at a temperature of 2-8°C during transit. For long-term storage beyond 48 hours, freezing at -20°C is recommended (Shariff, 2019). It is important to note that processing potentially infectious samples for virus isolation requires a Biosafety Level 4 (BSL-4) facility. However, the technique of sample irradiation has been explored as an effective method to inactivate the virus, thereby rendering the samples safe for subsequent molecular analysis in a lower-containment BSL-2 laboratory (Singh et al., 2019). Confirmatory diagnosis of human or animal NiV infection can be achieved through the isolation of the virus itself, in addition to performing serological tests and assays designed to amplify viral nucleic acids (Singh et al., 2019).

In response to the diagnostic challenges posed by outbreaks in remote settings, Molbio Diagnostics Pvt. Ltd. in Goa collaborated with the ICMR-National Institute of Virology (NIV) in Pune to develop a point-of-care (PoC) molecular test for NiV (Yadav et al., 2021). This test underwent a rigorous validation process by ICMR-NIV and received the necessary approvals from the Institutional Project Review Committee, the Institutional Biosafety Committee, and the Institutional Human Ethics Committee (Yadav et al., 2021). Another diagnostic advancement involved research where the DNA coding for the G protein of NiV was cloned and expressed using a baculovirus system (Eshaghi et al., 2004). The purified recombinant G protein was then successfully utilized in an ELISA format for the serological screening of serum samples obtained from naturally infected swine during the 1998-1999 outbreak. This method offers advantages over using the whole virus antigen, as the production of the recombinant protein is more efficient and less time-consuming. Furthermore, this antigen is non-

infectious, eliminating the need for high-level biocontainment facilities during the assay procedure (Eshaghi et al., 2004).

Many molecular diagnostic tests for NiV are designed to target the Nucleocapsid protein (N) gene, with specific regions selected for the design of primers and probes (Pollak et al., 2023). Given that NiV outbreaks often occur in rural and remote locations with limited infrastructure, there is a pressing need for diagnostic tools that can be deployed in decentralized laboratories or field settings. Isothermal NAAT platforms are particularly promising in this context, as they have lower infrastructure requirements compared to traditional PCR. When combined with safe and straightforward sample preparation methods, these isothermal assays can be effectively utilized in low-resource settings and require less extensive training for healthcare personnel (Pollak et al., 2023). Beyond immediate diagnostics, the genomic sequencing of NiV isolates from outbreaks, complemented by techniques like electron microscopy, has significantly enhanced the scientific understanding of viral divergence, structure, and various aspects of the virus's life cycle (Thakur & Bailey, 2019).

Control and Management

The clinical management of suspected or confirmed NiV cases requires immediate isolation and the strict enforcement of infection control measures to prevent transmission (Shariff, 2019). The mainstay of medical treatment is intensive supportive care, with a focus on supporting airway, breathing, and circulation. Maintaining proper fluid and electrolyte balance is also a critical component of care (Banerjee et al., 2019). Patients who develop severe pneumonia and progress to acute respiratory failure often require mechanical ventilation, with invasive ventilation being the preferred method in such critical cases (Banerjee et al., 2019).

There has been considerable and promising progress in the development of pre-clinical platforms for NiV-specific disease interventions. Several therapeutic and vaccine candidates have been extensively tested and have demonstrated success in animal models such as hamsters, African green monkeys (AGMs), and ferrets, showing good correlation with established models of pathogenesis (Thakur & Bailey, 2019). The ideal therapeutic agent or vaccine would be one that elicits a robust neutralizing antibody (nAb) response, as this has been consistently shown to correlate with protection in animal challenge studies. This scientific rationale justifies the strategy of targeting the NiV F and G surface glycoproteins as immunogens for vaccine development (Thakur & Bailey, 2019). A primary consideration for the eventual deployment of such a vaccine is that it would be needed most in low- and middle-income regions where NiV is endemic, despite its sporadic outbreak pattern. Consequently, it is crucial that any licensed vaccine is affordable, has an excellent safety profile, is thermostable to overcome cold-chain limitations, and is capable of inducing long-lasting immunity (Thakur & Bailey, 2019). One potential approach that holds promise is the development of a single-dose, combination, vectored vaccine that provides cross-reactive protection against both the Malaysia (NiV-M) and Bangladesh (NiV-B) strains, as well as against the related Hendra virus. Such a vaccine could be stockpiled for emergency use during outbreaks and would ideally induce a rapid onset of protective immunity (Thakur & Bailey, 2019).

Prevention and Treatment

At the present time, there are no specific medications or vaccines licensed for the treatment or prevention of Nipah virus infection in humans (Satterfield et al., 2016). The primary approach to managing infected individuals is therefore focused on symptomatic relief and the provision of intensive supportive care (Banerjee et al., 2019). The drug Ribavirin, a broad-spectrum antiviral, has been used empirically in some outbreaks in an attempt to alleviate symptoms such as nausea, vomiting, and convulsions, though its efficacy remains a subject of debate (Chua et al., 2000). Treatment protocols mainly concentrate on managing fever and addressing the severe neurological symptoms that characterize the disease (Lam & Chua, 2002).

For the general public, particularly those traveling to areas affected by the Nipah virus, taking precautionary measures is essential to minimize the risk of infection. This includes avoiding any contact with both domestic and wild animals, with particular emphasis on bats and pigs. Maintaining strict personal hygiene, including frequent handwashing, is also crucial (WHO, 2018, as cited in Ambat et al., 2019).

Antiviral Chemotherapy

Ribavirin, which has demonstrated clinical effectiveness against other viruses in the Paramyxoviridae family such as Respiratory Syncytial Virus, was used during the Malaysian outbreak on an empirical basis to treat infected patients (Chua et al., 2000). Some subsequent studies reported an associated decrease in mortality, while other analyses from the same outbreak found no significant reduction in deaths (Lam & Chua, 2002). Importantly, controlled testing in animal models later demonstrated that Ribavirin is not effective against NiV (de Wit et al., 2011, as cited in Thakur & Bailey,

2019). Despite this evidence, in the absence of any proven antivirals, the Indian NCDC guidelines continue to recommend the use of oral or parenteral Ribavirin for all confirmed cases, though it is not recommended for post-exposure prophylaxis (Shariff, 2019). The antiviral drug Acyclovir was used during the Singapore outbreak, but its effectiveness against NiV remains unproven and unclear (Chan et al., 2002). Chloroquine showed inhibitory effects in cell culture experiments but failed to prevent death in a hamster model, both when used alone and in combination with Ribavirin (Freiberg et al., 2010, as cited in Thakur & Bailey, 2019). In vitro studies have indicated that natural ligands of the host receptor Ephrin-B2, as well as soluble Ephrin-B2 itself, can block viral entry and are effective (Negrete et al., 2005, as cited in Thakur & Bailey, 2019). Favipiravir, an antiviral drug licensed in Japan for the treatment of influenza, has also shown promise and demonstrated effectiveness in a hamster model of NiV infection (Dawes et al., 2018, as cited in Thakur & Bailey, 2019). A highly significant development has been the demonstration that neutralizing human monoclonal antibodies are effective in protecting non-human primates from lethal NiV challenge (Georges-Courbot et al., 2006, as cited in Thakur & Bailey, 2019). In India, the use of anti-G and anti-F monoclonal antibodies is approved for emergency/compassionate use in outbreak situations (Yadav et al., 2021). From an infection control perspective, patients are typically discharged only after a negative RT-PCR result is obtained from a throat swab or blood sample. The exact period of communicability is unknown but is presumed to extend up to 21 days post-infection. Therefore, discharged patients are advised to remain in isolation at home until 21 days have passed since the confirmation of their infection (Shariff, 2019).

Surveillance

Effective surveillance is a cornerstone of disease management and preparedness for Nipah virus. Surveillance activities typically encompass both event-based surveillance and formal sentinel surveillance systems (Satter et al., 2023). In countries like Bangladesh, India, Malaysia, Singapore, and the Philippines, event-based surveillance often involves monitoring print and electronic media reports, as well as operating dedicated hotlines for healthcare personnel to report suspected outbreaks or clusters of unusual illness. This enables the rapid identification of potential outbreaks and deaths from unknown causes (Satter et al., 2023). Under sentinel surveillance protocols, any cluster of encephalitis cases is thoroughly investigated. A cluster is generally defined as two or more cases occurring within a 21-day period and within a short geographical distance (e.g., a short walking distance) of each other (Satter et al., 2023). In Bangladesh, for instance, the Institute of Epidemiology, Disease Control and Research (IEDCR) deploys a team of epidemiologists to investigate identified clusters. These investigations aim to identify suspected human cases, trace potential animal sources of infection, understand behavioral factors that may contribute to transmission, and assess possible environmental contamination (Satter et al., 2023). Maintaining vigilant and robust surveillance is considered absolutely crucial not only in areas that have previously experienced outbreaks, such as specific regions of India and Bangladesh, but also in neighboring countries within the South and Southeast Asian region that are at potential risk (Plowright et al., 2019).

II. CONCLUSIONS

Over the course of the past two decades, dedicated and significant research efforts have substantially enhanced the global understanding of Nipah virus pathogenesis, transmission dynamics, and epidemiology (Gurley et al., 2020). This accumulated knowledge base is expected to continue its rapid advancement in the coming decade, providing a solid foundation for the eventual initiation of human clinical trials for Nipah virus vaccines and the refinement of targeted preventive measures (Thakur & Bailey, 2019). By strategically utilizing this knowledge, the global health community can develop more effective clinical procedures and therapeutic medications to treat infected individuals, thereby reducing the high mortality and morbidity associated with this deadly virus (Singh et al., 2019). Preventing the spillover and spread of high-consequence zoonotic diseases like Nipah is a paramount objective that requires integrated efforts across agricultural and healthcare settings (Daszak et al., 2013). Scientists and public health experts have repeatedly emphasized the critical importance of establishing a robust network that seamlessly connects veterinary and medical services, fostering effective communication and coordinated action to address this cross-sectoral disease threat (One Health Commission, n.d., as cited in Bruno et al., 2022). Only by involving multiple sectors and steadfastly adopting a multidisciplinary "One Health" approach can the world develop targeted, concrete, and ultimately successful prevention and control methods for Nipah virus and other emerging zoonotic pathogens.

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