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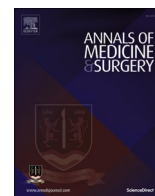
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## Short Communication

## A short communication of Nipah virus outbreak in India: An urgent rising concern

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## ABSTRACT

In the past two decades, countries like Malaysia, Singapore, Bangladesh, and India have recorded several cases of Nipah virus (NiV) infection. Following the 2018 NiV outbreak in the Kozhikode district of Kerala, India that claimed 17 lives, there has been a recent re-emergence of the virus in the same district, causing the recently reported death of a 12-year-old boy. Accordingly, population panic has heightened as inhabitants of these areas try to together combat the existing COVID-19 pandemic alongside the emerging NiV infection. Although the rate of transmission of NiV is low as compared to coronavirus disease 2019 (COVID-19), scientists suggest a higher mortality rate from NiV infection. In this manuscript, we aim to discuss the NiV infection in India as well as suggest recommendations to contain and ameliorate the severe impact of the virus on affected populations.

## 1. Introduction

In the early hours of Sunday, September 5, 2021, the people of Pazhur village in Kerala's Kozhikode district woke up to the news that a tree climber, Vichutti, had lost his son, Muhammad Hashim, after consuming the rambutan fruits he picked by the riverside. Hashim died due to Nipah virus (NiV) infection, the first case in Kerala after the state reported and controlled the May 2018 virus outbreak, during which 17 individuals lost their lives. The death of Hashim has created panic in Southern India as the state battles containing both coronavirus disease 2019 (COVID-19) and Niv concurrently.

Nipah virus (NiV) is a pleomorphic virus with an outer wrapping belonging to the *paramyxoviridae* family and the *henipavirus* genus. The genetic component of the virus consists of an RNA that is single-stranded, negative, unsegmented and encodes for six genes including nucleocapsid (N), phosphoprotein (P), matrix (M), fusion protein (F), glycoprotein (G) and RNA polymerase (L) [1]. As a zoonotic virus, bats

from the genus *pteropus* serve as natural reservoirs of NiV. The virus is categorized under the Category C priority pathogen and a biological safety level 4 (BSL-4) pathogen by the Centers for Disease Control and Prevention (CDC).

The first cases were reported in Malaysia and Singapore between 1998 and 1999 after its discovery in Sungai Nipah where it took its origin [2]. Following the initial outbreaks in Malaysia and Singapore, India recorded outbreaks in 2001 and 2007. Bangladesh also reported eight outbreaks from 2001 to 2012 [3]. In Kozhikode district, Kerala, India, another outbreak was reported on May 19, 2018 [3]. The most recent incidence of NiV infection was reported on September 5, 2021, in the same Kozhikode district, Kerala, India. As COVID-19 continues to rage in some countries, complications in rapid diagnosis and treatment of NiV infection can occur [4–10].

As a result of the high fatality rate of NiV infection, this paper outlines the epidemiology, aetiology, transmission, diagnosis, clinical management and prevention control measures of the NiV to share

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knowledge that is imperative to control the virus effectively.

## 2. Epidemiology and outbreak of Nipah virus in India

In India, Siliguri, West Bengal recorded a significant NiV epidemic in 2001 with 66 presumed cases and 45 deaths. The Nadia district in West Bengal experienced a minor outbreak in 2007 with five cases and a 100% fatality. These epidemics occurred over the border from the Nipah belt in Bangladesh. The Kerala districts of Kozhikode and Malappuram recorded a NiV outbreak in May 2018, although a southern state on the west coast that is geographically isolated from areas that were formerly affected and where date palm sap intake is not widespread. The index case remained undetected in Siliguri in 2001. However, the patient was hospitalised at the Siliguri District Hospital and later infected 11 patients at the same hospital.

Further transmission affected 25 employees and eight visitors after said infected patients were transferred to other hospitals [1]. In the 2007 epidemic, an individual developed the disease after consuming date palm-derived alcohol. The rest, including one healthcare professional, became infected from the initial case [2].

As of June 1, 2018, there had been 18 confirmed cases of NiV infection and 17 fatalities due to the virus [3]. All of the cases were in the economically productive age range, with no sex difference [11,12]. During the 2018 epidemic, no less than one healthcare practitioner acquired the virus in a healthcare facility [13–15]. The most recent epidemic of the NiV was reported on Sunday, September 5, 2021, in Kozhikode district, Kerala, India. A 12-year-old boy, Hashim, died after eating rambutan fruits gathered by his father, Vichutti, along the riverbank. As seen above, all NiV outbreaks occurring in India have been transmitted from person to person.

## 3. Aetiology of Nipah virus infection

The spread of the virus can occur through direct contact with infected animals or the consumption of food or fruits contaminated with the body fluids of infected animals like bats and pigs. Infection can also occur when an individual comes in close contact with an infected person or their bodily fluids, including urine, blood, nasal droplets, and saliva. Reports show that in Malaysia, humans became infected with the virus through pigs which act as intermediate hosts of the virus [16]. These pigs can become infected through the consumption of contaminated fruits by bats infected with the virus [17]. Similarly, humans can become infected through the consumption of infected pigs or bats. The virus can also spread from person to person through direct contact with infected individuals or contact with aerosols from said infected individuals.

A report in Bangladesh that showed some persons infected with the virus had eaten raw palm sap approximately 30 days before disease onset. This proposes that contaminated palm sap by infected bats may serve as the causative agent [18]. There was also a high rate of person-to-person transmission in Bangladesh [19,20]. Similarities exist between the NiV outbreaks in Bangladesh and India as they were both characterized by person-to-person transmission [20]. To note, these outbreaks were majorly healthcare-associated as hospital staff and caregivers were mostly affected [21]. Although the information is not proven, the Siliguri outbreak is said to have begun in Kerala where the index patient was reported to have caught the virus from infected fruit bats. Further infection occurred through hospital exposure; hence the rate of person-to-person transmission in Kerala was high and like those in Bangladesh and Bengal [21,22].

## 4. Relationship between coronavirus and Nipah virus

There have been speculations among scientists that the next pandemic agent after COVID-19 could most likely be NiV. However, in states like Kerala, COVID-19 precautions have helped mitigate the spread of the NiV. NiV infection, like COVID-19, is also a respiratory

disease and thus, shows similar symptoms. However, loss of sense of smell and taste, which has been noted as a characteristic symptom of COVID-19 infection, is not common with NiV infection. Similarly, some persons who contract NiV remain asymptomatic.

The WHO estimates that the NiV fatality rate is high (40–45%), making it far deadlier than COVID-19, which has a mortality rate between 0.1% and 19% depending on the region of infection. Unlike with COVID-19 when infected individuals are most infectious before symptoms appear, NiV patients demonstrate peak infectious potential during symptomatic stages. To note, although the fatality rate of NiV infection is high, it is less transmissible than COVID-19.

## 5. Clinical signs and symptoms

Variations occur with the incubation period of NiV across several regions. The incubation period in Malaysia was observed to range between four days to two months. The incubation period span ten days and 6–14 days in Bangladesh and Kerala respectively [22–24]. Clinical features of NiV infection are broad, ranging from asymptomatic to severe. Respiratory distress, nausea, vomiting, headache, fever, and acute encephalitis are major clinical features associated with NiV infection. Other symptoms, such as behavioural distortion, disorientation, pneumonia, and diminished consciousness, have been reported in some patients [25–27]. Muscle pain, cough, nervous system disturbances, seizures, and encephalitis alongside other general symptoms were observed in infected persons during the Kerala outbreak [28–34]. Higher rates of cases characterized by respiratory discomfort were particularly observed in Bangladesh and India outbreaks [35].

## 6. Diagnosis

Early detection serves as the rate-limiting step in containing the spread of the virus and mitigating its fatality rate. Diagnosis can be done in both live patients and deceased carriers. In live patients, samples like cerebrospinal fluid, throat swab, nasal swab, blood, and urine can be used for the diagnosis of NiV infection. Samples such as spleen, kidney and lung biopsy can be used for diagnosis in dead patients. Isolation and propagation of NiV-infected patients require enhanced biosafety level 3 and 4 facilities. A wide array of tests can be employed in the detection of NiV, including virus isolation and neutralization, immunohistochemistry, molecular and serological assays, and enzyme-linked immunosorbent assay (ELISA), and polymerase chain reaction (PCR) [36]. NiV culture can be performed using Vero cells and within three days, cytopathic effects can be observed [37].

PCR is the most sensitive and widely used method of diagnosing NiV. Several types of PCR tests have been developed for NiV detection including conventional reverse transcriptase (RT)-PCR, nested RT-PCR, and real-time RT-PCR (the most widely used test yielding a sensitivity of 1000 times more than conventional PCR) [38]. Noteworthy is the possibility of such techniques being compromised if the viral genome becomes mutated [36,38]. Although PCR is the most preferred diagnostic method, NiV-specific immunoglobulin M ELISA can be used as an alternative approach in the absence of PCR [39]. Immunohistochemical assays provide post-mortem confirmation of NiV diagnosis in fatal cases. Viral isolation and neutralization assays are employed for general confirmation of NiV and are confined to BSL-4 facilities with strict safety measures [36].

## 7. Treatment

Treatment available to infected individuals is currently limited to supportive care, as there are no approved treatments for NiV infection. Ribavirin and acyclovir have been administered during past outbreaks to treat NiV infection. Ribavirin was administered either intravenously or orally to patients presenting with NiV encephalitis in Malaysia and approximately a 36% decrease in the mortality rate was observed [40].

In Singapore, acyclovir was administered to all patients presenting with NiV encephalitis and only one case of death was reported. Although there is supporting evidence of the use of these drugs in managing NiV, their role in the treatment of NiV remains unclear [40,41]. Recently, there have been ongoing investigations on the potency of vaccine administration and the efficacy of antiviral therapies in the treatment of NiV infection. This shows hope for a better NiV prognosis in the future [42,43]. However, due to the increased mortality rate of NiV infection and its severe impact on community health, specific antiviral agents must be developed for the early treatment of infected individuals.

## 8. Prevention and control

Preventive and control measures focus on proper identification of infected individuals and further isolation to contain the outbreak. Transmission of NiV from patient to health worker or caregiver can be controlled through regular hand washing and avoiding shared foods and bedding with infected patients [4,5]. It is important to wear protective personal equipment (PPE), such as face masks and gloves while handling the corpse of an infected individual to prevent contracting the virus from the infected corpse [6–8,10,44]. In low-resource countries with limited access to PPE, handwashing with soap and water after contact with the corpse of an infected person can provide some level of protection against the disease [45,46]. The transmission of NiV to health workers can be mitigated by encouraging adequate handwashing practices, stringent use of PPE, and the isolation of infected patients [45].

Preventive measures, such as the bamboo skirt method, can be used to reduce date palm sap contamination. This bamboo skirt method typically involves the hanging of the pot over a bamboo skirt and covering its shaved part and mouth. Another method is the sap branch technique which involves the covering of the shaved part of the tree with branches from the same tree or with clothes or a mosquito net [47,48]. Fruits should be properly washed and after each preparation, individuals should ensure their hands are thoroughly washed to prevent the spread of the disease [49]. Awareness campaigns can be organized in communities to educate the public on the risk factors as well as buttress the importance of strict adherence to preventive measures in containing the spread of the virus [9,50–53].

Media communication like television, radio channels, posters as well as physical-based programs can be utilized to improve awareness of the virus among different populations, especially among impoverished populations [34,47,54–56].

## 9. Efforts to mitigate the disease

During the 2019 outbreak in Kerala, the Union Health Minister formed a specialized team to appraise and counter the NiV outbreak. This team was formed by physicians (neurologists and infectious disease experts), microbiologists and public health experts [57–59]. Pre-set guidelines to address the outbreak were already prepared following the experiences of previous outbreaks [60]. The main roles and responsibilities of this team included: Addressing the diagnostic and treatment guidelines, epidemiological and risk assessment studies, containment measures, addressing the dead body disposal protocols, emergency operations activation, and reporting events to the international authorities. Veterinary experts also played a major role in identifying and sting the diseased bats. Moreover, the directorate of health in Kerala as well as the State Programme Officer of the Integrated Disease Surveillance Programme put on efforts for infection control by establishing control rooms, contact tracing program, cremation guidelines, providing resources, and ensuring proper handling infected medical wastes management. To add, the Nipah cell (District Rapid Response Team), composing of public health experts as well as computers and information technology experts, developed a cyber space monitoring and worked on raising awareness through informative videos and posters [56,61,62].

Despite all these measures to control the disease, yet a lack of specific antiviral treatments and vaccination measures still impose a high mortality risk on the population. Health authorities should focus more on clinical trials to speed up the vaccination innovation, and to emphasize more on the effectiveness of the mentioned measures taken by the government in mitigating the disease.

## 10. Conclusion and recommendation

Over the past two decades, NiV outbreaks have been recorded in several countries ranging from Malaysia, Singapore, and Bangladesh, with the most recent reports in Kerala, India. Such outbreaks have posed a significant threat to the economy and community health of affected countries owing to the high mortality and mobility rate of the NiV infection. Furthermore, expert scientists have speculated that NiV may potentially classify as the next pandemic agent after COVID-19. Consequently, it is pertinent that preparedness and sufficient awareness among the public, especially those of affected regions, are implemented to control and effectively contain NiV outbreaks. Additionally, banning the transportation of pigs in affected regions and improved hygiene practices at pig operation centers are highly recommended. Moreover, collaborative efforts should be made toward the accelerated development of specific treatment regimens to prevent any further emergence of NiV.

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### Author contribution

**Olivier Uwishema:** Conceptualization, Project administration, Writing-review and Designing, **Kamsi Olivia Muoka:** Collection and assembly of data, **Olivier Uwishema** – Reviewed and edited the first draft, supervisor, **Jack Wellington** – Reviewed and edited the second draft, **Helen Onyeaka:** Reviewed and edited the final draft, Supervisor, **Christin Berjaoui** and **Olivier Uwishema:** Worked on revision, **Manuscript writing:** All authors, **Final approval of manuscript:** All authors.

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## Declaration of competing interest

No conflicts of interest declared.

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