บทความฟื้นวิชา **Review Article**

การกระจายทางภูมิศาสตร์และรูปแบบฤดูกาลของการระบาดของโรคติดเชื้อไวรัสนิปาห์
Geographical Distribution and Seasonal Patterns of Nipah Virus Disease Outbreaks

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บทคัดย่อ

ไวรัสนิปาห์เป็นปัญหาสาธารณสุขที่สำคัญ โดยองค์การอนามัยโลกจัดให้เป็นหนึ่งในไวรัสอุบัติใหม่ที่อันตรายที่สุด เนื่องจากสามารถก่อให้เกิดโรคทางเดินหายใจรุนแรงและโรคสมองอักเสบ ซึ่งมีอัตราการเสียชีวิตสูง การระบาดของไวรัสนี้ไม่เพียงส่งผลกระทบต่อสุขภาพของประชาชนเท่านั้น แต่ยังกระทบต่อระบบสาธารณสุขเศรษฐกิจ สร้างความตื่นตระหนกในสังคม การเปลี่ยนแปลงสภาพภูมิอากาศและการขยายตัวของเมืองทำให้มนุษย์มีโอกาสสัมผัสกับสัตว์ป่ามากขึ้น จึงยิ่งเน้นย้ำถึงความสำคัญของการทำความเข้าใจไวรัสชนิดนี้ เพื่อป้องกันการระบาด แม้ว่าไวรัสจะยังไม่กลับมาระบาดซ้ำในประเทศมาเลเซีย สิงคโปร์ และฟิลิปปินส์ แต่ในบังกลาเทศและอินเดียยังคงเกิดการระบาดอย่างต่อเนื่อง ซึ่งมักเกี่ยวข้องกับช่วงฤดูผสมพันธุ์ของค้างคาวและฤดูกาลเก็บเกี่ยว อินเดียพบการระบาดแล้ว 9 ครั้ง ขณะที่บังกลาเทศพบการระบาดเกือบทุกปี โดยมีลักษณะการระบาดตามฤดูกาลและพื้นที่เฉพาะข้อมูลเกี่ยวกับการกระจายทางภูมิศาสตร์และฤดูกาลของการระบาดไวรัสนิปาห์จึงเป็นประโยชน์ต่อการทำความเข้าใจการแพร่เชื้อข้ามสายพันธุ์ และสนับสนุนการวางกลยุทธ์ด้านสาธารณสุขได้อย่างมีประสิทธิภาพ

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Abstract

Nipah virus is a major public health concern, recognized by the World Health Organization as one of the most dangerous emerging viruses due to its ability to cause severe respiratory illness and encephalitis, with a high mortality rate. Its outbreaks have far-reaching consequences beyond health, affecting healthcare systems, economies, and causing widespread public anxiety. Climate change and urban expansion have increased human

contact with wildlife, highlighting the importance of understanding the Nipah virus for outbreak prevention. Although the virus has not re-emerged in Malaysia, Singapore, and the Philippines, it continues to cause outbreaks in Bangladesh and India often linked to the bat breeding season and harvest periods. Since the first outbreak, India has reported nine outbreaks, while Bangladesh experiences nearly annual occurrences, often showing seasonal patterns and geographic specificity. Understanding the geographical distribution and seasonal trends of Nipah virus outbreaks is essential for identifying cross-species transmission patterns and supporting effective public health strategies.

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Keywords: Nipah virus, Cross-species transmission, Zoonosis, Disease outbreak

Introduction

Cross-species transmission refers to the transmission of an infectious pathogen from one host species to another. Diseases that can be transmitted across-species to humans are referred to as zoonotic diseases or zoonoses. Cross-species transmission occurs mainly with viruses and can occur when there is contact between the main host of a virus and an alternative host which the virus can enter. Viruses that mutate rapidly are able to evolve and adapt to the new host quickly, leading to emergence in the new host. Cross-species transmission to humans can occur even when there is no direct contact between humans and the main host of a virus, given that there is an intermediate host with close contact to humans such as pigs and horses[(1)]. Many severe modern infectious diseases, including rabies, ebola, and avian influenza, are caused by zoonotic pathogens. The SARS-CoV-2 is another zoonotic pathogen that led to a pandemic in 2020 after it was successfully transmitted from bats to human hosts.

In September 1998, an outbreak of viral encephalitis primarily affecting pig-farmers occurred in Malaysia. The main presenting symptoms of those affected include fever, headache, dizziness, and vomiting[(2)]. The virus behind the outbreak was suspected to be related to the Hendra virus but identified to be distinct due to the fact that infections caused by the Hendra virus are mostly pulmonary while the infection caused by the new virus usually affects the central nervous system and does not affect any part of the respiratory system. The Hendra virus is also known to be transmitted from horses while the new virus was associated with contact with pigs[(3)]. Due to these differences, the virus was recognised as distinct and named the Nipah virus (NiV)[(3)].

In recent years, the NiV has emerged as a significant pathogen, posing serious public health challenges in several regions, particularly in South and Southeast Asia. This zoonotic virus, which primarily originates from fruit bats, has shown the ability to cause severe respiratory illness and neurological complications in humans, leading to high fatality rates. Understanding the biology of the Nipah virus is crucial, as it highlights the complex interplay between its viral structure, modes of transmission, and the ecological factors that facilitate its spread. Due to its rapid transmission and the potential for outbreaks, particularly in densely populated areas, researchers are focusing on elucidating its genetic characteristics and

virulence mechanisms. As the global interconnectedness increases, the study of the NiV biology is not only critical for the development of effective therapeutic and preventive measures but also for enhancing overall pandemic preparedness.

Methodology

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Literatue review

Nipah virus outbreaks

The historical context of Nipah virus outbreaks reveals a complex interplay between zoonotic transmission and human encroachment into wildlife habitats, particularly in South and Southeast Asia. The initial identification of the NiV occurred between 1998 and 1999 in the village of Sungai Nipah on the Malaysian peninsula, which is the origin of the name 'Nipah'. Since then, the NiV has re-emerged sporadically, with significant incidents reported in Bangladesh and India.

The NiV outbreak in Malaysia occurred from September 1998 to May 1999, causing 265 cases of acute encephalitis and 105 deaths, greatly impacting the pig-farming industry[4]. A study shows that 93.0% of patients in a Malaysian medical center diagnosed with the virus had contact with pigs 2 weeks before the onset of symptoms[2]. The disease primarily transferred to humans through contact with infected pigs, leading to pig culling to halt the outbreak. From 10 to 19 March 1999, 11 workers in a Singaporean abattoir got sick with the NiV-related encephalitis or pneumonia, leading to one death. Most case patients had contact with live pigs. To control the outbreak, the importation of pigs from affected Malaysian regions was banned on 3 March 1999, and abattoirs closed by 19 March 1999[5].

In 2001, Bangladesh experienced the NiV outbreaks. Since then, there have been yearly reports of recurrent the NiV outbreaks in various regions of Bangladesh. In Bangladesh, date palm sap is a traditional beverage. Since many cases have reported consuming raw date palm sap within 30 days prior to the commencement of the disease, it is believed that drinking raw date palm sap contaminated with the NiV is the cause of the NiV epidemics in Bangladesh[6]. People have contracted the virus through consumption of date-palm sap tainted by bat excreta, highlighting the critical link between human behaviors and viral transmission. The continuous dynamics of the NiV in its wildlife reservoir, particularly in *Pteropus medius* bats, further complicate this issue, as evidenced by findings that transmission occurs year-round and varies across regions, including outbreaks in Kerala, India, which showcased an increased transmission following declines in bat populations. As communities expand into these natural habitats, the risk of spillover events grows, necessitating proactive health measures[7].

In 2001, there was the NiV outbreak in Siliguri, West Bengal, India, with 66 suspected cases and 45 fatalities. In 2007, there was a small outbreak in West Bengal's Nadia area, with five cases and a 100.0% death[8]. These outbreaks happened over the Bangladeshi border from the Nipah belt. Later the NiV outbreaks occurred in Kerala state which is a southern state on the west coast that is physically remote from previously affected areas and where date palm sap intake is uncommon.

In 2014, an outbreak of the NiV occurred in two villages in southern the Philippines. Seventeen cases were confirmed and 10 horses died in the same time. The outbreak was linked to contact with contaminated fluids from the slaughter of infected horses and eating undercooked horse meat. Five patients, including two healthcare workers, contracted the disease through person-to-person transmission[9].

Since the NiV appeared in 1998 in Malaysia, the NiV disease outbreaks has been reported in five countries in South and Southeast Asia: Bangladesh, India, Malaysia, the Philippines, and Singapore. As of May 2024, there are 754 confirmed human cases and 435 deaths. Bangladesh has the most cases and deaths (341 cases and 241 deaths). followed by Malaysia (283 cases and 109 deaths), India (102 cases and 74 deaths), the Philippines (17 cases and 9 deaths), and Singapore (11 cases and 1 death)[10]. The distribution of the NiV disease outbreaks in those countries is shown in Figure 1

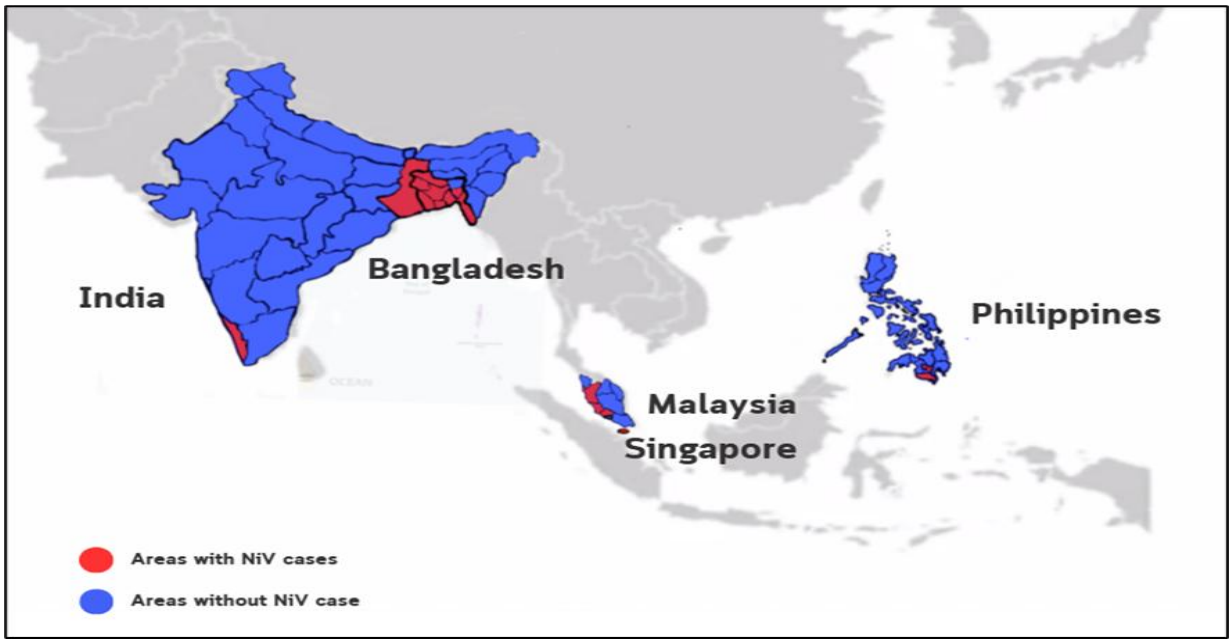

Figure 1 Distribution of Nipah virus disease outbreaks in humans

After the first NiV outbreaks in Malaysia, Singapore, and the Philippines, no NiV outbreak reemerges again in those countries. On the contrary, NiV outbreaks continuously reemerge many times in Bangladesh and India as shown in Table 1 and Table 2. Since the first NiV outbreak in India (2001), the NiV outbreaks happened nine times in eight years in which the outbreaks happened two times in 2024[11]. In Bangladesh, the situation is more serious. the NiV outbreaks continuously happened almost every year[12].

The NiV outbreaks in India and Bangladesh have a seasonal pattern. the NiV outbreaks in India were reported only in two states which are geographically far apart. The first two NiV

outbreaks (2001 and 2007) in India occurred in West Bengal state which locates in the eastern part of India and shares the border with Bangladesh. These former NiV outbreaks happened in the first four months of the year (January - April). After that, all of the subsequence NiV outbreaks in India occurred in Kerala state which locates in the west coast of southern part of India. The later consequence NiV outbreaks happened in the second four months of the year (May – August). Possibly, the causes of NiV outbreaks in these two states are different. In Bangladesh, among the eight administrative divisions, many cases of NiV infection were reported in four divisions (Dhaka, Khulna, Rajshahi, and Rangpur)[13]. Less cases were reported in Barisal, Chittagong, and Mymensingh divisions. Only Sylhet division, which is on the north eastern part of Bangladesh, has no case reported. Except the first outbreak in 2001, the record of NiV outbreaks during 2003 – 2012 reveals that the NiV outbreaks in Bangladesh happened in the first four months of the year. The emergence of NiV outbreaks in Bangladesh and in West Bengal state of India which is adjacent to Bangladesh are in the same period. Possibly, the causes of NiV outbreaks in these two areas are the same.

Table 1 Time periods of NiV disease outbreaks in Bangladesh in 2001 - 2012

Month / Year	1	2	3	4	5	6	7	8	9	10	11	12
2001				■	■							
2003	■											
2004	■			■								
2005	■	■	■									
2007	■	■	■	■								
2008	■	■		■								
2009	■											
2010		■	■									
2011	■	■										
2012		■										

Table 2 Time periods of Nipah Virus outbreaks in India in 2001 - 2024

Month / Year	1	2	3	4	5	6	7	8	9	10	11	12
2001	■	■										
2007				■								
2018					■							
2019						■						
2021								■				
2023								■				
2024						■		■				

Nipah virus

The scientific name of Nipah virus is *Henipavirus nipahense*, which classifies it within the Henipavirus genus in the family Paramyxoviridae[14]. It has an enveloped structure and contains a single-stranded, negative-sense RNA genome[15]. The genome codes for six key proteins necessary for its replication and ability to cause disease, including the nucleoprotein (N), phosphoprotein (P), matrix protein (M), fusion protein (F), glycoprotein (G), and large polymerase protein (L)[16]. Among these, the N protein is particularly important, as it encapsulates the viral RNA, protecting it and aiding in replication[17]. The viral envelope features two glycoproteins, G and F, which play crucial roles in infection. The G protein allows the virus to attach to host cells, while the F protein facilitates the fusion of the viral envelope with the host cell membrane, enabling the virus to enter the cell[15]. The G protein binds to specific receptors, such as ephrinB2, initiating a conformational change that activates the fusion process crucial for viral entry[18]. The duplication of the P gene leads to the production of multiple protein variants, with the V protein playing a critical role in evading the host immune response, as it can inhibit interferon signaling pathways[19]. Furthermore, the structural composition of these proteins is vital for the virus's replication and pathogenesis, illustrating a conserved motif present within the Paramyxovirinae family, suggesting evolutionary significance[20]. Such genomic and protein features underpin the virus ability to persist and adapt within its natural reservoir hosts, contributing to its zoonotic potential.

NiV is categorised into two genetic lineages: NiV-Malaysia (NiV-M), representing and NiV-Bangladesh (NiV-B). NiV-M includes strains associated with the 1998-1999 outbreaks in Malaysia, Singapore and the Philippines. whereas NiV-B encompasses strains responsible for recurring outbreaks in Bangladesh and India. NiV-B strains are particularly notable for higher human-to-human transmission rates compared to NiV-M[15]. However, despite their differences, they retain structural features that support their ability to infect a wide range of hosts and transmit between species[15].

Nipah virus transmission

The Nipah Virus can be transmitted from bats to humans via three main routes. The first route involves the consumption of fruits contaminated with the Nipah virus. In Bangladesh where date palm sap is harvested, it has been observed that *P. giganteus* bats often visit palm date trees undergoing sap collection and lick the sap, introducing their NiV-infected saliva to the sap[14]. During collection, this sap flows slowly overnight into an open clay pot, and is typically ingested as fresh raw juice just hours after collection[21]. Moreover, in regions like Thailand, *Pteropus lylei* bats commonly feed on fruits such as mango, banana, and tamarind, leaving traces of saliva containing NiV on the fruit's surface[15]. Research by Singh and colleagues shows that the NiV can survive in mango flesh, mango juice, and other fruit juices up to three days–depending on the fruit's pH-, heightening the risk of contact with NiV and a spillover[22].

The second route involves the initial transmission of the virus from livestock to humans (including swine, cattle, horses, and goats), followed by subsequent transmission to

humans via direct contact[14]. Between September 1998 and June 1999, there was a nationwide outbreak of viral encephalitis caused by the NiV in Malaysia. A study shows that 93.0% of the patients admitted to a medical centre in Kuala Lumpur had had direct contact with pigs two weeks before the onset of symptoms, demonstrating transmission of the NiV from pigs to humans[2]. This transmission occurs due to virus shedding where the pig's bodily fluids containing the virus such as saliva, urine, and respiratory secretions, come in contact with humans, facilitating its spread.

One of the fastest and most common ways the NiV can spread is via direct contact from human-to-human. Human-to-human transmission has been documented among family members and caregivers of infected individuals, particularly in healthcare settings. A study by Gurley and colleagues showed 36 cases of NiV illness were identified where 33 case-patients, 91.7%, had close contact with another NiV patient before their illness[23]. Authors concluded that contact with one patient carried the highest risk for infection. In such hospital settings, direct contact with an infected person's saliva or bodily fluids can easily occur leading to transmission. In this same study, reverse transcription-PCR was used to evaluate hospital surfaces where testing of environmental samples confirmed NiV contamination of hospital surfaces which along with medical equipment, bedding, or frequently touched objects, can serve as a source of infection if transferred to a person's mucous membranes (eyes, nose, or mouth). As an airborne virus, NiV spreads through respiratory droplets, where in confined spaces such as hospitals, coughing and sneezing makes risks of transmission even greater[24]. The illustration of cross-species transmission of NiV is shown in Figure 2

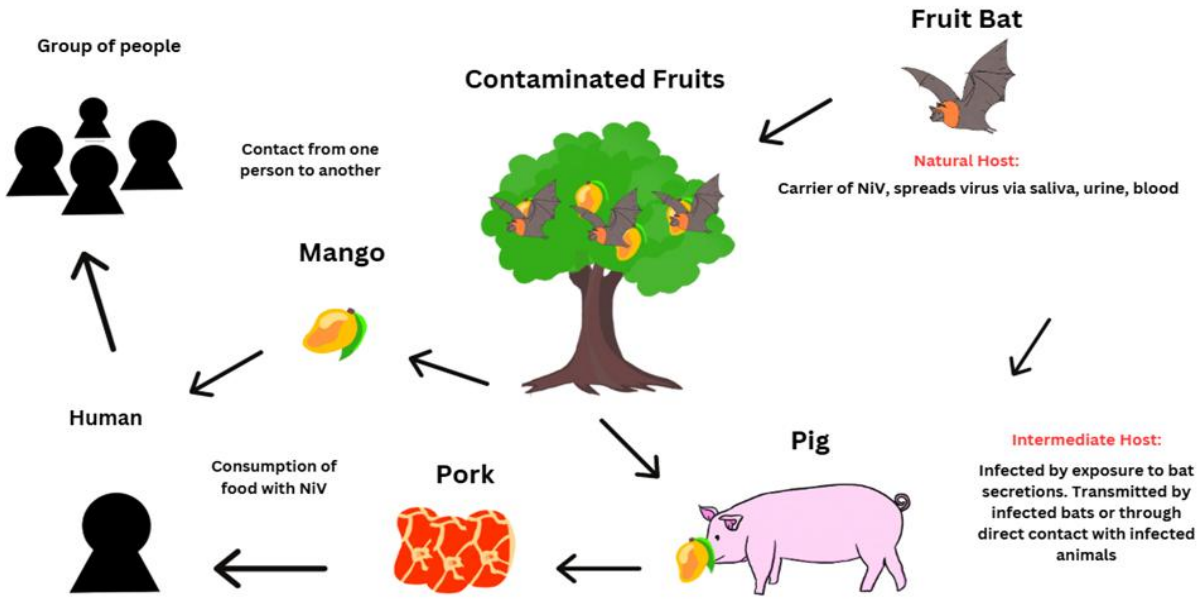

Figure 2 Cross-species transmission of NiV (Nipah virus)

Understanding the transmission and pathogenesis of NiV is crucial for developing effective preventive measures and therapeutics. Initially identified during an outbreak among pigs in Malaysia, NiV has demonstrated a significant capacity for human infection, with a case-fatality rate ranging from 40.0% to as high as 93.0% in subsequent outbreaks in Bangladesh and India[25]. Transmission occurs primarily through direct contact with infected

animals or their secretions, as well as through human-to-human contact, notably in healthcare settings. Noteworthy is the role of ephrinB2, the primary receptor for NiV, which is expressed on endothelial cells and neurons, facilitating the virus ability to cause severe neurological damage and endothelial syncytium formation a hallmark of infection[26].

The mechanisms of transmission and disease process of NiV involve complex interactions between the virus, its animal hosts, and human populations. Initially identified in fruit bats, NiV frequently transmits to humans through direct contact with secretions from infected animals, particularly in agricultural settings where pig farming is prevalent. The zoonotic nature of NiV exemplifies the dynamic relationship between emerging pathogens and environmental factors linked to ecological changes[27]. Upon infecting a host, NiV exhibits a significant pathogenicity profile, causing severe encephalitis with fatal outcomes in many cases. Critical to its virulence, the virus utilizes the ephrinB2 receptor on endothelial cells and neurons, which facilitates cell fusion and contributes to the characteristic syncytia observed during infection[26].

Discussion

Conclusion and Suggestions

Understanding the structure and classification of viruses is essential for comprehending their pathogenic mechanisms, especially in the case of NiV an emerging threat to public health. The classification of NiV, including its differing transmission routes among strains, influences pathogenicity and virulence, with receptor usage such as ephrinB2 and ephrinB3 being a key determinant of tissue tropism and disease severity. These insights have critical implications for designing effective vaccines and outbreak control strategies.

NiV is a zoonotic virus primarily harbored by fruit bats (*Pteropus* spp.) and capable of causing severe human infections with high case fatality rates. As a member of the *Paramyxoviridae* family, NiV has been responsible for outbreaks in South and Southeast Asia, raising urgent concerns about its transmission dynamics. The One Health framework which recognizes the interconnectedness of human, animal, and environmental health is central to managing such zoonotic threats. Evidence suggests that transmission can occur through contact with infected animals, consumption of contaminated food (e.g., raw date palm sap), or, in some cases, human-to-human transmission.

Recent virological surveillance in countries such as Sri Lanka reveals the co-circulation of multiple bat-borne viruses, including NiV, reinforcing the necessity of robust ecological monitoring. However, the rise of Nipah virus outbreaks cannot be viewed in isolation from broader environmental and anthropogenic drivers.

Deforestation and land-use changes are key ecological disturbances that have intensified human–wildlife interactions, increasing the likelihood of spillover events. The destruction of natural habitats forces bat populations to migrate closer to human settlements in search of food, often leading to viral shedding in areas of human activity. Similarly, climate change through its influence on bat migratory patterns, food availability, and breeding cycles can alter the seasonality and geography of outbreaks, as observed in

Bangladesh and India. These climate-linked ecological shifts are becoming increasingly relevant for disease forecasting and early warning systems.

Furthermore, population density and urbanization exacerbate the risk of rapid viral spread once zoonotic transmission occurs. High-density living conditions and insufficient public health infrastructure, particularly in rural and peri-urban areas, can facilitate clusters of human-to-human transmission and overwhelm local healthcare capacities.

To effectively address these interlinked factors, environmental management and urban planning should be integrated into public health policies. Strategies such as preserving bat habitats, regulating agricultural expansion, and improving land-use zoning can reduce the frequency of high-risk human–wildlife interactions. In addition, enhancing community education, improving diagnostic capacity, and strengthening cross-border surveillance are essential components of a multisectoral response.

In summary, addressing the challenge of NiV requires a multidisciplinary approach that combines virology, ecology, public health, and policy. Expanding study and intervention efforts to include deforestation, climate change, and population density as critical determinants will improve prevention strategies and help mitigate the risk of future outbreaks.

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