IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 1, November 2023

Review on NIPAH Virus

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Abstract: *Nipah contagion is an acute febrile illness that can beget fatal encephalitis. It's an arising zoonotic paramyxovirus aboriginal to south- east Asia and the western Pacific, and can be transmitted by its primary force of fruit batons, through intermediate beast vectors and by mortal- to- mortal spread. Outbreaks of Nipah contagion encephalitis have passed in Malaysia, Singapore, Philippines, India and Bangladesh, with the most recent outbreak being in Kerala, India in late. Extremely high case casualty rates have been reported from these outbreaks, and to date no vaccines or remedial operation options are available. Combining this with its propensity to present non-specifically, Nipah contagion encephalatis present a grueling opinion that should not be missed in cases returning from aboriginal regions. Raising mindfulness of the epidemiology clinical donation and threat factors of constricting Nipah contagion is vital to honor and manage implicit outbreaks of this complaint in the UK.*

Keywords: Nipah contagion

I. INTRODUCTION

A rare zoonotic disease is infection with the Nipah virus. It is caused by the Paramyxoviridae family member Nipah The Indian Flying Fox (Pteropus gi- ganteus) and the relatively smaller Greater short-nosed fruit bat (Cy- nopterus sphinx), both of which are widespread and common species in South Asia, have been identified as the main natural reservoir for the genus Pteropus. Insectivorous bats have not yet been isolated as a source of the Nipah virus. Fruit bats don't appear to have any diseases. A significant reservoir of other zoonotic viruses, like as the Melaka, Marburg, SARS, and Ebola viruses, has also been identified in bats.(1)

People and other animals, including pigs, can contract the disease from infected fruit bats. The initial transmission of an infection from an animal to a person is referred to as a “spillover event” and occurs when people come into close contact with an infected animal or its bodily fluids (such as urine or saliva). Person-to-person transmission of NiV is another possibility once it infects individuals.(6)

All around Southeast Asia, flying foxes can be found. The flying fox (genus Pteropus) has a global distribution that starts from the islands of Mauritius, Madagascar, and Comoro in the west Indian Ocean, moves through the sub-Himalayan regions of Pakistan and India, South-east Asia, the Philippines, Indonesia, New Guinea, the South-west Pacific Islands (to the Cook Islands), and Australia (Figure 1). In total, flying fox species number roughly 60. The body weight of flying foxes can vary from 300 g to more than 1 kg, and its wingspan can reach up to 1.7 m.(7)

An encephalitis (brain inflammation) is linked to a Nipah virus infection. Drowsiness, disorientation, and mental confusion follow a fever and headache that lasts for three to fourteen days after exposure and a five to fourteen-day incubation period. In a span of 24 to 48 hours, these indications and symptoms may intensify to coma. A respiratory disease was present in some individuals in the early stages of their infections, and pulmonary symptoms were also present in half of the patients exhibiting severe neurological symptoms.resentnon-specifically, Nipah contagion encephalitis presents a grueling opinion that shouldn't be missed in cases returning from aboriginal regions. Raising mindfulness of the epidemiology, clinical donation and threat factors of constricting Nipah contagion is vital to honor and manage implicit outbreaks of this complaint in the UK. (8)

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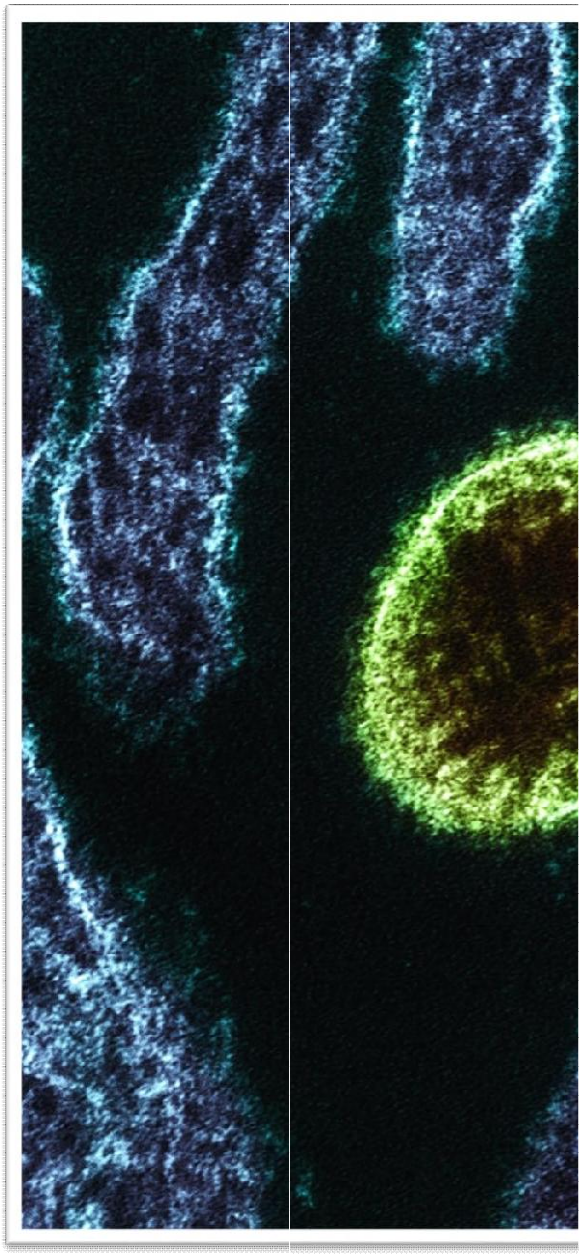

Figure 1: Nipah virus under the microscope

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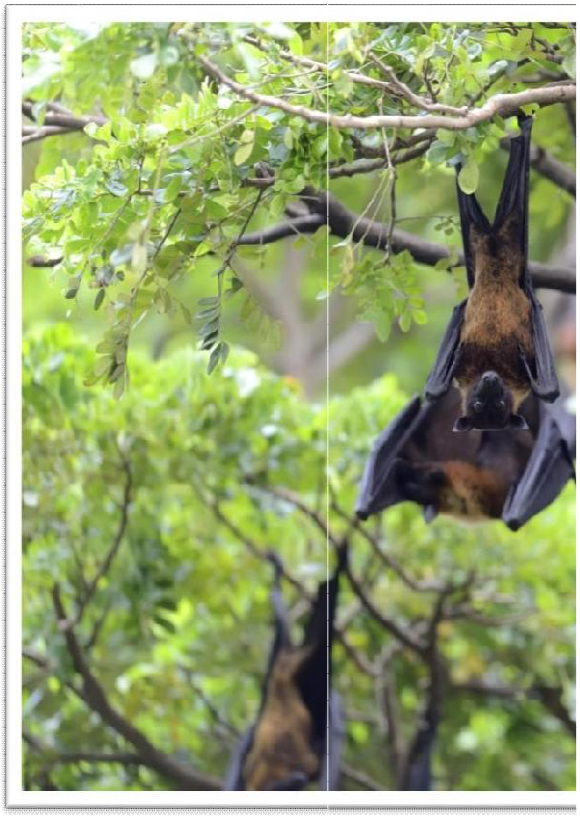

Figure 2: Flying fox

A NiV infection can result in mild to severe disease, as well as death, and is linked to encephalitis, or brain swelling.(9)

NiV encephalitis epidemics with significant case fatality rates have recently occurred in Bangladesh, Malaysia, Singapore, the Philippines, and India. The widespread dispersion of its natural host, along with NiV's potential for human-to-human transmission and the lack of effective treatments, underscore the worry that it might potentially start a worldwide pandemic.(2)

The World Health Organization (WHO) has identified the NiV virus as a global health concern and included it in the list of epidemic threats that are given priority in research and development efforts because of its high human mortality rate, zoonotic nature, potential for human-to-human transmission, and lack of a vaccine.(5)

II. HISTORY

MALAYSIA

In October 1998, pig farmers in a swine production area close to Ipoh, Malaysia, experienced a deadly encephalitis outbreak . When the outbreak in Ipoh ended in late February 1999, at least five individuals had died, but pig farmers and their families in the Bukeit Pelandok area of Negeri Sembilan state to the south had contracted a similar encephalitic sickness.

Initially declaration, it was thought that the sickness was Japanese encephalitis. It wasn't until March 19, Nipah 1999, that the presence of a novel paramyxovirus in multiple patients from both regions was identified.(3)

Pigs were sold to other farms throughout the nation by pig farmers impacted by the virus. The major pig farming communities in Negri Sembilan, around 300 km south of Ipoh, were Sikimat, Sungai Nipah Village, and Bukit Pelandok, where the outbreak had reached by February 1999. There were perhaps 180 patients and 89 fatalities from this second, more catastrophic epicenter.

Additional instances were reported from the vicinity of Sepang and Sungai Buloh in Selangor due to the covert movement of sick pigs. Abattoir workers in Singapore who had handled pigs imported from Malaysia were involved in

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11 cases—including 1 fatality—reported in March 1999. By that time, the epidemic had spread panic throughout the country and nearly brought the local pig farming sector to an end.(4)

It was discovered that dogs were also frequently aflicted(11).There's no proof that these outbreaks have spread from person to person. Ultimately, it was discovered that Pteropus bats were the infection reservoir in Malaysia [13], where the virus spread to pigs, the amplifying hosts, by eating fruit that had been bitten by a bat(12).

The Actions Taken For Control The Spreading of Nipah Virus

Movement control on pigs

Any movement of pigs or pig meat, whether local, intrastate, or interstate, was prohibited following the legislation's of as a disease.

Public announcements and media releases were utilized to inform people about the limitations.

Increased DVS and police patrols on routes from affected regions were used to enforce the restriction.

Transporting pigs to government abattoirs from beyond designated zones was permitted as long as DVS personnel escorted each consignment and the transportation was done under permit.(10)

Mass culling of active disease farm

Around contaminated sites, buffer zones with a radius of 10 km and infected zones with a radius of 2 km were established. Over the course of two months, every pig in the buffer zone—901, 228 pigs from 896 farms—was slaughtered.

The culling operation included the participation of the Army, the Department of Veterinary Services, the Department of Transportation, and other relevant governmental and non-governmental organizations.

The hogs were killed by shooting and buried in deep holes in the affected region, either on or off the property.

Cemetery sites and buildings were cleaned using detergents and chlorineated lime.(10)

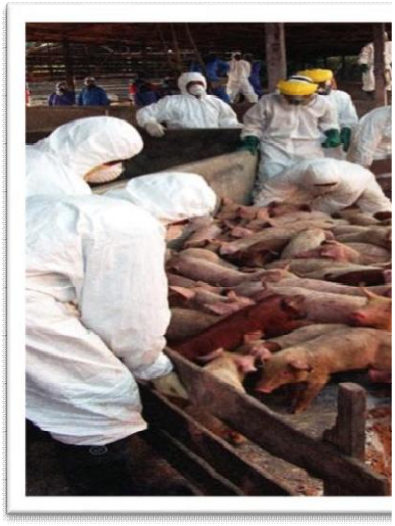

Figure 3

Figure4

Figure 3 and 4 Mass culling of pigs

SINGAPORE

A similar outbreak of encephalitis among Malaysian pig farmers in the months prior was followed by an outbreak among abattoir workers in Singapore in March 1999, which was caused by the recently identified Nipah virus (NV)(13).

Based on elevated IgM in serum, eleven patients were diagnosed with acute Nipah-virus infection. Reverse transcriptase PCR was used to detect the Nipah virus in the deceased patient's tissue and CSF(14).Pigs from Malaysian locations aflicted by the Nipah virus were imported and killed two to three weeks before to the onset of human illness, which is in line with the typical incubation period of a paramyxovirus. The number of case patients who interacted with live pigs was substantially higher than that of control individuals(15).

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BANGLADESH

Between 2001 and 2004, there were four Nipah virus outbreaks identified in central and western Bangladesh(16).

The ecological pattern of Nipah virus outbreaks varies greatly throughout Bangladesh. Since 2001, when the Nipah virus was discovered to be the cause of the first cases of human encephalitis in Bangladesh and India(17),outbreaks have been documented nearly yearly in Bangladesh and more infrequently in adjacent India(18). Bangladesh experiences seasonal outbreaks, with the majority of infections falling between December and April and concentrating in the nation's center and northwest regions(19). In contrast to the epidemics in Malaysia, those in Bangladesh were associated with the consumption of fresh or fermented sap (tari) from silver date palm trees (Phoenix sylvestris), rather than an intermediary animal host(20).

Naturally occurring reservoir hosts are Pteropus bats(21).Pteropus bats can be found all over Bangladesh(22).Still, the country's northwest and center are home to the majority of spillovers. The main distinction between the villages in Bangladesh where outbreaks have been reported and other communities is that a greater percentage of the population in these villages report drinking fresh date palm sap(22).Some of these regional and temporal variations may be determined by weather, specifically temperature and precipitation. For instance, when the weather is at its coolest and the sap is at its sweetest, communities like to gather it(23), hence risky behavior may rise in the winter months that are cooler. Prolonged precipitation may lower the risk since it can contaminate the sap collected in open pots. NiV has also been demonstrated to endure longer in fruit juice at lower temperatures, which implies that it might likewise endure longer in date palm sap at lower temperatures(24).

Eleven instances of NiV infection cases (10 laboratory confirmed and one probable) and eight related deaths were recorded from seven districts across two divisions in Bangladesh between January 4, 2013, and February 13, 2023. After 2015, when the nation reported 15 NiV cases and 11 related deaths, this is the largest number of NiV cases and deaths that have been documented (WHO). Six NiV cases and four related deaths (6/4) were reported by the Dhaka division from the districts of Shariatpur (1/0), Rajbari (4/3), and Nasingdi (1/1). The districts of Naogaon (2/1), Natore (1/1), Pabna (1/1), and Rajshahi (1/1) recorded five cases and four related deaths (5/4), according to the Rajshahi Division. The startlingly high average case fatality rate is 73%. Four of the eleven cases involved females, while seven were males(25).

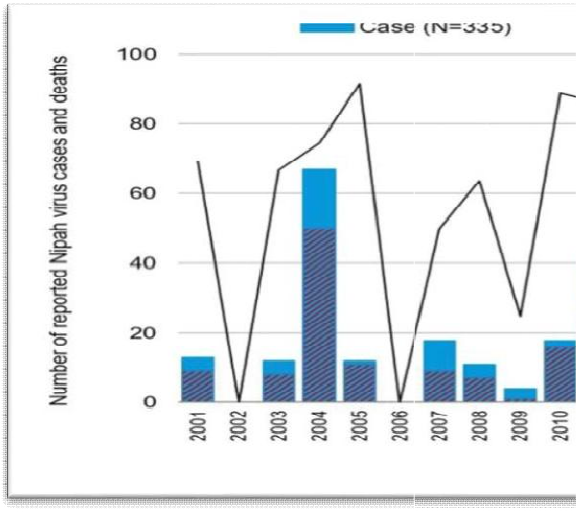

Figure 5 Number of reported Nipah virus cases and deaths from 2001 to 2023, Bangladesh.

INDIA

In Siliguri, West Bengal, India, an outbreak of febrile sickness with altered sensorium was noted in January and February of 2001. A significant commercial hub, Siliguri is home to about 500,000 people. Its borders with Bangladesh, China, Nepal, and Sikkim are close by. The hospitalized patients, their family members, and the medical personnel of four different hospitals were all affected by the outbreak. At first, it was thought to be Japanese encephalitis, which is endemic in this region, but the age range of those infected and the epidemiologic characteristics pointed to another

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illness. When the outbreak occurred, laboratory tests were performed, but they were unable to identify an infectious agent(26). In 2007, a small epidemic occurred in West Bengal's Nadia area, resulting in five illnesses and one fatality. These outbreaks spread from Bangladesh's Nipah belt across the border. Even though Kerala is a southern state on the west coast that is geographically distant from areas that were previously impacted and where date palm sap intake is not common, the districts of Kozhikode and Malappuram reported a NiV epidemic in May 2018.(27). There were 17 NiV-related deaths and 18 confirmed cases of infection as of June 1, 2018(28). No sex difference was seen, and all cases fell within the age range of economically active individuals.(29).

The government of India's Ministry of Health and Family Welfare announced six laboratory- confirmed cases of the Nipah virus in the Kozhikode district of Kerala between September 12 and 15, 2023, including two fatalities(30).Public mobility is restricted in several areas of Kerala state, while schools and workplaces are shuttered in Kozhikode as part of the outbreak containment measures. In order to help laboratory inquiry, a transportable BSL-3 laboratory is scheduled to be established in Kozhikode, along with a team of experts assigned to support local authorities. The Nipah virus reported in this outbreak is the same as the one that was discovered in Bangladesh earlier this year, according to laboratory research(31).

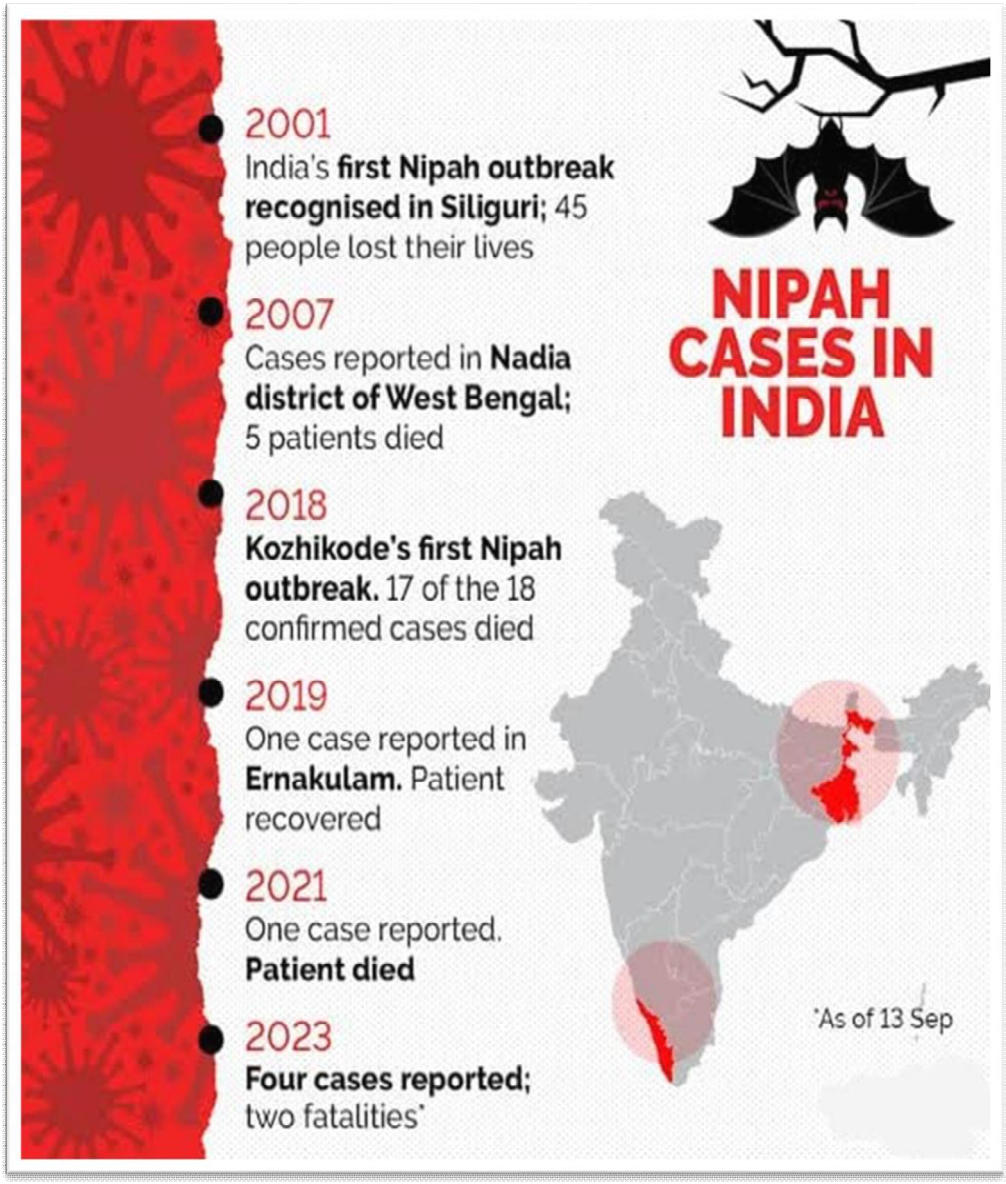

Figure 6 Nipah virus outbreak in kerala

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Structure of Nipah virus

NiV is a negative-sense, enclosed, single-stranded RNA virus that has multiple accessory proteins in addition to its six structural proteins. The NiV virus's envelope membrane contains two types of glycoproteins: fusion proteins (NiV-F) and attachment proteins (NiV-G). NiV-F mediates the fusion of virus-cell and cell-cell membranes at a neutral pH1, while NiV-G binds to cellular receptors(32). NiV, an RNA virus with a negative sense, encapsulates its RNA-dependent RNA polymerases (RdRp) within virions. The RdRp complex is made up of phosphoproteins (NiV-P) and large polymerase proteins (NiV-L). The ribonucleoprotein (RNP) complex is made up of nucleocapsid proteins (NiV-N), non-segmented RNA genome, NiV-L, and NiV-P. Located in the core of the NiV virion, the RNP complex is in charge of replicating the viral DNA. The viral envelope and the RNP core are separated by matrix proteins (NiV-M).Paramyxoviruses contain a variety of accessory proteins in addition to the six structural proteins that are encoded by their genomes.

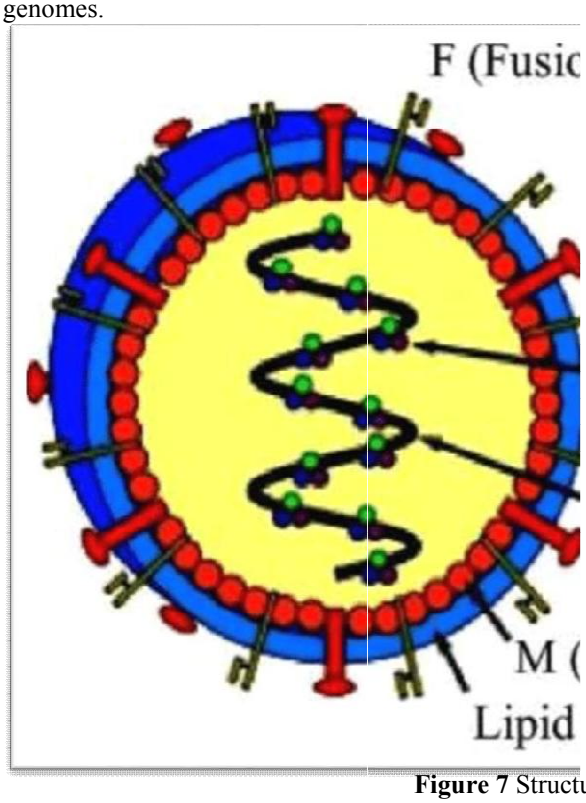

Figure 7 Structure of nipah virus

The majority of auxiliary proteins are translated from the P gene by utilizing different open- reading frames and nucleotide inserts. The three auxiliary proteins V, W, and C are encoded by the NiV P gene. These trio NiV is expected to counteract cellular anti-viral activity with the aid of accessory proteins, and Exist in the NiV virions' lumen(33).Most of the physical traits that NiV and other paramyxoviruses have in common are shared under EM(34).For instance, the majority of paramyxovirus particles are filamentous or pleomorphic spheres. On the virus envelope, F and G are spikes that measure 5-8 nm in length and can occasionally group together to form unique clusters. M is thought to associate with the RNP core and forms clusters beneath the membrane(35). The helical RNP core contains a 15-19 kb RNA genome with a herringbone shape. The RNP core forms a ring-like structure in cross-section, which can be observed under the membrane of infected cells and virus particles using EM16(36).

Life cycle of Nipah

NiV's life cycle begins when it enters host cells. NiV-G specifically bind to ephrin-B2 and/or -B3 receptors on the host cell. NiV-G tetramers are rearranged by this binding.

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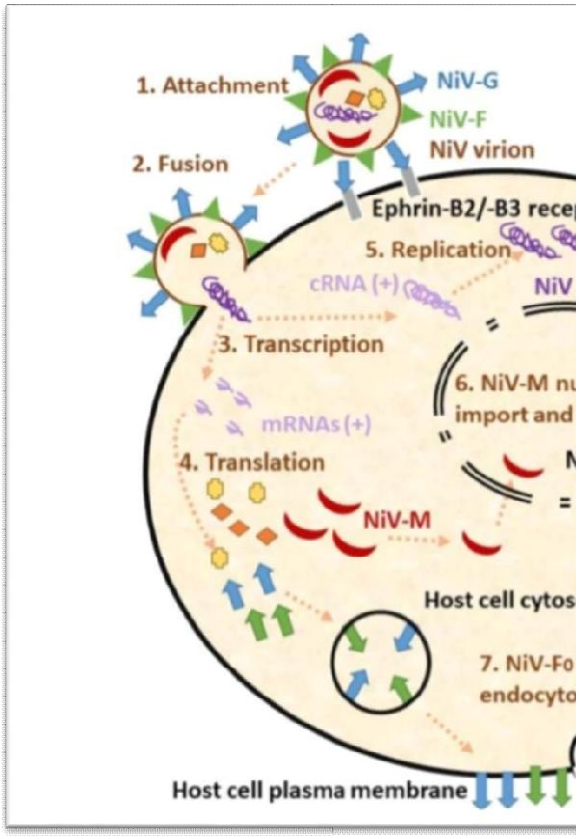

Figure 8 Life cycle of Nipah virus.starting with the infection of the host cell and ending with the generation of offspring NiV virions. The NiV life cycle's essential phases are arranged numerically.

NiV-F undergoes a series of conformational modifications as a result of the rearranged NiV-G(37), which results in the fusion between viral envelopes and host cell plasma membrane(38).The RNP complex and host cell components assist in the transcription of the viral genome RNA into viral mRNAs, which is necessary for the translation of viral proteins, once the virion has been released into the cytoplasm of the host cell. Transcriptase or replicase activities can change the RNP complex into the RdRp complex, which is needed for the replication of viral genomic RNAs(39).The plasma membrane receives the transportation of NiV-M, NiV-F, and NiV-G. The offspring virion must be released from the host cell by NiV-M(40).

Transmission of NiV

In Malaysia, the illness was spread to humans by NiV-infected pigs, the virus's intermediate hosts(41).Pigs contract the virus from bats when they eat fruits that have been partially eaten or contaminated by NiV-infected bats(42).Direct contact with infected pigs was the means by which the virus was transferred from pig to human, and fomites, aerosols, or direct touch may all be used to infect humans.

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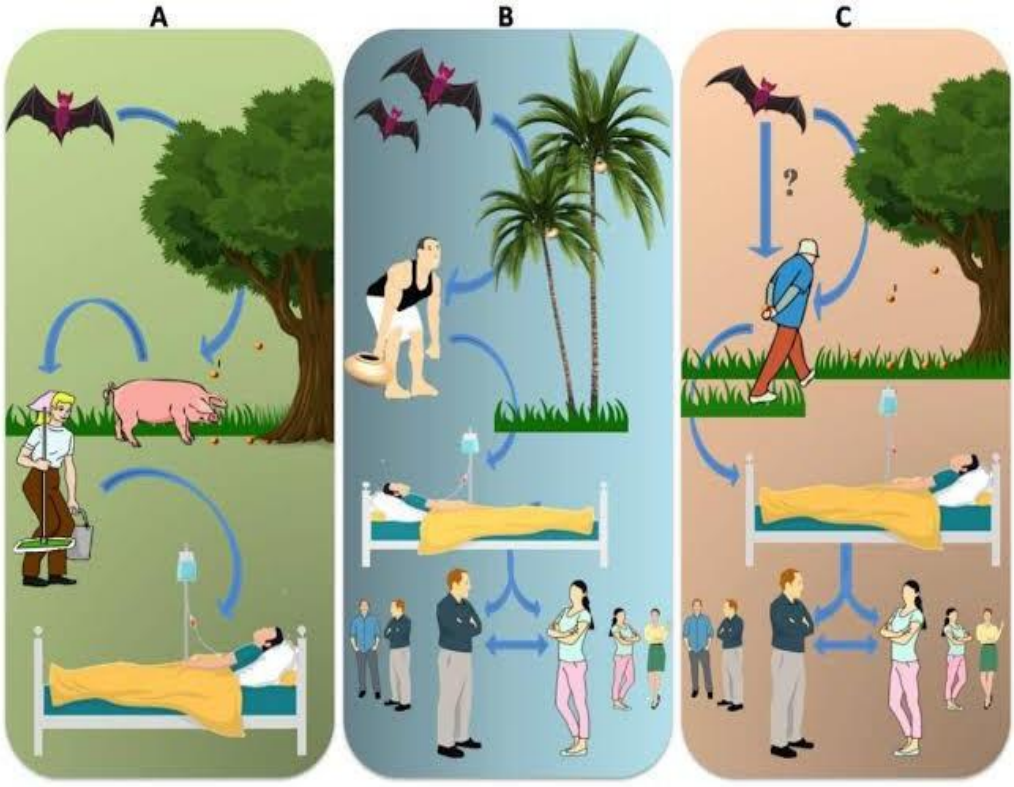

Figure 9 Transmission of NiV

Workers in slaughterhouses frequently come into contact with excretions and secretions from sick pigs, including their urine, saliva, pharyngeal, and respiratory secretions, as well as raw pig meat and other NiV-contaminated goods(43).A significant respiratory route of transmission for NiV is thought to be the aerosol dispersed from pigs, which causes severe respiratory irritation in humans(44).Pig farmers residing near pig sties became infected as a result of the importation of pigs from Malaysia to Singapore(43).

According to investigations conducted in Bangladesh, a small number of patients had eaten raw palm sap approximately 30 days before the illness manifested itself, indicating that the palm sap may have been contaminated with bat secretions carrying the NiV virus(45).A high incidence of transmissions between people was also noted throughout the pandemic(46).

West Bengal and Kerala outbreaks in India and Bangladesh have comparable epidemiologic features when it comes to direct human-to-human transmission of NiV without the need for intermediate hosts(47).Most hospital employees, caregivers, and bystanders were impacted by the primarily nosocomial epidemics(48).In Siliguri, outbreaks are said to have started with bats.The initial sick person in Kerala, known as the index patient, is thought to have acquired NiV from infected fruit bats; however, this theory is not supported by any evidence.Since all other patients acquired the illness by nosocomial transmission, Kerala's person-to-person transmission frequency was high and comparable to that of West Bengal and Bangladesh(49).

Pathogenesis of NiV

NiV can be diagnosed in epithelial cells during the early stages of infection, particularly in the bronchiole(50).There have been reports of viral antigens in the lungs, particularly in the bronchi and occasionally even in the alveoli.Acute respiratory distress syndrome (ARDS)-like illness eventually develops as a result of the release of cytokines from the infected respiratory tract's enlarged epithelium(51).During the later stages of infection, the airway epithelium additionally secretes inflammatory mediators as interleukin granulocyte-colony stimulating factor(52).The virus spreads to the endothelium's cells through the respiratory epithelium.As the illness progresses, the virus may enter the bloodstream. Multi-organ failure can result by targeting the brain and other organs in addition to the respiratory,

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digestive, and excretory systems. It has also been observed that leukocytes can contract NiV infection in hamster animal models, which can have fatal results(53).

The blood arteries of the cerebrum known as the choroid plexus allow the virus to reach the central nervous system (CNS). This infection has the potential to compromise the blood–brain barrier (BBB), which could result in a number of neurological issues.Necrosis may result from nonliving virus particles present in an infected human central nervous system. According to a number of new research using animal models, the virus may be able to penetrate the central nervous system through the olfactory nerve right away.Eventually, the infection may spread through the olfactory bulb. In the end, the virus travels throughout the ventral cortex at the side of the tubercle that detects smell(54).

Diagnosis

Reverse transcriptase polymerase chain reaction is the recommended and most sensitive diagnostic technique for NiV encephalitis (PCR)(55).NiV can be detected by PCR using urine samples, blood, nasal/throat swabs, and cerebrospinal fluid (CSF) collected during the acute phase of infection.

NiV particle isolation and propagation require biosafety level 4 laboratory facilities; at the moment, there are no quick diagnostic procedures for NiV; instead, most testing takes place in central laboratories in endemic nations (56).The Rare and Imported Pathogens Laboratory in Porton Down, UK, is the official location for doing NiV PCR in the country(57).

In patients with NiV encephalitis, thrombocytopenia, leukopenia, and abnormal liver function tests have been observed(58) and other non-haemorrhagic viral CNS diseases are similar in their CSF chemistry(59).

NiV's neuroradiological characteristics have been described and can aid in the diagnosis of those who have been exposed. Extensive cortical involvement, especially in the temporal lobe and pons, has been demonstrated by magnetic resonance imaging (MRI), and diffusion weighted imaging (DWI) reveals several bilateral abnormalities(60). These alterations are consistent with vasculitis- associated microangiopathy brought on by NiV and differ from the defining characteristics of HSV and JEV. Patients with late-onset and relapses of encephalitis have different MRI findings, and their neuroimaging shows confluent hyperintense cortical lesions that are probably the product of long-term micro-embolic damage from vasculitis(61).

Treatment

NiV outbreaks are more potent when they spread quickly through nosocomial and zoonotic pathways and have an asymptomatic incubation period. NiV infection symptoms start off as low fevers that come and go, eventually leading to severe cases of acute respiratory distress syndrome, acute encephalopathy, altered sensorium, and disorientation(62).Since there are currently no specific antivirals or antibodies that are effective against the virus, NiV infection requires careful supervision.Rescue patients with NiV problems are given supportive therapy with broad spectrum RNA virus antivirals such as Ribavirin together with other medications for deep vein thrombosis, anticonvulsive during seizures, and mechanical ventilation for respiratory system failure(63).During the prior NiV outbreaks in Malaysia and Singapore, two medications were used: ribavirin and acyclovir(64). In the open-label study against the Malaysian NiV epidemics, ribavirin decreased the mortality toll by 36%; however, later investigations in animal models were unable to demonstrate its effectiveness(65).A purine analogue called favipiravir (T-705) that inhibits RNA- dependent RNA polymerase made it to clinical trials for the Ebola virus, and other influenza antivirals have also proven effective against NiV in animal models using Syrian hamsters(66).The Hendra virus subunit vaccine, which is authorized for use in Australian equines, and the monoclonal antibody vaccine (m102.4), which targets the NiV recombinant viral envelope protein, have both demonstrated their effectiveness in a variety of animal models. The latter vaccine has been given to critically ill NiV patients out of compassion(67).

Vaccines

Numerous vaccine approaches for NiV have been proposed, and several of them have undergone testing in animal models. The subunit vaccination strategy based on the G glycoprotein (sG) of HeV and NiV has received the greatest research. HeV-sG triggers an immune response that is cross-protective against both HeV and NiV(68).It has since been developed into Equivac, a HeV vaccination for horses that is approved in Australia. Additionally, recombinant vaccines based on virus vectors have been created. The F or G glycoproteins are expressed on the surface of these recombinant viruses(69).Vaccines against virus-like particles made from mammalian cells have also been created(70).After a single

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dose, all of these methods have completely protected against oro-nasal NiV challenge in distinct animal models. Both the sG vaccination for horses and the VSV- vectored Ebola vaccine (rVSV-ZEBOV) are promising candidates for potential human application due of their efficaciousness(71).

Prevention

Periodically, it is important to make sure that public health and medical experts are aware of diseases that have been neglected and comparable ones, and that government and medical authorities in areas where outbreaks have occurred before are ready to contain any future outbreaks.Research aimed at comprehending the bat ecology, its vulnerability to transmitting NiV, and its exact prevalence may be able to mitigate the risk associated with human encroachment into their natural habitat. Monitoring and sero-surveillance for NiV antibody and NiV using ELISA and PCR technique in humans and bats can assist in preventing the potential for an epidemic in the areas where it is most common(72).

Reducing the amount of bodily fluids and close contact between patients and caregivers/attendants could stop outbreaks like the one that occurred in Kerala. Only wear masks and gloves when handling food items, mats and sheets, clothing, and patient aid supplies of all kinds. It is important to make sure that the attendant or caregiver wears masks, gloves, and patient aids are burned properly. Medical professionals should wear appropriate personal protective equipment (PPE) when consulting encephalitic patients exhibiting NiV symptoms in order to limit the risk of getting the disease and its nosocomial dissemination. Upon confirmation, these patients should be placed in isolation from the public. The ideal course of action is to incinerate the corpse; nevertheless, for religious reasons, Kerala has followed deep burial of sick bodies up to a depth of ten feet, along with the use of personal protective equipment (PPE) and thorough cleaning of the handling personnel and burial site. Healthy individuals may contract NiV from the corpse's tissues or bodily fluids(73).Thus, in order to reduce the possibility of the virus spreading from corpse to human, burning or deep burial are required.However, as no such data are currently available, it is unknown how long the infectious virus can persist in carcasses. Developing countries that cannot afford the overwhelming demand for personal protective equipment (PPE) should make sure that attendants and caregivers wash their hands with soap and water or use disinfectants like 70% alcohol to wipe their hands and body extremities.

It should be completely forbidden to purchase and consume raw fruits and products under unsanitary conditions in places where the prevalence of NiV is high.Similar to the ingestion of raw date palm sap contaminated with bat excreta causing recurring outbreaks in Bangladesh, bat- bitten fruits eaten raw are thought to be one of the numerous causes of the recent outbreak in Kerala(74).An appropriate understanding of and adherence to hygienic practices could reduce the chance of contracting and transmitting infections. When predicting an outbreak time, strategies such as public broadcasting, leaflets and posters, as well as the usage of social media for proper awareness, could be used(75).

III. CONCLUSION

Nipah viral outbreaks that have been reported in different regions of the world represent a significant risk to the international population. These outbreaks have had a devastating effect on the economies of the affected nations, leading to high rates of sickness and mortality and ultimately a decline in national stability. Controlling and managing epidemics of any kind may be aided by population readiness and knowledge. Future outbreaks could be significantly reduced by listing the contributing elements, conducting surveys and studies to better understand the dynamics of the virus among interspecies groups, and implementing preventive measures. To suppress any potential sporadic epidemic of a similar sort, authorities and governments should implement and adhere to preventive and containment measures.

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IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 1, November 2023

[3]. Referencr-Lessons from the Nipah virus outbreak in Malaysia Lai-Meng LOOI MD, FRCPath and Kaw-Bing CHUA* MD, FRCPath Department of Pathology, University of Malaya and *National Public Health Laboratory, Ministry of Health, Malaysia

[4]. Nipah Virus–Another Threat From the World of Zoonotic Viruses Krzysztof Skowron1 , Justyna Bauza-Kaszewska2 , Katarzyna Grudlewska-Buda1, Natalia Wiktorczyk-Kapischke1, Maciej Zacharski3*, Zuzanna Bernaciak1 and Eugenia Gospodarek-Komkowska1 1 Department of Microbiology, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun,´ Bydgoszcz, Poland, 2 Department of Microbiology and Food Technology, Jan and J ˛edrzej Sniadecki University of Technology ´ in Bydgoszcz, Bydgoszcz, Poland, 3 Department of Biochemistry and Molecular Biology, Wrocław University of Environmental and Life Sciences,

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