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Comprehensive Review On Nipah Virus

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Abstract: The Nipah virus (Niv) is a zoonitic paramyxovirus that mostly infects fruit bats and can occasionally spread to people through intermediary species like pigs. It causes severe respiratory and neurological sickness with a high fatality rate. In South and Southeast Asia, including Malaysia, Singapore, Bangladesh, and India, Niv epidemics have been documented. Niv has a high case fatality rate; in certain outbreaks, mortality rates can range from 40% to 75%. Because of its capacity to cause serious illness and epidemics, as well as the lack of an effective treatment or vaccination, Niv is regarded as a high-risk virus..

Index Terms - Nipah virus (Niv), neurological, neurological, species, respiratory

I. INTRODUCTION

One of the viruses on the WHO priority list of those that are likely to produce outbreaks and require immediate attention in terms of research and development is NiV [1]. Pteropus bats, the infection's reservoir, are found all over the planet. In the future, spillover incidents are probably going to occur in new places where they live. The most recent instance of this is an outbreak that has occurred in a new region of Kerala, India [2].The medical community has been baffled by the Nipah virus's high fatality rate, extensive species tropism, numerous viable modes of transmission, propensity for person-to-person transmission, and verified cases of infection among healthcare professionals during outbreaks. The virus and its clinical effects remain largely unknown despite ongoing efforts to uncover its mysteries. [3] Over 250 cases of febrile encephalitis among agricultural and slaughterhouse workers have been linked to the disease, which has been dubbed Nipa after its original epidemic in a Malaysian town in 1998–1999, causing serious economic hardship and raising public concerns. [4] The household Paramyxoviruses was previously identified as a class of viruses that tended to create low-mortality outbreaks and had a limited host range. However, the rise of the extremely pathogenic Hendra virus and its closely related NiV as a cause of deadly encephalitis has signaled a shift in Paramyxoviridae trends. [5]

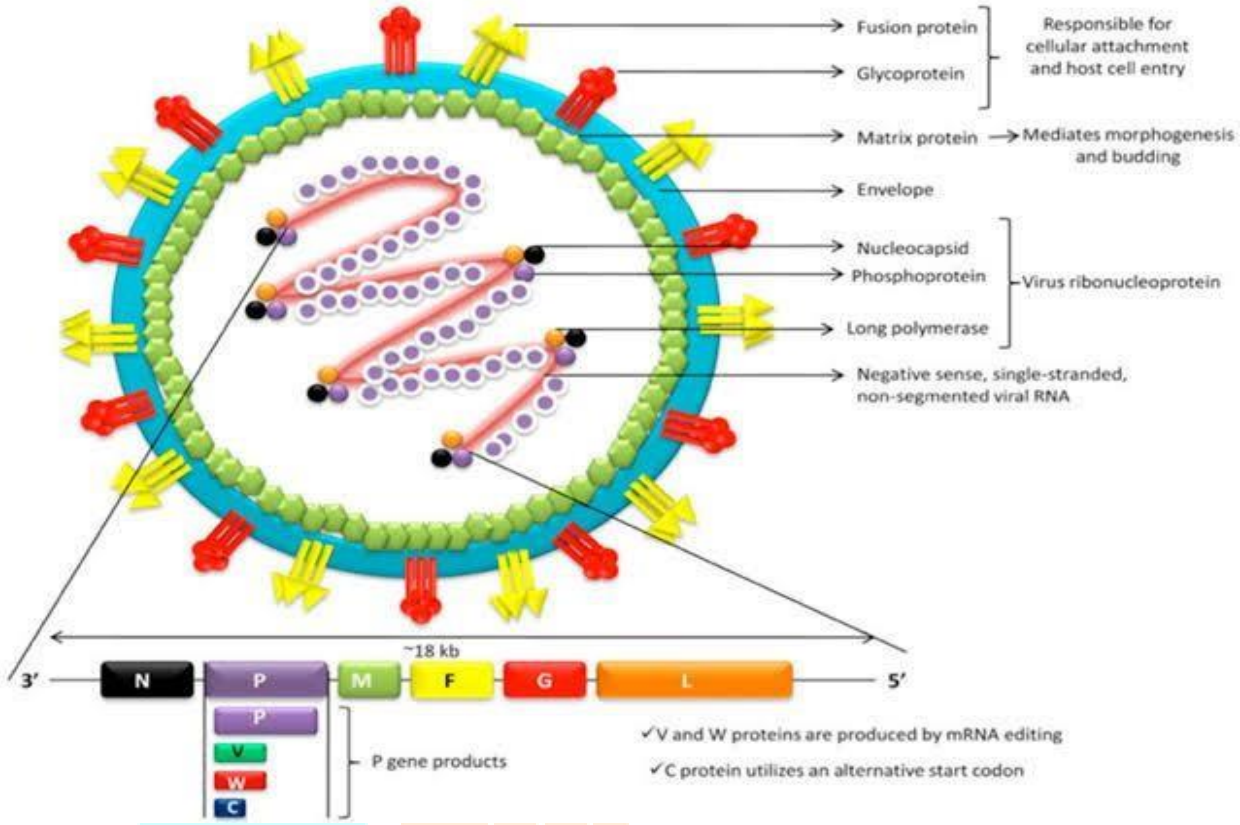


Figure 1:-Structure of Nipah virus

EPIDEMIOLOGY

In Malaysia, human NiV infection was initially discovered between 1998 and 1999. [6] Sungai Nipah (Nipah River village) is where the name "nipah" originates. In September 1998, several instances from the Malaysian state of Perak were recorded, exhibiting fever, headache, and decreased awareness. A JE outbreak was first announced after four individuals tested positive for IgM Antibodies against Japanese Encephalitis (JE). The outbreak worsened even after control measures were put in place. More clusters were discovered in the Port Dickson District, 300 kilometers to the south, by the end of the year [7]. The mode of transmission was one of the many noteworthy features of the Indo- Bangladesh epidemics, including the most recent one in Kerala. Luby et al. discovered a strong correlation between NiV sickness and eating raw date palm sap tainted by fruit bats [8].

MALAYSIA / SINGAPORE

The animals who were afflicted themselves displayed a slight respiratory ailment. Large numbers of animals are grown together in slaughterhouses and pig farms in Malaysia, which is where the outbreak started and where animal-to-animal transmission is most likely to occur. The outbreak was successfully contained by the culling of more than a million pigs, followed by their deep burial and fast lime cleansing, among other control measures [9]. In Malaysia, human NiV infection was initially discovered in 1998 and 1999 [10].

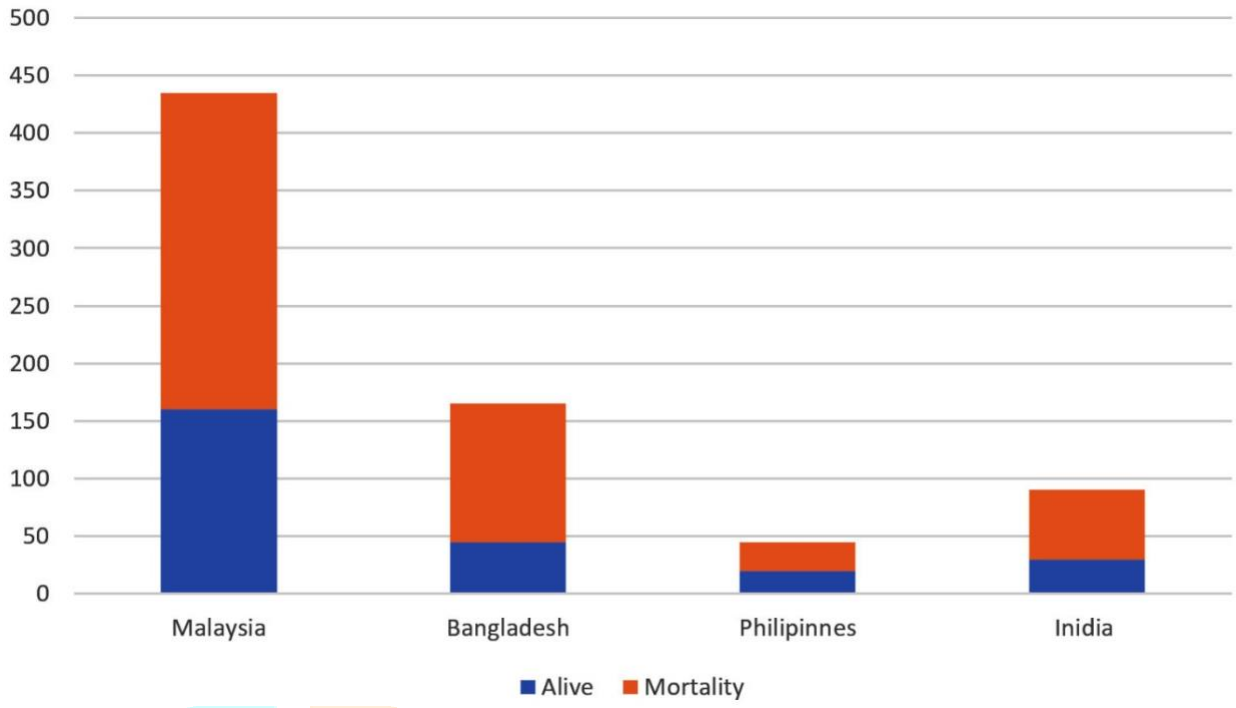


Figure 3: The overall count of cases reported for every outbreak [11]

In 2001, a significant outbreak occurred in Siliguri, West Bengal, resulting in 66 probable cases and 45 deaths. In 2007, a lesser outbreak occurred in Nadia district, West Bengal, resulting in five cases and 100% fatalities. These outbreaks occurred in Bangladesh, on the other side of the Nipah belt. Kerala, a southern west coast state that is geographically remote from previously impacted areas, announced an outbreak of NiV in May 2018 in the districts of Kozhikode and Malappuram. In this region, it is uncommon to consume date palm sap. As of June 1, 2018, there were 17 fatalities and 18 confirmed cases [12]. Most likely, the main cause of this was a lack of adherence to recommended safeguards.Additionally, the variation in transmission rates was influenced by the strain differences (BD vs. MY). According to a study by Clayton et al., ferrets infected with the BD strain exhibited greater blood levels of RNA and more viral shedding in their oral secretions. This could help to explain the Indo-Bangladesh Outbreak's higher rates of secondary attacks and more severe infection. Notably, viral shedding was seen throughout the incubation phase as well [13].

BANGLADESH

Although conclusive proof has not yet been found, eating fruit that has been bitten by a bat has also been suspected as a possible mechanism of transmission. Consumption of date palm sap and person-to-person transmission have been Identified as the main routes of transmission in Bangladesh [14].

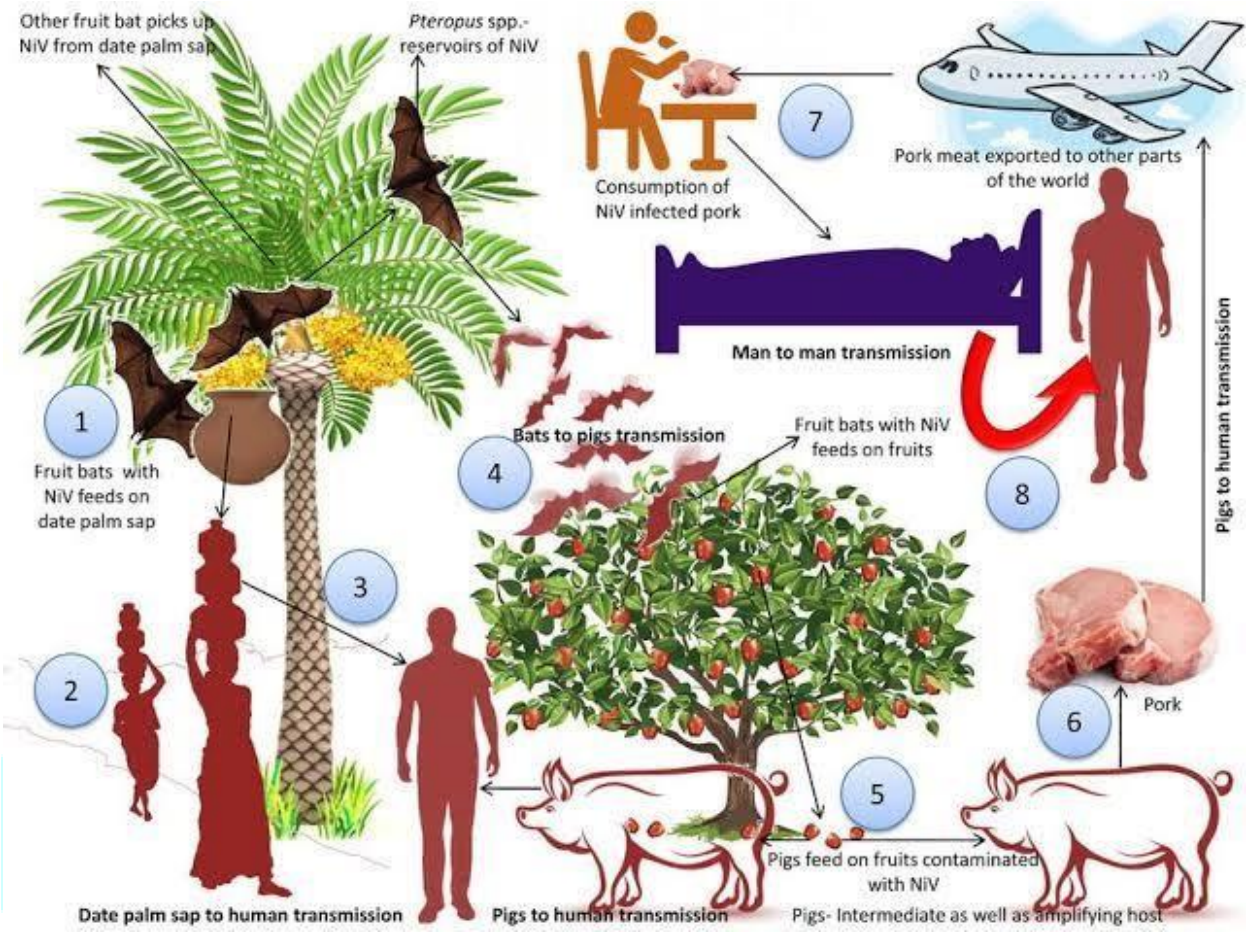


Figure 4: Niv's Transmission Cycle [15]

Three routes of NiV transmission from bats to humans have been discovered by epidemiological studies conducted in Bangladesh. Consuming fresh date palm sap is the method most commonly implicated. Especially in west central Bangladesh, date palm sap is extracted between December and March. Sap slowly pours into an open clay pot overnight after a tap is carved into the tree trunk. Studies using infrared cameras verify that P. giganteus bats often visit date palm sap plants and drink the sap while it is being collected. [16] One family reported in 2004 that their son regularly played with their two goats.the Goats developed a temperature, frothing at the mouth, difficulty walking, and walking in circles. When the goats were sick, the parents think their son came into contact with goat feces.

The two goats perished. The infant had encephalitis within two weeks of the goats' deaths, and antibody testing identified it as Nipah encephalitis (unpublished data). Third, some people could come into close contact with bat fluids that are infected with NiV. Tree climbers had a higher chance of contracting NiV infection than controls during the 2004 Goalando outbreak (odds ratio 8.2, 95% CI 1.3, undefined). [17] According to Figure 5, the Nipah virus is zoonitic, meaning it can spread from animals to people

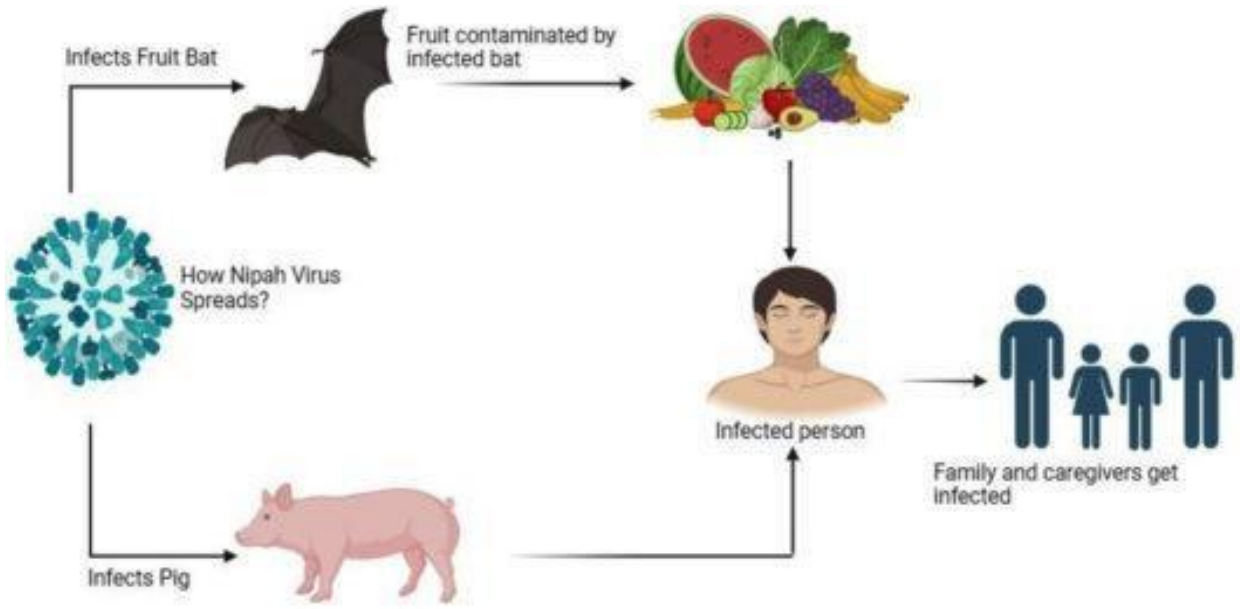


Figure 5, the Nipah virus is zoonitic, meaning it can spread from animals to people [18].

Domestic animals are a second way that bats might spread NiV to humans in Bangladesh. Fruit bats frequently drop partially consumed fruit that is dripping with saliva. Bangladeshi domestic animals forage for this kind of diet. Sometimes domestic animals are fed date palm sap that has been tainted by bat feces and is therefore unsafe for human consumption. It is possibl for domestic animals to contract NiV and spread the virus to people and other animals. In Meherpur, Bangladesh, in 2001, contact with a sick cow was significantly linked to Nipah infection (OR 7.9, 95% CI, 2.2, 27.7, p=.001). [19]

NIV TRANSMISSION FROM PEOPLE TO PEOPLE

15–27 days after the index patient's initial illness, four people who were caring for him—his mother, son, aunt, and a neighbor—became ill (Figure 2). The aunt of the Index patient was looked after by a well-known religious13 days later, a local leader who resided close fell ill. Many of the religious leader's family members and fellow followers paid him a visit when he fell very unwell. Twenty-two people contracted Nipah after coming into contact with the religious figure. After getting sick, one of these followers relocated to his family's home in a nearby village, where a friend and two family members took care of him. As his condition worsened, these three caregivers and a rickshaw driver fell unwell and assisted in moved to different facilities. Twenty-five employees and eight guests were infected via later transmission in two of the facilities [21]. Could certain NiV strains with genetic traits that cause person-to-person transmission be linked to person-to-person transmission? The closely comparable strains found in Malaysia did not cause frequent person-to-person transmission and caused less frequent and severe respiratory disease than those found in Bangladesh. Nonetheless, the trend of the outbreaks in India and Bangladesh indicates that person-to-person transmission depends less on a particular strain and more on the traits of the sporadic Nipah transmitter. Secondary NiV cases would be more likely to turn into NiV transmitters if the NiV strain was essential to person-to-person transmission. compared to primary instances (because secondary patients would have already chosen strains that are more likely to spread from person to person). However, secondary patients were no more or less likely than main cases to become Nipah transmitters in Bangladesh's seven-year study of human Nipah infection [22].

PROPERTIES OF NIPAH VIRUS

NiV has a filamentous nucleocapsid and is an envelope virus. It has a single-stranded, negative-sense, non-segmented genome that ranges in size from 120 to 500 nm. Due to a longer non-coding area for all genes except the L gene and an enlarged open read frame for the P gene, the genome is larger than that of other paramyxoviruses, including about 18,250 nucleotides [23]. Viral particle generation, budding, and interaction between the ribonucleoprotein (RNP) complex and the surface glycoprotein are all mediated by the viral matrix protein (M) of the plasma membrane. In the cytoplasm, replication takes place [24].

CLINICAL FEATURES

NiV can incubate for four to twenty-one days. NiV is extremely deadly and mostly causes respiratory illnesses and severe encephalitis. Only a tiny portion of affected People don't have any symptoms. [25] In a randomized controlled experiment among Malaysian pig farmers, Goh et al. found that 65% of patients had headaches and nearly all patients (n=91/94, 97%) complained of fever. Additionally, it demonstrated that over 50% of the patients had altered awareness and brain system involvement, indicating that encephalitis's aftereffects may cause death [26]. Fever, headache, myalgia, vomiting, altered sensorium, respiratory symptoms (from tachycardia to acute respiratory distress), and involuntary movements or convulsions were among the symptoms seen in patients during the Siliguri outbreak. [27] The National JALMA Institute for Leprosy C other Micro- bacterial Diseases, which is part of ICMR Tajganj, Agra, has two biosafety level 3 (BSL 3) facilities for the Microbiology Laboratory and one for animal experimentation. Four labs with BSL-4 facilities are available. Table 2, where the virus can be examined without running the risk of fleeing or potentially infecting more people Figure 3 [28] The most typical signs of encephalitis include altered mental state, areflexia, hypotonia, segmental myoclonus, gaze palsy, and limb weakness. These symptoms appear within a week. Patients rapidly deteriorate, and within a few days, they go into a coma and pass away. Twenty percent of survivors have residual neurological abnormalities, which might include depression, localized neurological problems, and fatigue. [29]

PATHOGENESIS

The only zoonotic paramyxoviruses are henipaviruses. Their wide host range and high case fatality rates make them remarkable as well. Their nonsegmented negative-stranded RNA genome is made up of helical nucleocapsids that are enveloped to produce pleomorphic, spherical, or filamentous virus particles. The genomes of Hev and NiV are both noticeably bigger than those of other paramyxoviruses [30]. This explains why NiV has a broad host range. Although a porcine model has shown signs of direct invasion through olfactory neurons, the haematogenous pathway is the primary method of invasion of the central nervous system [31]. Even though human virus levels are modest, the viremic spread is the major diffusion pathway. It is possible to separate the virus from the cerebrospinal fluid in the central nervous system. Damage to the endothelial cells of the small blood arteries is the hallmark of henipavirus infection. This allows the virus to progress into different organs and pass through the blood-brain and blood-air barriers, which causes the infection to spread throughout the brain and lungs. [32]

Nerves involved in smell. It is still unclear how this pathway spreads throughout the brain, despite the fact that it correlates with a direct entry into the central nervous system through oropharyngeal innervations [35]. The virus infects its host by entering through the oro-nasal pathway. Due to the fact that human tissues have only been examined near the end of the illness, the first replication site is not known. Nonetheless, lymphoid and pulmonary tissues had high antigen concentrations, suggesting that these tissues were likely the sites of early replication [36].

TESTING IN LABORATORY NUCLIC ACID AMPLIFICAT TESTING

The technique known as Polymerase Chain Reaction (PCR) is utilized to detect the RNA (viral genetic Kumar DS, Venkatesh G, Tosh C, and Kulkarni DD. Current situation of Nipah virus infection. Material) in a clinical specimen, including tissue, blood, CSF, and respiratory secretions (Indian J Virol. 2013;24(3):398-408.17). PCR techniques can be used to swiftly and accurately detect Nipah virus RNA. [37] NAAT: the procedure targets both human and animal populations and takes two to three hours. It is extremely sensitive and used to identify current viral infections [38].

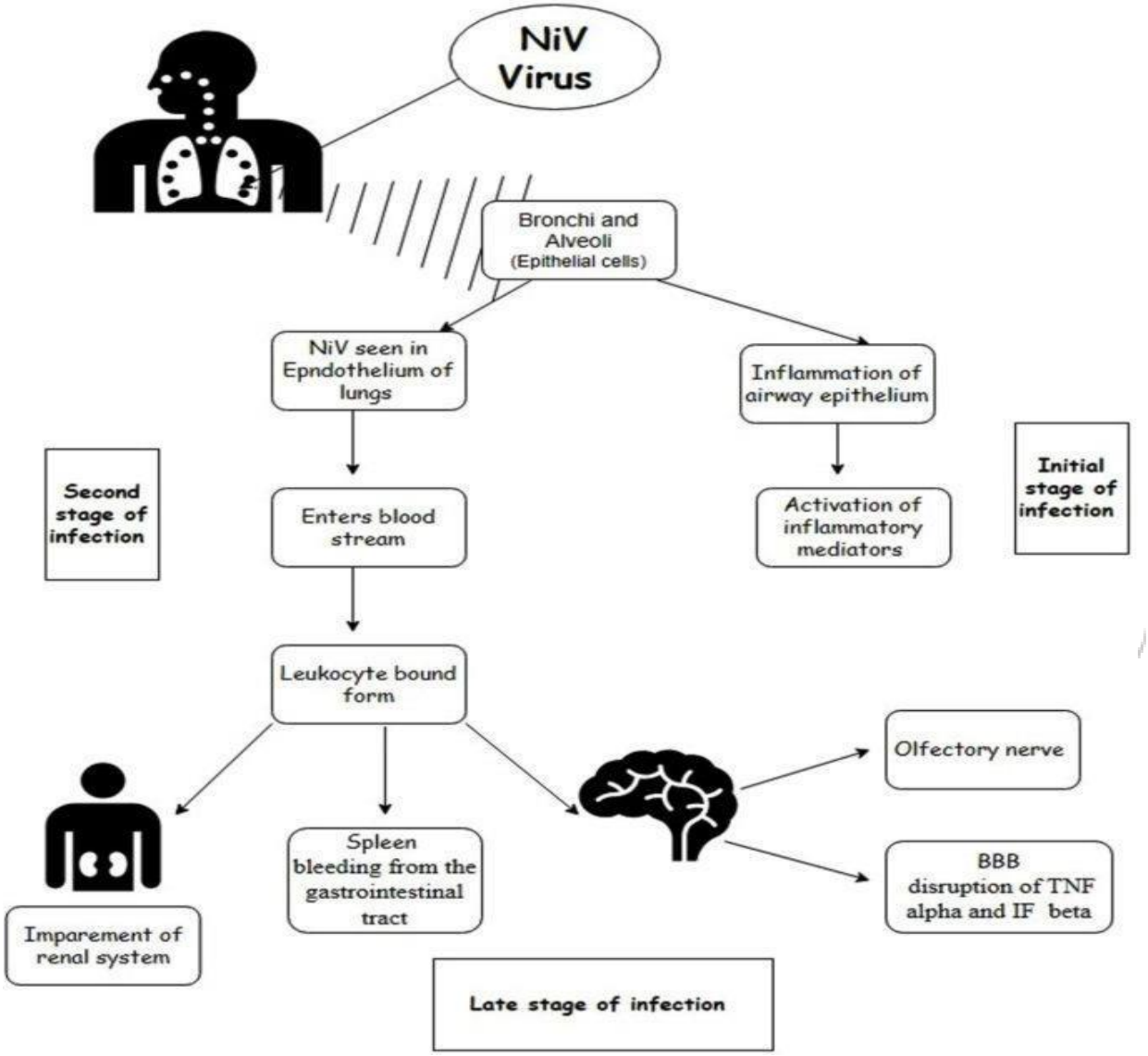


Figure 7: Niv's pathophysiology [33, 34]

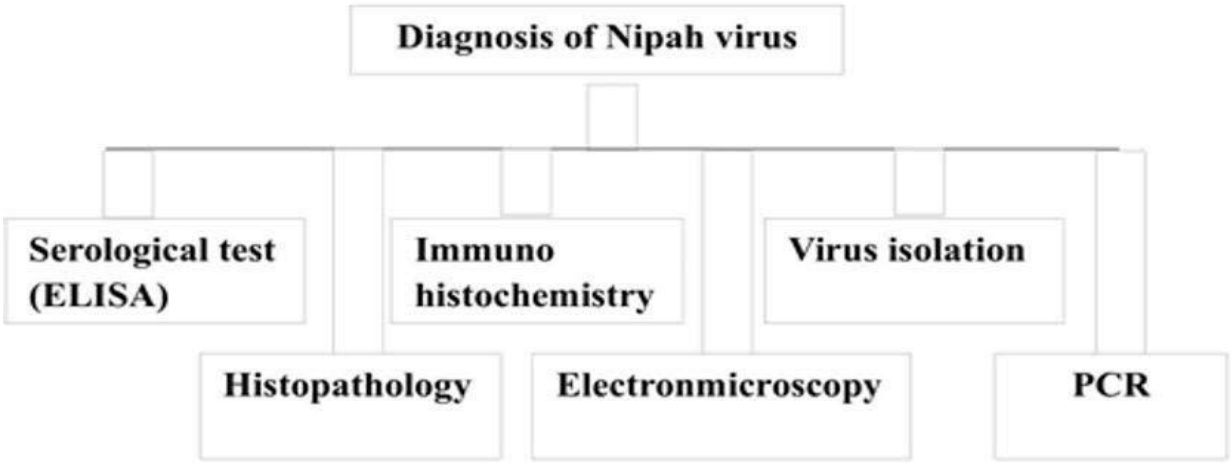
SEROLOGY

To find out if the body has developed antibodies in reaction to a Nipah virus infection, blood samples can be analyzed. In addition to IgM and IgG antibodies made against NiV, it directly detects the presence of the NiV antigen. Serological assays like the enzyme-linked immunosorbent assay (ELISA) can detect antibodies unique to the Nipah virus. ELISA tests for both humans and animals and takes roughly three to four hours to complete [39].

DIAGNOSIS

A number of assays can be used to diagnose NiV infection during both the acute and convalescent phases of the illness. Viral isolation, nucleic acid amplification testing, and serological testing can all be used to

confirm a Nipah virus infection. NiV isolation and propagation require BSL-4 facilities. Samples of blood, urine, CSF, and throat and nasal swabs can be taken from suspected patients. Samples can be taken from the kidney, spleen, lung, lymph nodes, and other organs in experimental animals. [40]



Immunohistochemistry

Figure 7. Nipah Virus Diagnosis

Study 1: As previously reported, control ferrets 1-0 and 2-0 both developed histological lesions, including extensive NiV antigen deposition indicative of acute NiV infection [41].

PCR

Conventional Polymerase Chain Reaction (PCR) has been widely used in the past for the detection of viral isolates in human and animal reservoirs. However, with advancements in rapid detection methods, tests based on conventional PCR targeting the N (nucleocapsid protein) gene have been developed by the US Centers for Disease Control and Prevention (CDC) [42]. On traditional PCR are no longer used for diagnostic reasons since they are regarded as inferior. In order to quickly describe field specimens or laboratory material, a particular TaqMan Real-Time PCR (RT-PCR) of the Nipah nucleoprotein was created in 2004. This method works well for quickly detecting NiV RNA for diagnosis since it is sensitive and dependable. [43]

SERUM NEUTRALIZATION TEST

Although a BSL-4 laboratory is needed, this is regarded as the gold standard test. Test sera are allowed to infect Vero cells after being cultured with the virus. Tests can be read after three days, and positive sera prevent the onset of cytopathic consequences. A modified neutralization test has been developed that may be read at 24 hours. [44]

MANAGEMENT AND CONTROL

Patients must be segregated, and strict infection control procedures must be followed. The mainstay of treatment for NiV infection is supportive preservation of breathing, circulation, and airway. Electrolyte and fluid equilibrium is preserved. Mechanical ventilation is required for patients with acute respiratory failure and severe pneumonia. It is preferable to use invasive mechanical ventilation. Antiviral Drug Treatment In Malaysia, patients with respiratory syncytial virus were treated with ribavirin, which works well against other

paramyxoviruses. Chong and associates [45] Controlling infections and using other precautions, such as hand Safe treatment of dead corpses, barrier nursing, and good hygiene all contribute to reducing the transmission of viruses in hospitals and homes. It's also important to utilize personal safety equipment like gloves, glasses, and masks (which offer enough filtration against airborne infections) correctly. [46, 47]

HISTORY

When a neurological and respiratory disease outbreak on pig farms in Peninsular Malaysia in 1998 resulted in 265 human cases and 108 fatalities, the first instances of Nipah virus infection were discovered [48,49,50,51]. The increasing overlap between bat habitats and piggeries in the Malaysian Peninsula is believed to be the cause of the Nipah virus's transmission from flying foxes to pigs. In one incident, the pigs were exposed to urine, feces, and half consumed fruit due to fruit orchards near the piggery [52].

TREATMENT

The only available treatment for NiV-infected people is supportive care. Extra care is taken when managing these patients since direct human-to-human contact is the greatest risk factor for infection transmission. There aren't any approved therapeutic interventions available to treat NiV. Even though antiviral therapy looks like the best option, there are surprisingly few intervention techniques available today. Two medications, ribavirin and chloroquine, have been identified; however, it is unclear if they have any therapeutic effects. On the other hand, in vitro research has shown that ribavirin effectively inhibits NiV replication. A male survivor of the most recent Kerala Nipah outbreak was also observed using ribavirin without any respiratory conditions. Ultimately, the male survivor's semen was found to contain NiV RNA on days 16 and 26 after the disease began. However, the conclusion whether the virus was alive in semen or it can be transferred through sexual routes could not be drawn [53,54] There are currently no specific medications or vaccinations available to treat or prevent Nipah virus infection. Nipavirus has been identified by the World Health Organization (WHO) as a priority disease under the WHO Research and Development Blueprint. Healthcare providers recommend extensive supportive care as the main treatment strategy in cases of severe respiratory and neurological problems brought on by Nipah virus infection [55].

PREVENTION

In order to prevent the spread of infection from one person to another, infection control measures like patient isolation, PPE use, and hand cleanliness are implemented. Contacts found via contact tracing undergo testing and are monitored until the results are negative. It has been discovered that NiV has contaminated hospital surfaces around patients [56]. Foodborne transmission is the first area that needs focused action; to prevent this, fruits should be washed and peeled before consumption, and those that have obvious biting or tampering should be thrown out [57].Two strategies for preventing human illness are suggested by the epidemiology of NiV transmission in Bangladesh. The first is reducing the amount of fresh date palm sap that Bangladeshi peasants are exposed to that is infected with NiV. Date palm sap is a seasonal national delicacy that millions of people enjoy each year and gives low-income collectors a vital source of income. Limiting bat access to date palm trees where the sap would be consumed fresh and shifting more production to molasses, where the sap is boiled at temperatures higher than those at which NiV can survive, are two ways to make date palm sap consumption safer. Date palm sap collectors have occasionally used a variety of techniques to prevent bats from accessing date palm trees [58].

VACCINE

Numerous NiV vaccination approaches have been created, and a number of them have undergone testing in animal models. A subunit vaccination based on the G glycoprotein (sG) of HeV and NiV has been the most researched strategy. HeV-sG triggers an immunological response that is cross-protective. Versus NiV as well as HeV [59]. Another tactic would be to use the present Ebola vaccination technique, which involves ring immunization around a community using vaccinations that have been stockpiled. Large- scale NiV clinical trials have not yet been carried out as of 2018, as the virus's intermittent outbreaks make it impossible to carry out such studies. Additionally, although no vaccine has been approved for usage as of yet, the Food and Drug Administration may let vaccinations that demonstrate efficacy in animal models to translate to human infections. Since the efficacy of all currently being developed potential NiV vaccines is still being evaluated on animal models, they are all in the pre-clinical stage. In animal models, a number of vaccines that use sG protein and various adjuvants, such as oligodeoxynucleotide, have shown a protective effect. The Equivac HeV vaccine, which was created with an immune-stimulatory adjuvant, is the most efficacious vaccination in this class. After a single injection, hamsters, ferrets, and African Green Monkeys have similarly demonstrated full protection from other vaccines that use the outer-membrane G/F proteins [60].

FUTURE CHALLENGES

Creating and sustaining a supply of accurate, focused, and reasonably priced testing instruments to facilitate quick diagnosis in labs situated in areas where the virus is probably present in wildlife reservoirs is a significant future issue. For early outbreak diagnosis and timely execution of preventive measures, coordination between human and animal virologists and active collaboration between institutions are essential [61]. Developing and guaranteeing a supply of reliable, specific, and reasonably priced reagents to build a quick diagnostic capability in labs in areas where the virus is anticipated to appear in International cooperation is required to create quality control systems for testing laboratories. There is an active NiV infection in Indian bats, as evidenced by the presence of NiV antibodies in the bat populations of northeastern to northwest states like Haryana [62].

CONCLUSION

Niv is now a lethal zoonotic illness. Because bats are found all over the planet, outbreaks are likely to happen in new places. The virus can be spread to humans or other animals, like pigs, by the fruit but (genus Pteropus). The Nipah virus naturally inhabits fruit bats belonging to the pteropodidase family. There isn't a particular medication or vaccination for humans or animals

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