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NIPAH VIRUS INFECTIONS: CURRENT INSIGHTS AND FUTURE PERSPECTIVES

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ABSTRACT

Nipah virus (NiV) is an extremely contagious zoonotic type of virus that has become one of the biggest issues of health protection in Asia. NiV belongs to the family Paramyxoviridae and the genus Henipavirus and was identified in 1998 as one of the biggest epidemics among Malaysian pig farmers. The virus has replicate outbreaks in South and Southeast Asia and above all, in Bangladesh and India, where the case-fatality reaches very high levels. The main natural reservoirs of the virus are fruit bats belonging to genus *Pteropus* and the virus can be transmitted either by direct contact with infected animals or by consuming tainted food or transmission among humans. The clinical manifestation of Nipah virus infection include highly febrile condition with a sudden onset or acute encephalitis or respiratory failure. The capability of the virus to overcome the species barrier, its high pathogenicity and the absence of any effective form of treatment or vaccine make the virus to reach Biosafety Level-4 (BSL-4) pathogen. Besides health hazards, Nipah epidemics have produced high socio-economic cost such as mass slaughter of pigs in Malaysia and interference with agriculture trade. The recurring epidemics advocate the need to enhance surveillance, adopt a One Health approach and come up with the preventive measures including vaccines, antiviral drug development and community awareness strategies. This descriptive review has provided information about the etiology, pathogenesis, epidemiology, outbreak history and strategies to prevent Nipah virus.

KEYWORDS: Nipah Virus Emerging Infectious Diseases Fruit Bats Encephalitis Zoonosis Paramyxoviridae Epidemiology.

INTRODUCTION

Nipah Virus (NiV) is a novel form of zoonotic virus that is known to be highly dangerous to human health since it is accompanied by high fatality and epidemic potential. The initial outbreak happened in Kampung Sungai Nipah, Malaysia in 1998-99[15] where pig farmers were infected by pigs which had picked the virus during a hunting spree from fruit bats and died of encephalitis.[7] After this there have been numerous outbreaks in Bangladesh and India, there have been sporadic attacks in the Philippines and Singapore.[20] The World Health Organization (WHO) has classified this virus as a priority pathogen, since it has an epidemic potential and no specific medical counter measures exist.[5]

NiV infection in its onset resembles an ordinary case of flu that may soon degenerate into an acute respiratory syndrome or a deadly encephalitis and kill an individual within few days. There is a possibility of long-term neurological complications which include personality change and convulsions that arise in the survivor. Genuine animal hosts of Nipah virus are *Pteropus* fruit bats.[19] The bats excreting the virus through saliva, urine and feces bypass the symptoms, hence they can be silent bearers of the disease. Seasonal phenomena are also critical to the predisposition of human infections as in the gathering of the sap of the date palm commonly polluted by fruit bats. Nipah virus is more than just a health burden since its occurrence in Malaysia, close to a million pigs had to be destroyed resulting in significant losses within the livestock industry.[14] The Nipah virus is a typical example of the predicament engulfing wild domesticated animals and human beings and the need to employ a one Health approach in the management of emerging infectious diseases.[3]

EPIDEMIOLOGY

Geographic Distribution

Discovered first in Malaysia and Singapore (1998 and 1999). Repeated cases of outbreak in Bangladesh and India. Occasional instances among the Filipines.[36] Nipah virus outbreaks in Southeast Asia confirmed 754 cases and 435 fatalities, indicating an global health risk that needs to be addressed urgently.[37]

Transmission Dynamics

Malaysia: Pig-to-human. Bangladesh/India: Bat to human and human to human. [36] In India reason for the outbreaks was mostly person to person transmission.[39]

Mortality Rate

Ranges between 40 percent (Malaysia) and 75 percent (Bangladesh/India) according to the outbreak. When compared to the previous decade (2004-2013), which exhibited a mortality rate of 54.1% virus mortality rate in the 2014–2023 decade was found to be 80.1% a notable 24% increase. From the various countries assessed for overall fatality starting from 1994-2023, India experienced greatest mortality rate of 82.7%, with Bangladesh at 62.1%, followed by Philippines at 52.9%, with Malaysia at 28.9% and Singapore was found at 21%.[38]

Seasonality

Bangladesh and India both have outbreaks mainly in winter (December, January May), when date palm sap is being collected.[40]

At-Risk Populations

Farmers, pig handlers, fruit pickers, health care workers and communities that consume uncooked or contaminated date palm sap were found to be the high risk carriers for the transmission of the disease.[40]

WHO Classification

Nipah virus infection has a pandemic potential and listed as a priority disease under WHO R&D Blueprint as there is no effective chemoprophylaxis available to the affected patient and only supportive care and preventive strategies can be adopted in this context.[40]

Table 1: Major Nipah virus outbreaks and their outcomes.[1,40,43,44,46]

Year	City/Region	Cases & Deaths	Approx. Fatality Rate
1998–1999	Malaysia	~265 cases, 105 deaths	~40%
2001	Bangladesh	13cases, 9 deaths	~69%
2004	Bangladesh	36 cases, 27 deaths	75%
2005	Bangladesh (Tangail)	12 + 11 deaths	92%
2007	India (Nadia)	suspected ~50, deaths ~5	—
2018–2024	Kerala, India	~21 deaths	~89% (2018)
2023	Bangladesh	11 cases,8 deaths	~73%
2024–2025	Kerala, India	Multiple reported cases	—

Major Outbreaks[1,40,43,44,46,47]

Malaysia & Singapore (1998)

First epidemic in Kampung Sungai Nipah. 40 per cent mortality, 265 human cases. Transmitted by intermediate host. More than 1 million pigs were culled in an effort to contain.[44,47]

Bangladesh (2001 and beyond)

An outbreak almost yearly. Related to contaminated by bats intake of sap of date palm trunk. Elevated case fatality rate: this is commonly 70-75 percent. Transmission person-to-person reported.[43]

India

2001 (Siliguri, West Bengal): 66 cases; 74 percent mortality. Key hospital related transmission. 2007 (Nadia, West Bengal): 5 cases, 100 percent mortality. 2018 (Kerala): 23 cases, 91 % mortality. Public health action kept the outbreak in check. Kerala: 2019 & 2021 Sporadic cases, well contained. 2023 (Kerala): Scarcely any cases at high degree of awareness.[1]

Philippines (2014)

Infection between human beings and infected horses. Cases-17, deaths-9.[48]

ETIOLOGY

Taxonomy

Family: Paramyxoviridae Genus: Henipavirus

Similar Viruses: Hendra virus (Australia)

Structure

Nipah virus is a single stranded, negative-sense, enveloped virus.[12] It has six structural proteins: Nucleocapsid protein (N) -wraps up the viral material.[11] Phosphoprotein (P) Assistance in replication.[18] Matrix protein (M) -gives structural integrity.[11] Fusion protein (F) - mixes with host cell membranes.[4] Glycoprotein (G) - attaches to the host cells receptors (Ephrin-B2/B3).[25] Large polymerase protein (L)-was able to participate in transcription and replication.[17]

Reservoir Hosts

Pteropus species of fruit bats are natural reservoirs. They do not get sick but excrete the virus in the urine saliva and in partially consumed fruits.[42]

Intermediate Hosts

There were amplifying hosts (pigs, Malaysia outbreak).[18] Equines (Australia, Hendra virus). [16]

Transmission of Humans

Close contact with infected animals (pigs, bats). Through contaminated food (saps, fruits of date palms). Close contact human-to-human, hospital involving and body fluids. The tropism wide severity of the disease outcomes is explained by the capacity of the virus to use Ephrin B2 and Ephrin B3 receptors expressed in large numbers of mammalian tissues (lungs, brain, blood vessels).[41]

PATHOGENESIS

Nipah virus is a disease causing agent that attacks the respiratory system and the nervous system resulting in serious cases of respiratory distress and death of the victim due to encephalitis.[24]

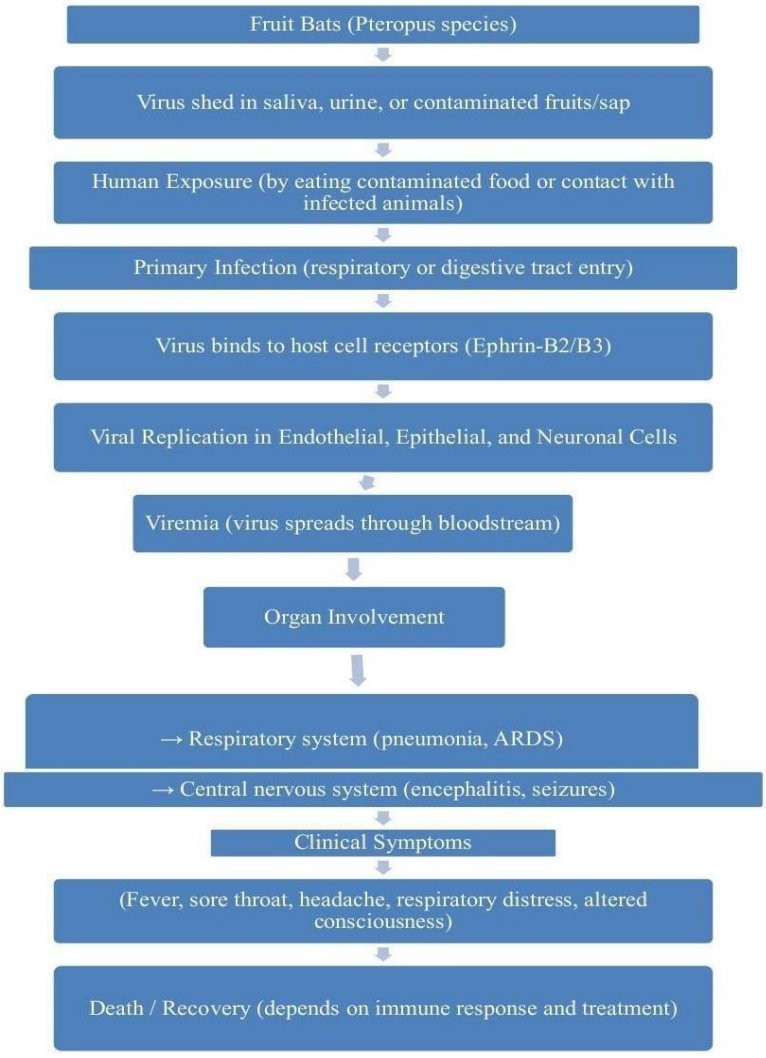

Fig. 1: Pathogenesis pathway of Nipah Virus infection.[24,41]

Entry and primary infection

Respiratory (infection by droplets) and digestive (contaminated food) tract, or infection by contact with mucous membranes.[26] The glycoprotein (G) interacts with Ephrin-B2 and B3 methods at the host cells. It worthlessly replicates itself and propagates ubiquitously. Entry is made possible by fusion protein (F). Viral replication takes place in endothelial cells, epithelial cells and neurons. The virus travels in blood (viremia).[27]

Immune Evasion

NiV manages to inhibit interferon signaling pathways and impairs the fast response of the host immune system. This enables high viral replication and dissemination of the system.[28]

Organ Damage

Respiratory System: Leads to severe pneumonia, pulmonary edema, as well as hypoxia.[29] Central Nervous System: There is inflammation in the brain (encephalitis), seizures, confusion, coma.[30] Blood Circulation System: Multiple organ dysfunction leading to microhemorrhage due to infection of endothelial cells forms.[31]

Clinical Symptoms

Headache, sore throat, fever, nausea and muscular pain. Developing: Dyspnea, cough. Severe: Neurological signs and symptoms- dizziness, altered consciousness, seizures, encephalitis. Fatality: Death in a severe case within 514 days.[36,42]

Therapy for Nipah Virus infection

Conventional / Supportive Treatment

At the moment, the Nipah virus infection has no definite antiviral medication or authorized vaccine. The treatment primarily involves supportive care which entails: Keeping the electrolytes and hydration. Treating hot blood, seizures and breathing difficulties. Intensive care support on severe cases such as administering mechanical ventilation to patients with acute respiratory failure. The treatment of such complications as encephalitis with corticosteroids and medications.[32]

Under Research or Clinical Trials

Antiviral Drugs

A number of antiviral agents and monoclonal antibodies have demonstrated positive proofs in animal testing and in the initial human experimentation:

Ribavirin - an antiviral which was used in the case of Malaysia outbreak; it was not very effective however it improved the condition slightly in mild cases.[33]

Remdesivir - demonstrated to be supportive of animals in the preclinical trials on Nipah and Hendra viruses.[34] Favipiravir (T-705) - has been shown to have antiviral activity against laboratory models. m102.4 monoclonal antibody - This antibody has been generated by immuno- reacting against the G glycoprotein of the virus; it has been shown to be successful in animals and is used on a compassionate basis in both Australia and the U.S. in case of emergency exposure.[49]

Vaccine Development

A number of such vaccine platforms are under research. The University of Oxford has developed ChAdOx1 NiV vaccine with 100 percent protection in animal testing (similar platform as AstraZeneca COVID-19 vaccine). The Hendra virus developed HeV-sG subunit vaccine can also cross-protect animals against Nipah virus. There is currently no Nipah vaccine that has been approved to be used in humans, but WHO has included it as a priority pathogen in R&D Blueprint to accelerate vaccine development. Alternative and/or Herbal Treatments (None): *Andrographis paniculata* (Kalmegh), *Tinospora cordifolia* (Giloy) and Curcumin are some of the Ayurvedic and herbal compounds under investigation due to their antiviral, immunomodulatory and anti- inflammatory effects. None of them, however, have been shown to treat Nipah virus infection clinically, but might have supportive immune effects.[35]

Table 2: Comparative Analysis Table: Nipah Virus vs COVID-19.[1,50]

Characteristic	Nipah Virus	COVID-19 (SARS-CoV-2)
Pathogen Transmission Source	Bats (sap) to humans (animals)	Possibly bats (or pangolins) (airborne droplets /aerosols) to humans
Human-to-Human Transmission	Only when it is direct contact	Very efficient air borne Transmission
Incubation Period	4-14 days	2-14 days
Common Symptoms	Fever, headache, muscular pain, respiratory disorder, encephalitis	Fever, cough, loss of smell/taste, tiredness, respiratory disease

CONCLUSION

Nipah virus is a deadly zoonotic agent that poses critical repercussions to the health of society, agricultural and economic stability. Its jumping capacity from bats to domestic animals and

human beings and the human-to-human transmission system makes it a lethal pathogen with pandemic potentialities.

There is no preventive or control measures due to unavailability of vaccines and certain antiviral agents. The strategies need to be directed towards: not eating raw sap of date palm sap, decreasing the contact between man and bats, training in the endemic areas and enhancing the infection control in the hospitals. Multinational coordination is required during vaccine design, antiviral investigation and One Health vigilance.

Altogether, the Nipah virus is not only a local issue but a threat to global health security for which we should be prepared, monitored and responded to in a systematic manner to avert any outbreaks in the future.

Future Perspectives

International collaboration is ongoing with the development of broad-spectrum antivirals and humanized antibodies and the next-generation vaccines. One Health surveillance, enhancement of biosafety laboratories capacity and awareness creation by the community are all important measures to successful management and prevention.

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