Review Article

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Nipah Virus - A Review

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ABSTRACT

Nipah virus (NiV) is a zoonotic virus (it is transmitted from animals to humans) and can also be transmitted through contaminated food or directly between people. In infected people, it causes a range of illnesses from asymptomatic (subclinical) infection to acute respiratory illness and fatal encephalitis. Outbreaks of Nipah virus (NiV) have been reported from countries like Malaysia, Singapore, Bangladesh, the Philippines, and India. Aerosol transmission, human-to-human spread, high mortality rate, and absence of efficacious vaccines and drugs make NiV a priority pathogen on the list of emerging pathogens.

Introduction :

Outbreaks of Nipah virus (NiV) have been reported from countries like Malaysia, Singapore, Bangladesh, the Philippines, and India. the primary reservoir reported is Pteropid fruit bats. Approximately 250 million people are at risk of exposure in outbreak-prone areas of Bangladesh and India, with upcoming outbreaks in non-endemic areas, its bit unpredictable to judge the risk now. Aerosol transmission, human-to-human spread, high mortality rate, and absence of efficacious vaccines and drugs make NiV a priority pathogen on the list of emerging pathogens.

Virus :

Nipah virus (NiV) is a paramyxovirus whose reservoir host is fruit bats of the genus Pteropus. Occasionally the virus is introduced into human populations and causes severe illness characterized by encephalitis or respiratory disease. Its name came from the village in the Malaysian peninsula where pig farmers became ill.

Nipah Virus is a spherical virus that is single stranded negative sense RNA. It consists of F fusion protein, G attachment protein, nucleocapsid, phosphoprotein, Viral RNA, M matrix protein and a bilayer lipid envelop. The virus is mostly found in neuronal cells, lung fibroblasts cells and monocytes. It can replicate very well and almost anywhere at the site of entry. It infects other cells either through release of infectious virus particles or by cell-to-cell spread mechanisms.

Two different strains of NiV have been isolated. The Malaysian strain varies slightly from the Bangladesh/India strain since NiV in Malaysia was cause by P. vampyrus and by P. giganteus in Bangladesh. This variation leads to the difference in clinical symptoms seen in both cases. What is been observed is that, Bangladesh strain has a higher mortality rate and is capable of transferring from human-to-human.

Transmission :

Mode of transmission -

Transmission to humans may occur after direct contact with infected bats, pigs or people, with the latter presumably through droplet transmission of bodily fluids

Bats to human - In Bangladesh and India, outbreaks have known to occur due to consumption of fruits or fruit products (such as raw date palm juice) contaminated with urine or saliva from infected fruit bats.

Animals to human - During the first recognized outbreak in Malaysia, which also affected Singapore, most human infections resulted from direct contact with sick pigs or their contaminated tissues. Unprotected exposure to secretions from the pigs, or unprotected contact with the tissue of a sick animal, has led to transmissions amongst humans.

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There are currently no studies on viral persistence in bodily fluids or the environment including fruits.

Human to human - Human-to-human transmission of Nipah virus has also been reported among family and care givers of infected patients. Interestingly, during the later outbreaks in Bangladesh and India, Nipah virus spread directly from human-to-human through close contact with people's secretions and excretions. In Siliguri (India) outbreak in 2001, transmission of the virus was also reported within a health-care setting, almost 75% of cases occurred among hospital staff or visitors. While in Bangladesh, during 2001-2008 outbreaks were due to human-to-human transmission through providing care to infected patients.

Signs and symptoms :

Human infections range from asymptomatic infection to acute respiratory infection (mild, severe), and fatal encephalitis. The incubation period (interval from infection to the onset of symptoms) commonly observed ranges from 4 to 14 days. However, an incubation period as long as 45 days has been reported in literature.

Sometimes NiV infection can be mild but most cases suffer from acute neurological signs which start with flu-like symptoms such as fever and headache. Most patients develop encephalitis that leads to altered sensorium confusion and coma in almost 97% of the cases. Some suffer from nausea and vomiting (19%) and some from respiratory disorders (51%). In severely ill patients' complications like septicemia, renal impairment and bleeding from GI (gastrointestinal) tract may occur.

Those who survive are left with mild to severe neurological damage. In few cases it is also observed that the initial infection is asymptomatic, but it can develop into a severe neurological disease up to four years later. Nearly 20% of patients are left with residual neurological consequences such as seizure disorder and personality changes. While a small subset of people who recover subsequently relapse or develop delayed onset encephalitis.

Approximately 40% to 75% case fatality has been reported. Case fatality varies depending on diagnostic tools, local infrastructure and management to contain the virus early.

Diagnosis :

Basic challenge and hindrance in diagnosing the outbreak includes nonspecific initial signs and symptoms of Nipah virus infection, and the diagnosis is often not suspected at the time of presentation. This delay in diagnosis, rather delay in suspicion is major hindrance in effective and timely infection control measures, and outbreak response activities.

In addition, availability of advanced diagnostics, ease of transportation of samples, quality, quantity of samples can affect accuracy of laboratory results. Diagnostic tool includes clinical history during the acute and convalescent phase of the disease. The main tests used are real time polymerase chain reaction (RT-PCR) from bodily fluids and antibody detection via enzyme-linked immunosorbent assay (ELISA). Polymerase chain reaction (PCR) assay, and virus isolation by cell culture, have been used as a part of diagnostic algorithm.

Treatment :

Although WHO has identified Nipah as a priority disease so far there are currently no drugs or vaccines specific for Nipah virus infection.

Intensive supportive care to treat severe respiratory and neurologic complications is recommended. Though ribavirin use has been tried in few,but no clinically significant benefit has been documented so far.

Outbreaks in India :

On 19th May 2018, a Nipah virus disease (NiV) outbreak was reported from Kozhikode district of Kerala, India. This is the first NiV outbreak in South India. During this outbreak, there have been 17 deaths and 18 confirmed cases as of 1st June 2018. The two affected districts are Kozhikode and Malappuram.

A man (age 52 years), also from Cuddalore district of Tamil Nadu and working at Guruvayur in Kerala, was admitted to JIPMER on 10th June 2019 with symptoms of Nipah. His blood samples were sent to

the Virological Institute in Pune, and these have proved negative for Nipah. Doctors confirmed he was having encephalitis, and he died 2 days later. Although from Tamil Nadu state, where he reported after becoming ill, the patient was apparently infected in Kerala state.

In 2001, from January 31st to February 23rd, 66 people were infected with Nipah Virus and 45 of them died in Siliguri, West Bengal, India. Siliguri is a commercial center that shares borders with China, Bangladesh and Nepal. This outbreak occurred among hospitalized patients, family of these patients and medical staff of 4 different hospitals.

In 2007 from 9th to 28th April in the village Belechuapara in Nadia, West Bengal, another outbreak was reported. This time 5 cases were reported and all of them succumbed to disease.

The one question that arises here is how did Nipah Virus originate and travel to India? What is known is that this virus can spread through fomites but in 2001 outbreak in Bangladesh and India no intermediating vector was found between the bats and humans. It was later found that the virus was transmitted directly to humans due to the consumption of date palm sap in Bangladesh. It is not known how the virus first entered Siliguri or who the index case was, but most of the reported cases in 2001 were clustered around one hospital called Medinovva Hospital. When a team of epidemiologists and physicians from the National Institute of Virology, Pune, India, along with local public authorities visited Siliguri and reconstructed the scenario they found a clear linage in 43 reported cases.

Outbreaks in other countries :

Human Nipah virus (NiV) infection was first recognized in a large outbreak of 276 reported cases in peninsular Malaysia and Singapore from September 1998 through May 1999. Most patients had contact with sick pigs. Patients presented primarily with encephalitis; 39% died. Autopsy studies noted diffuse vasculitis most prominently involving the central nervous system with intense immunostaining of endothelial cells with anti-Nipah virus hyperimmune serum.

In 2001, an outbreak of human disease was reported in Bangladesh. However genetic sequencing confirmed this virus as Nipah virus, but a strain different from the one identified in 1999.

Prevention :

Controlling Nipah virus in pigs. As on date, no vaccines are available against Nipah virus. Based on the prior experiences during the outbreak of Nipah involving pig farms in 1999, it has been found that, routine and thorough cleaning and disinfection of pig farms with appropriate detergents may be effective in preventing infection.

In case of suspected outbreak, the animal premises should be quarantined immediately. Sometimes, culling of infected animals (with close supervision of burial or incineration of carcasses) may be necessary to reduce the risk of transmission to people. The movement of animals from infected farms to other areas should be restricted or banned and can reduce the spread of the disease.

Nipah virus outbreaks have involved pigs and/or fruit bats, hence it becomes mandatory to establish an animal health/wildlife surveillance system, to detect Nipah cases. Indirectly it helps in giving early warning for human public health authorities and veterinary authorities.

Reducing the risk of infection in people :

Raising awareness of the risk factors and educating people about the measures they can take to reduce exposure to the Nipah virus is the only way to reduce prevent infection in people.

Reducing the risk of bat-to-human transmission.

- Efforts to decrease bat access to date palm sap and other fresh food products
  - Keeping bats away from sap collection sites with protective coverings (such as bamboo sap skirts) is proven to be helpful.
  - Avoid consuming raw date palm juice, it should be boiled, and all fruits should be thoroughly washed and peeled.
  - Discard the fruits with signs of bat bites.

Reducing the risk of animal-to-human transmission.

- It is advisable to wear protective clothing while handling sick animals or their tissues, and same precautions should be taken during slaughtering and culling procedures.
- people should avoid contact with infected pigs.

Reducing the risk of human-to-human transmission.

- Caution should be taken while handling, Nipah virus-infected people and personal protective equipment should be worn.
- Regular hand washing should be carried out before and after caring for or visiting sick people.

Controlling infection in health-care settings

Standard infection control precautions should be advised while handling specimen.

Contact and droplet precautions should be used in addition to standard precautions.

Airborne precautions may be required in certain circumstances, particularly while handling clinical specimens.

Key Facts :

- Clinical presentations vary from asymptomatic infection (subclinical) to acute respiratory infection and fatal encephalitis.
- The case fatality rate is estimated at 40% to 75%.
- Case fatality rate can be curtailed with good epidemiological surveillance and appropriate clinical management.
- Nipah virus can be transmitted to humans mainly through animals but can be transmitted through food and human contacts as well.
- There is no treatment or vaccine available for either people or animals. The primary treatment for humans is supportive care.
- The Nipah virus outbreak in Kerala during 2018 in India, claimed 21 lives out of 23 cases, with a case fatality rate of 88.9% (deaths/laboratory-confirmed cases, 16/18).
- Highlights of this outbreak include good laboratory training, increased diagnostic capacity for Nipah virus and other pathogens of high consequence. one more important tool which worked during this outbreak include good hospital infection control rapid detection and response.

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