Review

Nipah Virus: An Emergent Deadly Paramyxovirus Infection In Bangladesh

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Abstract

Nipah virus, a member of the genus Henipavirus, a new class of virus in the Paramyxoviridae family, has drawn attention as an emerging zoonotic virus in south east and south asian region. Case fatality rate of Nipah virus infection ranges from 40-70% although it has been as high as 100% in some outbreaks. Many of the outbreaks were attributed to pigs consuming fruits partially eaten by fruit bats, and transmission of infection to humans. In Bangladesh, 7 outbreaks of Nipah virus infection were identified during the period 2001–2007. In Bangladesh, Nipah virus infection was associated with contact with a sick cow, consumption of fresh date palm sap (potentially contaminated with pteropid bat saliva), and person-to-person transmission. In the most recent epidemic at least 15 people died due to Nipah virus infection in Hatibandha, Lalmonirhat district in a remote northern Bangladesh town in 2011 adding to the previous death toll of 113 in the country . Human infections range from asymptomatic infection to fatal encephalitis. Infected people initially develop influenza-like symptoms of fever, headaches, myalgia , vomiting and sore throat. This can be followed by dizziness, drowsiness, altered consciousness, and neurological signs that indicate acute encephalitis. Some people can also experience atypical pneumonia and severe respiratory problems. The virus is detected by ELISA, PCR, immunofluoroscent assay and isolation by cell culture. Treatment is mostly symptomatic and supportive as the effect of antiviral drugs is not satisfactory, and an effective vaccine is yet to be developed. So the very high case fatality addresses the need for adequate and strict control and preventive measures.

Key words: Nipah virus, paramixoviridae, pteroid bat, Bangladesh.

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Introduction

Nipah virus is an emerging zoonotic virus. In infected people, Nipah virus causes severe illness characterized by inflammation of the brain or respiratory diseases. It can also cause severe disease in animals such as pigs, resulting in significant economic losses for farmers[1].

Nipah virus is closely related to Hendra virus. Both are members of the genus Henipavirus, a new class of virus in the Paramyxoviridae family. Although Nipah virus has caused only a few outbreaks, it infects a wide range of animals and causes severe disease and death in people, making it a public health concern[2].

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Historical Background

Nipah virus was first identified and confirmed in Malaysia in 1999 when the virus crossed the species barrier from bats to pigs and then infected humans, inducing encephalitis with upto 40%

mortality. The survivors were inflicted with residual neurological problems[3] .The virus itself was named after a town in Malaysia. The outbreak was attributed to pigs consuming fruits partially eaten by fruit bats, and transmission of infection to humans. Similar outbreaks in China and Singapore followed[4,5].Case fatality rate of the 2001 outbreak which took place in Siliguri, India, near the northern border of Bangladesh was 68%. The patients affected by this outbreak presented with both encephalitis and respiratory symptoms. In Bangladesh, 4 outbreaks of Nipah virus infection was identified during the period 2001–2004. Outbreaks were different in Bangladesh due to lack of identifiable intermediate animal hosts (i.e. pig). 2004 outbrak included a number of victims under 19 years of age who collected and ate fruits, partly eaten by bats under the trees before dawn[6].

Epidemiology

In the period between 1998-2008 has infected 477 people and killed 252. Outbreaks of Nipah in south Asia have a strong seasonal pattern and a limited geographical range. Case fatality rate of Nipah virus infection ranges from 40-70% although it has been as high as 100% in some outbreaks[7,8].

Signs and symptoms

Human infections range from asymptomatic infection to fatal encephalitis. Infected people initially develop influenza-like symptoms of fever, headaches, myalgia, vomiting and sore throat. This can be followed by dizziness, drowsiness, altered consciousness[9], and neurological signs that indicate acute encephalitis. Some people can also experience atypical pneumonia and severe respiratory problems, including acute respiratory distress[10]. Encephalitis and seizures occur in severe cases, progressing to coma within 24 to

Table 1: Morbidity and mortality due to Nipah or Nipah-like virus,Asia-Pacific Region, 1998-2008[7]

Year/Month	Location	No. of cases	No. of Deaths	Case fatality
Sep 1998-Apr 99	Malaysia	265	105	40%
March 1999	Singapore	11	1	9%
Feb 2001	Siliguri (India)	66	45	68%
Apr-May 2002	Meherpur, Bangladesh	13	9	69%
Jan 2003	Naogaon, Bangladesh	12	8	67%
Jan 2004	Goalondo, Bangladesh	29	22	76%
Apr 2004	Faridpur, Bangladesh	36	27	75%
Jan –Mar 2005	Tangail, Bangladesh	12	11	92%
Jan -Feb2007	Thakurgaon, Bangladesh	7	3	43%
Mar-Apr 2007	Kuushtia, Bangladesh	8	5	63%
April 2007	Nadia, India	5	5	100%
Feb2008	Manikganj &Rajbari, Bangladesh	11	6	55%
Apr2008	Shatkira &Jessore, Bangladesh	2	1	50%
Total		477	248	52%

48 hours. The incubation period varies from four to 45 days. Most people who survive acute encephalitis make a full recovery, but around 20% are left with residual neurological consequences such as persistent convulsions and personality changes. A small number of people who recover subsequently relapse or develop delayed onset encephalitis[11,12]. In the long term, persistent neurological dysfunctions are observed in more than 15% of people. The case fatality rate is estimated at 40% to 75%; however, this rate can vary by outbreak depending on local capabilities for surveillance investigations[1, 13].

Diagnosis

Nipah virus infection can be diagnosed by a number of different tests[1]:

- serum neutralization
- enzyme-linked immunosorbent assay (ELISA)
- polymerase chain reaction (PCR) assay
- immunofluorescence assay
- Virus isolation by cell culture.

The virus

Nipah virus is closely related to Hendra virus. Both are members of the genus Henipavirus, a new class of virus in the Paramyxoviridae family, both viruses are public concern for their wide host range, ability to jump species barrier, high mortality they cause[14]. This family of viruses typically possesses a single stranded nonsegmented RNA genome of negative polarity that is fully encapsidated by proein. the helical nucleocapsid structure is surrounded by membrane derived from the plasma membrane from which the viruses bud. The paramyxovirus envelope contains two transmembrane glycoproteins (G, H or HN) and a separate fusion (F) protein [15,16]

Natural host: fruit bats

Fruit bats of the family Pteropodidae – particularly species belonging to the Pteropus genus – are the natural hosts for Nipah virus. These bats are migratory, and there is no apparent disease in fruit bats[17].

It is assumed that the geographic distribution of Henipaviruses overlaps with that of Pteropus category. This hypothesis was reinforced with the evidence of Henipavirus infection in Pteropus bats from Australia, Bangladesh, Cambodia, China, India, Indonesia, Madagascar, Malaysia, Papua New Guinea, Thailand and Timor-Leste. Recently, African fruit bats of the genus Eidolon, family Pteropodidae, were found positive for antibodies against Nipah and Hendra viruses, indicating that these viruses might be present within the geographic distribution of Pteropodidae bats in Africa[1].

Nipah virus in domestic animals

Nipah outbreaks in pigs and other domestic animals (horses, goats, sheep, cats and dogs) were first reported during the initial Malaysian outbreak in 1999. Many pigs had no symptoms, but others developed acute feverish illness, laboured breathing, and neurological symptoms such as trembling, twitching and muscle spasms. Generally, mortality was low except in young piglets.

These symptoms are not dramatically different from other respiratory and neurological illnesses of pigs. Nipah should be suspected if pigs also have an unusual barking cough. Nipah virus is highly contagious in pigs. Pigs are infectious during the incubation period,which lasts from 4 to 14 days[1, 18,19].

Situation in Bangladesh

In Bangladesh, 7 outbreaks of Nipah virus infection were identified during the period 2001–2007. In Bangladesh, Nipah virus infection was associated with contact with a sick cow, consumption of fresh date palm sap (potentially contaminated with pteropid bat saliva), and person-to-person transmission [20,21].The Malaysian outbreak was associated with a single strain. By contrast, viruses isolated in Bangladesh represent diverse strains . Hypothetically, a single

strain of Nipah virus could result in a narrower range of clinical presentations than those found during epidemics associated with genetically diverse strains. Thus, Nipah virus illnesses occurring in Bangladesh potentially provide insight into broader clinical manifestations of Nipah virus infection[22]. Unlike Malaysia and Singapore person to person transmission was found to be an important mode of spread of Nipah virus in Bangladesh. Handling or exposure to secretions of the patients was a suggested risk factor[23].

A study conducted on the Nipah virus infection in Bangladesh during the period of 2001-2004 identified 92 patients with confirmed and probable cases of Nipah virus infection Among 92 patients with Nipah virus infection, 67 (73%) died. Although all age groups were affected, 2 outbreaks principally affected young persons (median age, 12 years); 62% of the affected persons were male. Fever, altered mental status, headache, cough, respiratory difficulty, vomiting, and convulsions were the most common signs and symptoms. Clinical and radiographic features of acute respiratory distress syndrome of Nipah illness were identified during the fourth outbreak. Patients died with Nipah virus have a temperature $>37.8^0$C, altered mental status, difficulty breathing, and abnormal plantar reflexes. Patients with Nipah virus infection who had well defined exposure to another Nipah virus infected patient, the median incubation period was 9 days (range, 6–11 days)[22].

So, far Nipah virus outbreaks have been confined to western districts of Bangladesh.In the most recent epidemic at least 15 people died due to Nipah virus infection in Hatibandha, Lalmonirhat district in a remote northern Bangladesh town [23,24,25].

Treatment

No drugs or vaccines are available to treat Nipah virus infection. Intensive supportive care with treatment of symptoms is the main approach to managing the infection. Ribavarin may alleviate the symptoms of nausea, vomiting, and convulsions[26,27] Treatment is mostly focused on managing fever and the neurological symptoms. Severely ill individuals need to be hospitalized and may require the use of a ventilator[7].

Prevention and Control

Controlling Nipah virus in domestic animals

There is no vaccine against Nipah virus. Routine cleaning and disinfection of pig farms (with sodium hypochorite or other detergents) is expected to be effective in preventing infection[1]. If an outbreak is suspected, the animal premises should be quarantined immediately. Culling of infected animals – with close supervision of burial or incineration of carcasses – may be necessary to reduce the risk of transmission to people. Restricting or banning the movement of animals from infected farms to other areas can reduce the spread of the disease. As Nipah virus outbreaks in domestic animals have preceded human cases, establishing an animal health surveillance system to detect new cases is essential in providing early warning for veterinary and human public health authorities[1].

Reducing the risk of infection in people

In the absence of a vaccine, the only way to reduce infection in people is by raising awareness of the risk factors and educating people about the measures they can take to reduce exposure to the virus.

Public health educational messages should focus on the following[1].

- Reducing the risk of bat-to-human transmission. Efforts to prevent transmission should first focus on decreasing bat access to date palm sap. Freshly collected date palm juice should also be boiled and fruits should be thoroughly washed and peeled before consumption.
- Reducing the risk of human-to-human transmission. Close physical contact with

Nipah virus-infected people should be avoided. Gloves and protective equipment should be worn when taking care of ill people. Regular hand washing should be carried out after caring for or visiting sick people.

- Reducing the risk of animal-to-human transmission. Gloves and other protective clothing should be worn while handling sick animals or their tissues, and during slaughtering and culling procedures.

Controlling infection in health-care settings

Health-care workers caring for patients with suspected or confirmed Nipah virus infection, or handling specimens from them, should implement standard infection control precautions. Samples taken from people and animals with suspected Nipah virus infection should be handled by trained staff working in suitably equipped laboratories[1].

Efforts in development of an effective vaccine: A vaccine is being developed. A recombinant sub-unit vaccine formulation protects against lethal Nipah virus challenge in cats.21 ALVAC Canarypox vectored. Nipah F and G vaccine appears to be a promising vaccine for swine and has potential as a vaccine for humans[7]. Addition of a cholesterol group to HRC peptides active against Nipah virus targets these peptides to the membrane where fusion occurs, dramatically increasing their antiviral effect because of increased ability to penetrate CNS[28].

Conclusion

Nipah virus is a newly emerging potentially deadly infectious agent in this region. This situation may be made worse by mutation in the virus with the spread and progression of infection in human population with irrational, inadequate or inappropriate therapeutic measures. The main strategy is to prevent Nipah virus infection in humans before it grows beyond manageable proportion. Establishing appropriate surveillance systems will be necessary so that Nipah virus outbreaks can be detected quickly and

appropriate control measures can be initiated.

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