

Mini Review**Nipah Virus (NiV): Diagnosis, pathophysiology and treatment**

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Abstract

Nipah virus infection is a developing disease in Southeast Asia. It belongs to the family *Paramyxoviridae* of Henipavirus Genus. The name Nipah originated from a village named "Sungai Nipah" in Malaysia where pig farmer diagnosed with encephalitis. A recent outbreak revealed that this virus was also associated with a neurological disease in horses and human in the Philippines. The present study is aimed to discuss the various methods for Diagnosis, prevention and possible treatment of the Nipah virus. It was considered that transmission of virus was through respiratory droplets, an open contact with throat and nasal secretion of the pig or due to the exposure with the tissue of sick animal. Moreover the virus has been disseminated in Malaysia from the fruit bats (natural host) to the amplification host and finally to humans. Date palm sap is very commonly used for the preparation of products like molasses which is used as a sweetener in sweets and cakes and sometime administered in raw form. The establishment period of Nipah virus generally varies from 4 days to 14 days but it can be increased up to 45 days to 2 months. Infection in humans begins from without symptoms and ends with fatal encephalitis. In starting days, affected people shows influenza like symptoms with high fever, headache, weakness and sore throat. This infection can be screened by the identification of antigen, virus isolation and serology. Exposure should be avoided with the fruits bats and with their secretions. On the other side, some other pharmacologically effective treatments are still under process in preclinical trials.

Keywords: Encephalitis, Hyperthermia, Nipah virus, Respiratory droplets, Serology

Introduction

Nipah virus infection is a developing disease in Southeast Asia. It belongs to the family *Paramyxoviridae* of Henipavirus Genus. In the beginning, Nipah virus was screened and analyzed in 1998-1999 during a disruption of respiratory illness and encephalitis among pig farmers and the individual who was in close contact with pigs in Malaysia and Singapore. The name Nipah originated from a village named "Sungai Nipah" in Malaysia where pig farmer diagnosed with encephalitis. Nipah virus is closely related to "Hendra virus" so bat species were quickly culled for examination and flying foxes which belongs to the genus *Pteropus* were finally identified as the main cause for Nipah Virus. Nearly 100 deaths were reported over 300 human cases. More than a million pigs were euthanized in order to stop this outbreak which caused an astounding trade loss for Malaysia. After this crash, No consecutive cases, neither swine

nor human, have been reported in Singapore and Malaysia (MMWR, 1998). In 2001, Nipah virus was again diagnosed as originative agent in a crash of human disease occurring in Bangladesh.

Genetic screening identified this virus as Nipah virus. But different strain was identified which was not similar to that was identified in 1999. In the same year, another case was reported in Siliguri. India reports that person to person nosocomial transmission is possible to cause Nipah infection. Most of these kinds of cases seem to be acquired directly from bats by drinking raw date palm sap which a commonly consumed local delicacy. This sap is supposed to be infected or contaminated when bats stay and exposed sap collection sites at night. The disease can be transmitted person to person as well if there will be any close and unprotected contact. It is still ambivalent that how Nipah virus is circulating in these bats species. On the other hand, seropositive bats with infected RNA have also been identified in those areas where not a single case reported with infection. A recent outbreak revealed that this virus was also associated with a neurological disease in horses and human in the Philippines (MMWR, 1999; WHO, 2009).

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Transmission

During the starting crashes in Malaysia and Singapore, Most of the human infected with virus is due to that of the direct contact with diseased pig or their contaminated tissues. It was considered that transmission of virus was through respiratory droplets, an open contact with throat and nasal secretion of the pig or due to the exposure with the tissue of sick animal. In swine, it has confirmed that transmission through the placenta is carried out by iatrogenic mean and the same has been suggested for semen but not confirmed (Luby et al., 2006). Moreover the virus has been disseminated in Malaysia from the fruit bats (natural host) to the amplification host and finally to humans. Whereas no amplification was required because people were directly being infected by fruit bats somehow. On the other hand in India and Bangladesh outbreaks, contamination of fruit and fruit product carried out with urine or saliva from infected fruit bats which leads to infection (Luby et al., 2012). It seems that other people are infected due to their occupational work in trees (Montgomery et al., 2008). Date palm sap is known as most similar risk factor in Bangladesh which is some extent identical with the epidemiology of Nipah virus (Ali et al., 2010) in these countries, date palm sap is very commonly used for the preparation of products like molasses which is used as a sweetener in sweets and cakes and sometime administered in raw form. The coolest month (December to February) is most

suitably preferred for the collection of date palm sap so that sap collection should be quantitatively better due to favorable humidity and temperature. In Bangladesh the collection of date palm sap is carried out by harvesters by making a cut of V shaped gouge into a date palm tree and collected in hanged container (WHO, 2009).

Sign and Symptoms

The establishment period of Nipah virus generally varies from 4 days to 14 days but it can be increased upto 45 days to 2 months (Chua, 2003). The clinical development is described by hyperthermia followed by convulsions and death due to encephalitis or respiratory diseases. Infection in humans begins from without symptoms and ends with fatal encephalitis. In starting days, affected people shows influenza like symptoms with high fever, headache, weakness and sore throat. This may be followed by ruination in dimensional perception and stability, which makes the person abnormal sleepy with altered consciousness, few times followed by nausea and vomiting which are the key sign of acute encephalitis (8). Atypical pneumonia and severe respiratory problems can also be experienced by patients infected with Bangladeshi strain (Hossain, 2008).

In severe cases, encephalitis and convulsions may occur

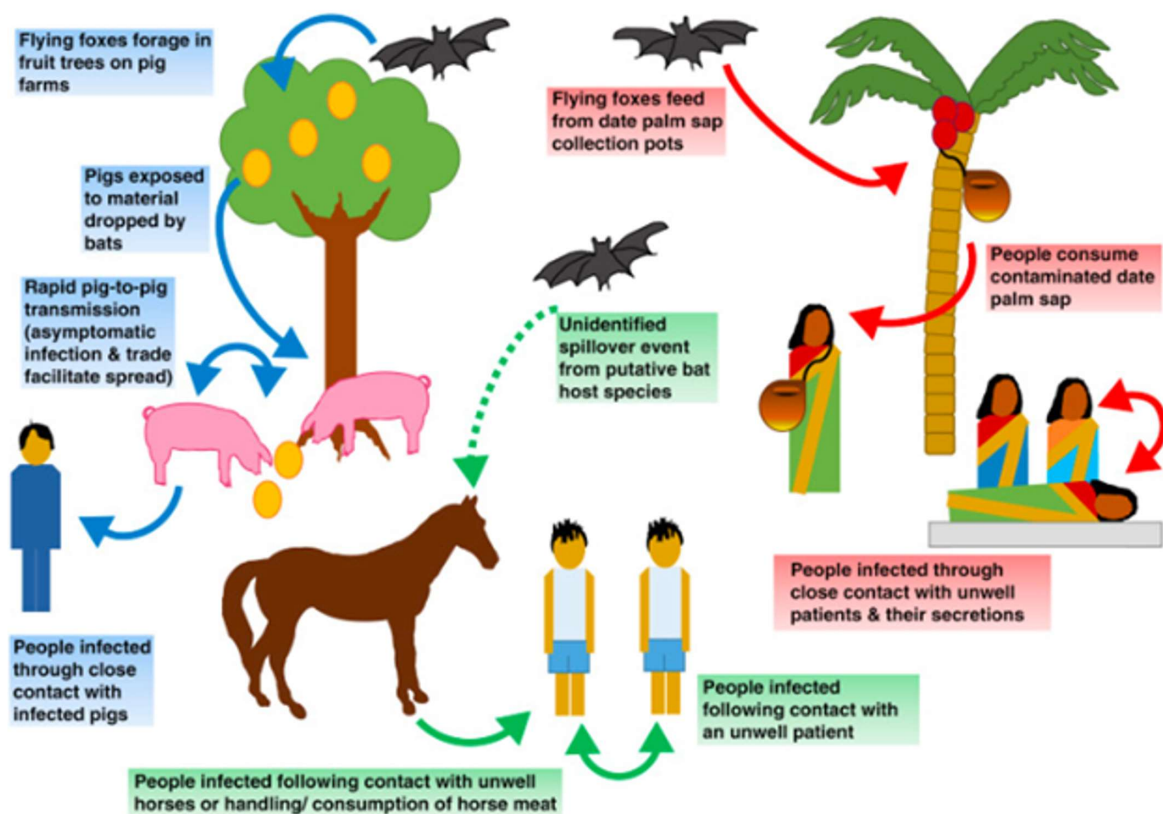


Figure. 1 Transmission of Nipah virus through various modes

which leads to coma within 1 to 2 days. The case fatality rate assessed approximately 40 % to 100% during infrequent outbreaks (Table 1). The only people make full recoveries who survive acute encephalitis. Nearby 20 % are left with neurological symptoms like as constant seizures and personality changes (WHO, 2009; Wahed, 2011).

Table 1. Case Fatality Due to Nipah Virus (Rahmana et al., 2012; Institute of Epidemiology, 2013)

Year	Country	Case	Death	Case fatality (%)
1998-1999	Malaysia	265	105	40
1999	Singapore	11	1	9
2001	India	66	49	74
2001	Bangladesh	13	9	69
2003	Bangladesh	12	8	67
2004	Bangladesh	67	50	75
2005	Bangladesh	12	11	92
2007	Bangladesh	18	9	50
2007	India	05	5	100
2008	Bangladesh	11	9	82
2009	Bangladesh	04	1	25
2010	Bangladesh	16	14	88
2011	Bangladesh	44	40	91
2012	Bangladesh	12	10	83
2013	Bangladesh	24	21	87

Pathophysiology

Nipah virus is the main cause of encephalitis in infected persons. And this virus can also leads to respiratory diseases. The proliferative period Nipah virus disease in Malaysia was evaluated to be 10 days; from the starting of symptom to the death in severe case, the time was found to be approximately 16 days (Chong, 2002). Patients usually represented with fever & changed mental status or lowered consciousness during the

Nipah virus crash in Malaysia and Singapore (Chong, 2002; Goh, 2000). Neurological character of disease increased with time and converted to coma which results in death in fatal cases. Most of the cases show the requirement of mechanical ventilation. Promulgation of focal lesions in brain mainly in subcortical and deep white matter of cerebral hemisphere revealed by the MRI during acute and chronic illness (Goh, 2000; Lee, 1999; Sarji, 2000). In Malaysia, Nipah virus was isolated with the help of cotton swabs from throat, nose, urine and secretion of trachea. Cerebrospinal fluid is also used as a medium for the collection of NiV (Nipah Virus) (Goh, 2000; Chua, 2001). Only the cases from the 1998-1999 outbreaks in Malaysia were used to perform postmortem autopsies. Some histopathological changed were visualized in the central nervous system, lungs & spleen of patients (Chua, 1999; Wong, 2002).

As a result of autopsies, vasculities in small blood vessels and capillaries was observed. The observed vasculities was described by segmental endothelial extermination, karyorrhexis & mural necrosis. Lesions were visualized in the vascular system of grey and white matter. Other than vasculities, alveolar hemorrhage, pulmonary edema & aspiration pneumonia were observed often in the pulmonary system. No vasculities was observed in the spleen while decrease in white pulp and acute necrotizing inflammation were visualized (Wong, 2002).

Diagnostic tests

This infection can be screened by the identification of antigen, virus isolation and serology. Detection can be carried out with the help of histopathology. Respiratory

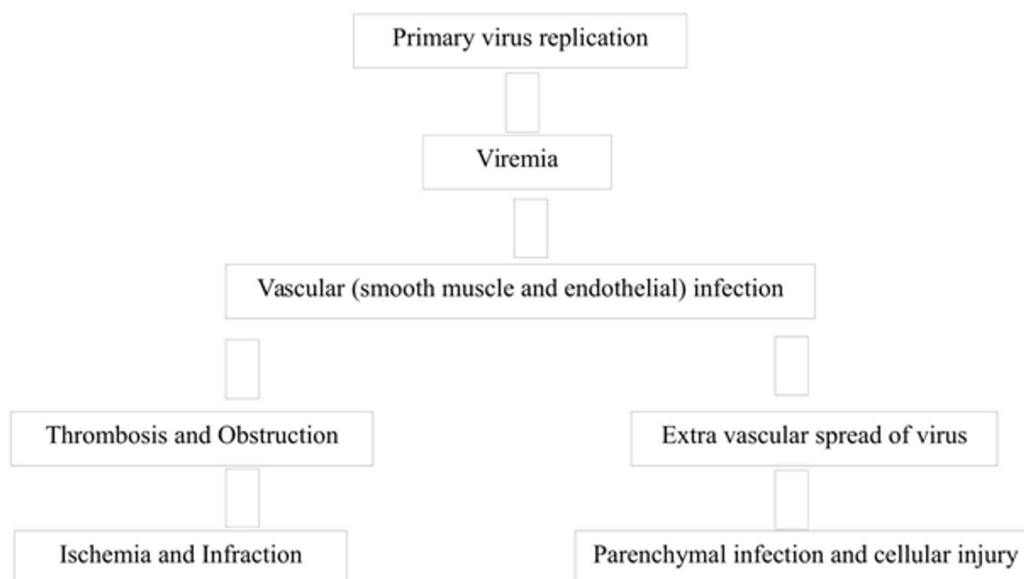


Figure 2. Pathophysiology of Nipah virus (Kum Thong Wong et al., 2002)

secretion, blood and different type of tissue have been used for the detection of Nipah virus in swine. The virus can also be screened in the feline blood, urine and respiratory secretion. On the other hand the virus diagnosed in dogs in brain, spleen, kidney, adrenal gland, lungs & liver as well. People should take important precaution while collecting sample from animal. Sampling procedure should be standardized and to ensure the safety of person limited sampling techniques should be used. Respiratory secretion and tissue sample be capable of quick diagnosis with the help of reverse Transcription-Polymerases chain reaction (RT-PCR) assay. A few number of laboratory are dealing in the isolation of viruses. Moreover Nipah virus should be cultured under high security condition as it is a BSL4 pathogen. Vero cells are used for the isolation of virus but some other cell lines may also be used for isolation purpose such as BHK, RK-13, Porcine spleen cells. This virus could be grow in embryonated chicken eggs, although this system is not usually implemented because of the ease of culture in cells. Identification of isolated virus can be carried out by various methods like as RT-PCR, immunostaining and virus neutralization. Immuno-electron microscope can produce the beneficial results in the detection of virus. Difference between the Hendra virus and Nipah virus can be identified with the help of RT-PCR and virus neutralization methods. Immunofluorescence and immunoperoxidase assays are useful in the diagnosis of viral antigen. In humans, few serological tests are performed to diagnose Henipavirus-specific IgG or IgM such as ELISAs & serum neutralization. The presence of antibodies in patient during the illness against Nipah virus can be diagnosed in serum or Cerebrospinal fluid (CSF) (Daniels, 2001).

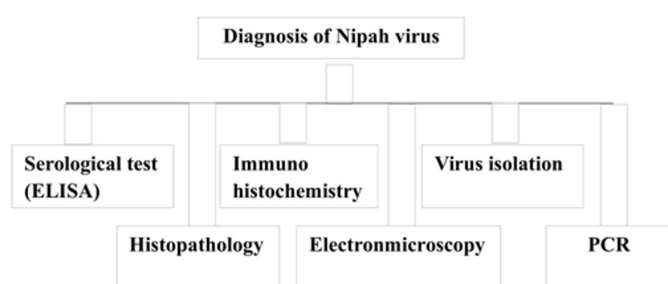


Figure 3. Diagnostic tests for Nipah Virus (NiV)

Control and Treatment

Supportive treatment is must because some patient needs mechanical ventilation. In some cases, Ribovirin was found to be effective but when checked pre-clinically, a mild effect or no effect seen. On the other side, some other pharmacologically effective treatments are still under process in preclinical trials.

Pigs are the most important category of host animal which are

associated with the dissemination of Nipah virus. The active effort for prevention of this species from this fatal disease may be helpful to decrease the risk of infection in human beings. Animal with any kind of disease should not be used for food because these slaughter process can be a major way of contact between human and viruses. Exposure should be avoided with the fruits bats and with their secretions because, at night, Bats visit collection sites of date palm sap and spread contamination with their urine and saliva. So it has been advised to avoid drinking an unpasteurized juice in native region. So to avoid drinking of these raw date palm saps, people from those endemic region use protective covering of bamboo sap skirts. Before eating, fruit should be cleaned thoroughly by washing. Peeling or cooking. Nipah virus has been categorized under the class of BSL4 pathogen; an appropriate biologically secure precaution should be used while handling infected animals, body fluid or tissue samples. Special type of gloves, masks, goggles, boots and protective clothing should be used by people who have close contact with infected animals because this disease can be easily transmitted from one person to another. Patient should be isolated from other patients to avoid transmission. Vaccines are not yet available for humans. (Geisbert, 2014).

Conclusion and future perspectives

Nipah virus is one of the pathogens in the WHO R&D Blueprint list of epidemic threats needing urgent R&D action. From 1998 to 2015, more than 600 cases of Nipah virus human infections were reported. Subsequent outbreaks in India and Bangladesh have occurred with high case fatality. Nowadays, the demand for natural product and plant based medicine is growing throughout the world. Herbal preparation can be more potentiating than allopathic medicines and they can be easily administered for long time.

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Conflicts of interest: Nil

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