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Review - Nipah virus: An emerging zoonotic disease

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Abstract
Nipahvirus or Nipah viral encephalitis is an emerging zoonotic disease. It is a negative - sense, non-segmented, single stranded RNA virus of the family of paramyxoviridae, genus Henipavirus and is closely related to hendra virus. The natural reservoir of Nipah virus is pteropid bats (flying foxes) also called fruit bats on the genus of Pteropus. Viral infection is mainly acquired by bats saliva, urine, faeces and birth fluids. Virus affected animals mostly having severe febrile encephalitis. First line of treatment is Ribavirin can reduce the mortality of acute Nipah encephalitis. Diagnosis may be done with polymerase chain reaction and serological test like Enzyme – linked immunosorbant assay.

Keywords: Nipah virus, Nipah viral encephalitis, pteropid bats, ribavirin

Introduction
Nipah virus was first appeared in pigs at Malaysia and Singapore and humans are affected in Malaysia, Singapore, India and Bangladesh. The natural reservoir of Nipah virus are Fruit bats (Suborder- Megachiroptera) and insectivorous bats (suborder – Microchiroptera) in peninsular Malaysia is responsible for Nipah viral infection. In Malaysia there are 13 species of fruit bats (including 2 flying fox) and >60 species of insectivorous bats are present due to its high diversity of bats fauna Johara *et al*., (2001) [9]. Intermediate host of the Nipah virus is pigs. The first outbreak of Nipah virus appeared in Malaysian pig farm which contain high level of fruit tress which attracted by bats and leave their saliva, urine, faeces and birth fluids. Nipah virus infection is also affected in dogs, cats, horses and goats. The first human case of Nipah virus noticed in Kampung sungai Nipah, Malaysia in 1998. That's why the virus name noticed as Nipah virus. In 1999, pigs as well as human beings of some part of the Malaysia are affected by Nipah virus had the symptoms of acute encephalitis (Chua *et al*., 1999) [4]. In 2004, similar symptoms were noticed in Bangladesh peoples due to eating of fruits or raw date palm juice which is affected by saliva or urine of fruit bats. In Earlier reported cases of encephalitis in 265 peoples with 105 deaths in Malaysia and 11 encephalitis cases with respiratory illness and one death noticed in Singapore abattoir workers who handled pigs from outbreak areas of Malaysia (Chua *et al*., (2000) [3]. Outbreak of Singapore is inhibited by import of pigs from Malaysia were prohibited and in Malaysia, outbreak ended by culling of 1 million pigs in the outbreak areas. Nipah virus killed approximately 70% of the peoples infected in Bangladesh compared to 40% in Malaysia. Virus transmits to 2 times to the west Bengal (Chadha *et al*., 2006) [1] at the time of epidemic year in Bangladesh (2001 and 2007).

Transmission
Transmission of Nipah viral infection from infected secretions of bats to the pigs. The virus is believed to have jumped from fruit bats of the Pteropus species to domestic pigs paddocked under the trees where such bats roost. These contaminated fruits taken for humans and animals leads to infection of Nipah virus infected pigs can transmit disease by direct contact of their respiratory secretions to other animals. Peoples are affected by Nipah virus due to eating of fruits or raw date palm juice which is affected by saliva or urine of fruit bats. Contamination of drinking water infected with faeces, urine, parturition fluids. Virus can transmit from one person to another through respiratory droplets (Gurley *et al*., 2007) [7].

Signs and Symptoms
Animals
40% of the mortality mostly occurs in piglets. However morbidity is high in all age groups of animals. Nipah virus mostly affects the respiratory as well as the nervous systems. It is also called as porcine respiratory and encephalic syndrome (PRES) and Barking pig syndrome

(BPS). Common symptoms of muscle tremor with limb weakness and laboured breathing can occur. CNS infection leads to head pressing, twitching, trembling, muscle fasciculation, nystagmus, tetanic spasms, seizures and respiratory infection leads to nasal discharge, open mouth breathing, convulsion and death can occur (Hooper *et al*., 2001) [8]. In dogs distemper like symptoms are noticed with pyrexia, dyspnoea and purulent oculo – nasal discharge.

Humans

Generally, Nipah virus infection can be asymptomatic to nonspecific influenza like symptoms can appear. Some common signs of fever, headaches, sore throat, confusion, disorientation, vomiting and muscle pain (myalgia), and segmental myoclonus are occur. Nipah virus can affect the CNS leads to severe vasculitis of small blood vessels result in endothelial damage, Hypertension, tachycardia and rapid deterioration with irreversible hypotension which leads to death. In severe cases, respiratory infection leads to dyspnoea (Wong *et al*., 2002) [12]. In advance cases, fatal encephalitis (inflammation of brain tissue), drowsiness, dizziness, altered consciousness and neurological signs are appearing finally coma within 24 – 48 hours.

Case Definitions

Suspect Nipah Case

Person from a area/ locality affected by a Nipah virus disease outbreak who has:

- Acute Fever with new onset of altered mental status or seizure and/or
- Acute Fever with severe headache and/or
- Acute Fever with Cough or shortness of breath

Probable Nipah Case

Suspect case-patient/s who resided in the same village where suspect/confirmed case of NIPAH were living during the outbreak period and who died before complete diagnostic specimens could be collected

OR

Suspect case-patients who came in direct contact with confirmed case-patients in a hospital setting during the outbreak period and who died before complete diagnostic specimens could be collected.

Confirmed Nipah Case

Suspected case who has laboratory confirmation of Nipah virus infection either by:

- Nipah virus RNA identified by PCR from respiratory secretions, urine, or cerebrospinal fluid.
- Isolation of Nipah virus from respiratory secretions, urine or cerebrospinal fluid.

Definition of a Contact

A Close contact is defined as a patient or a person who came in contact with a Nipah case (confirmed or probable cases) in at least one of the following ways.

- Was admitted simultaneously in a hospital ward/ shared room with a suspect/confirmed case of Nipah virus disease
- Has had direct close contact with the suspect/confirmed case of Nipah virus disease during the illness including during transportation.
- Has had direct close contact with the (deceased) suspect/confirmed case of Nipah virus disease at a funeral or during burial preparation rituals
- Has touched the blood or body fluids (saliva, urine, vomitus etc.) of a suspect/confirmed case of Nipah virus disease during their illness
- Has touched the clothes or linens of a suspect/confirmed case of Nipah virus disease

These contacts need to be followed up for appearance of symptoms of NipahV for the longest incubation period (21 days), or preferably double incubation period, of 42 days.

Diagnosis

Incubation period in pigs is approximately 4 to 14 days, human beings at 4 to 20 days and some cases reported in 45 days. The current infection can be diagnosed by high or four fold rises in specific IgM or IgG antibody (Ab) was detected in serum sample by Enzyme – linked immunoassays (ELISA) and modified ELISA developed based on relative reactivity of sera with Niv antigen. Tissue samples from necropsy – showed micro-infraction in CNS. Blood and cerebrospinal fluid samples taken at before death of affected animals to culture the virus. The vero cells inoculation with cerebro spinal fluid (CSF) samples taken from the fatal cases of encephalitis causing a syncytial formation. The RT- PCR – in that RNA was extracted from human brain tissue (Fatal cases only). Two sets of primers were used for RT-PCR reaction (Chadha *et al*., 2006) [1].

- Primary set NVNBF – 4 (5’ – CAATGGAGCCAGACATCAAGAG-3’) and NVNBR4 (5’-CATAGAGATGAGTGTAAAAGC-3’) amplified a 159 nucleotide (nt) region of the N gene of Niv.
- Primer set of NVBMFC1 (5’- CAATGGAGCCAGACATCAAGAG- 3’) and NVBMFR2 (5’- CGGAGAGTAGGAGTTCTAGAAG-3’) amplified a 320 nt-region of the M gene of Niv.
- The recommended samples in humans are:
- Throat swab in viral transport medium
- Urine 5 ml in universal sterile container
- Blood in red vacutainer (5ml)
- CSF (1-2 ml) in sterile container

Differential Diagnosis

In earlier time the pigs which are affected by the Nipah virus had respiratory illness and it was ascribed as Japanese encephalitis (JE). JE is a mosquito born disease which is mostly endemic in a particular area where the pigs are mostly present. Pigs are the amplifying host of the JE (Chua *et al*., (2000) [3]. Symptoms which appear in the humans were distinct or deferred from JE.

Nipah virus is differ from the JE by mostly affected the adult rather than children, members of the same households are mostly affected so, the viral infection had higher attack rate. But in JE, symptomatic encephalitis can occur in only 1 in 300 affected peoples but in Nipah virus affected peoples all had encephalitis.

The Nipah virus outbreak is related to hendra virus but it had a clear-cut difference from hendra virus (Rogers *et al*., 1996) [11]. Hendra virus transmitted from horse and all affected animals had respiratory infection with severe menigo – encephalitis (Field *et al*., 1997) [6] (Osullivan *et al*., 1997) [10]. But in all Nipah virus animals do not had pulmonary involvement (Hooper *et al*., 2001).

Prevention and Control

- Transmission of Nipah virus can be effectively controlled by strict hygienic measures such as avoid consumption of partially bat eaten fruits and undercooked meat of infected animals.
- Avoid direct close physical contact of affected peoples
- Wear proper mask which contain NH-95 grade while attending patients with symptoms
- Proper sanitation of hands at regular interval
- Avoid visitors to enter the farm
- Proper cleaning of contaminated areas with using of 4% sodium hypochlorite.
- Proper isolation and quarantine period for the farm.
- Mass eradication of the infected animal in the farm and after culling proper burial site are selected and disinfected with chlorinated lime.
- Educative campaigns should be created to make public aware of this viral zoonotic diseases.
- Most important biosecurity measures to avoid the likelihood of the bats reservoir coming into contact with pigs.

Treatment

Currently there is no known treatment or vaccine available for either human or animals. Intensive supportive care with treatment of symptoms is the main approach to managing the infection in people.

There is no proven treatment recommended for Nipah virus disease. Some observational data suggests that Ribavirin may be of use in reducing mortality among patients with encephalitis caused by Nipah virus disease. There is no data/evidence of its usefulness as a prophylactic drug (Chong *et al*., 2001) [2].

There are research project going on by using Monoclonal antibodies as treatment for Nipah Virus disease.

Systemic treatment only now currently available, there is no proper vaccination and drug available for treating the virus.

First line of treatment is Ribavirin can reduce the mortality of acute Nipah encephalitis (Chong *et al*., 2001) [2].

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