

# Nipah virus outbreaks in Bangladesh: a deadly infectious disease

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**Abstract:** During 2001-2011, multidisciplinary teams from the Institute of Epidemiology, Disease Control and Research (IEDCR) and International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) identified sporadic cases and 11 outbreaks of Nipah encephalitis. Three outbreaks were detected through sentinel surveillance; others were identified through event-based surveillance. A total of 196 cases of Nipah encephalitis, in outbreaks, clusters and as isolated cases were detected from 20 districts of Bangladesh; out of them 150 (77%) cases died. Drinking raw date palm sap and contact with a case were identified as the major risk factors for acquiring the disease. Combination of surveillance systems and multidisciplinary outbreak investigations can be an effective strategy not only for detection of emerging infectious diseases but also for identification of novel characteristics and risk factors for these diseases in resource- poor settings.

**Keywords:** Nipah virus, outbreak, surveillance, transmission, communicable disease, Bangladesh.

## Introduction

Nipah is a recently detected viral zoonotic disease caused by Nipah virus originating from a new genus - the Henipa virus.<sup>1, 2</sup> *Pteropus* bats are the zoonotic host of the virus and pigs are the likely amplifying host.<sup>2, 3</sup> The virus was first identified in Nipah village of Malaysia in 1998,<sup>2, 4</sup> since then three other countries have reported human cases of Nipah virus infection, including Bangladesh.<sup>5-7</sup> The Institute of Epidemiology, Disease Control and Research (IEDCR), a government mandated institute, conducted disease surveillance and outbreak investigations for Nipah encephalitis in Bangladesh. We present a review of the methods used for detecting these cases and their novel characteristics and risk factors

through outbreak investigations during 2001-2011.

## Methods

We reviewed IEDCR strategies and guidelines from its records to explore the mechanism for detection of Nipah cases and clusters. We also reviewed the method of hospital-based Nipah surveillance jointly conducted by IEDCR and the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b). Outbreak investigation reports were studied to identify the sources of information through which these outbreaks were detected. The Nipah surveillance database was used to describe the demographic and clinical characteristics of the identified Nipah cases. Published reports

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on Nipah encephalitis in Bangladesh and unpublished outbreak investigation reports were reviewed to identify the risk factors for Nipah encephalitis in Bangladesh.

## Results

To detect disease outbreaks, IEDCR conducts both 'event-based surveillance' and 'surveillance for specific disease or conditions'. Up to April 2010, as part of the event-based surveillance, IEDCR conducted unstructured monitoring of newspapers and television channels for reports of suspected disease outbreaks. In April 2010, IEDCR started a more structured surveillance of suspected disease outbreak reports in 10 national newspapers and eight national television channels. Any reported cluster or outbreak of known illness and even report of a single death from unknown disease is captured through this surveillance method. In addition to the media surveillance, IEDCR has two hotline numbers for healthcare providers to report disease outbreaks. Through district and sub-district rapid response teams, IEDCR verifies the existence of any outbreak and conducts investigation.

To identify outbreaks of encephalitis through enhanced surveillance networks and to identify risk factors for transmission of Nipah encephalitis, IEDCR in collaboration with the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) has been conducting surveillance for Nipah encephalitis in Bangladesh since 2006. Initially, this surveillance programme started in 10 hospitals. Currently, the surveillance is functioning in five hospitals in northwestern and central Bangladesh. Clinicians of sentinel hospitals identify and list all encephalitis cases presenting in the surveillance hospitals. A case of encephalitis is defined as any person with history of acute onset of fever or axillary temperature of  $>38.5^{\circ}\text{C}$  and evidence of acute

brain pathology manifested by altered mental status or new onset of seizure or neurological deficit. Any cluster of encephalitis cases, defined by two encephalitis cases within 21 days of each other and within half an hour walking distance from each other, identified through the sentinel hospitals are investigated by a trained team of epidemiologists from IEDCR and icddr,b.

As part of the cluster investigation the IEDCR and icddr,b team conducts search for encephalitis cases in the community adjacent to the cluster and carries out epidemiological research to identify risk factors. In case of outbreaks of encephalitis that are detected through event-based surveillance or sentinel surveillance, a team of epidemiologists, veterinarians and anthropologists conduct outbreak investigations. These investigations include identification of alive or deceased human cases suspected of having Nipah encephalitis, identification of possible animal sources of the infection, assessment of environmental contamination, and study of possible behavioural factors contributing to the outbreak and case control study to identify possible risk factors. For each case of Nipah encephalitis, four age-matched neighbourhood controls are selected for case control study. Exposure histories of both cases and controls within 30 days prior to the onset of illness are collected.

In case of any encephalitis cluster or outbreak, investigation teams collect blood from the suspected encephalitis cases and samples are sent to IEDCR. Initially, samples were sent to Centers for Disease Control and Prevention, USA (CDC) for testing. Later in 2007, a Nipah laboratory was set up at IEDCR for safe specimen handling and testing. Virologists of IEDCR conduct enzyme-linked immunosorbent assay to identify IgM and IgG antibodies against Nipah virus.

In Bangladesh, Nipah outbreak was first confirmed in 2003, when a team from Centers for Disease Control and Prevention, Atlanta, USA (CDC), icddr,b and the Government of Bangladesh retrospectively investigated two outbreaks of suspected encephalitis with human deaths which had occurred in Meherpur district in 2001 and in Naogaon in 2003.<sup>7</sup> Including these two, 11 outbreaks of Nipah encephalitis have been detected in Bangladesh since 2001. Five of these outbreaks were detected from newspaper reports of human deaths from unknown illness, three were reported by sentinel hospitals, one was reported from a private hospital and others were reported by the civil surgeon of a district. During this period, 196 cases of Nipah encephalitis were detected from 20 districts of Bangladesh in outbreaks, clusters and as isolated cases; out of these 150 (77%) cases died.

The Nipah cases were mostly distributed in the northwestern and central part of Bangladesh. Outbreaks occurred during December to May, which coincides with the winter season in Bangladesh. Cases were distributed in all age groups. Median age was 25 years (range: 0.5–75 years) and 124 (63%) cases were males. Median duration from onset of illness to death was six days (range: 1–47

days). In the course of illness, 123 (63%) Nipah encephalitis cases developed acute respiratory distress syndrome (Table 1).

Drinking raw date palm sap collected during winter months, which is a delicacy in rural Bangladesh, was first identified as a risk factor for Nipah infection in an outbreak in Tangail in 2005.<sup>8</sup> This has also been identified as a risk factor in three more outbreaks so far. Several sporadic cases have also reported history of drinking raw date palm sap within 30 days before the onset of illness. Close contacts with a sick person or his/her secretions and contact with sick animals were the other two risk factors identified through case control studies in different outbreak investigations (Table 2).

*Pteropus* bats were found to be positive for Nipah antibodies in different outbreak areas.<sup>7</sup> A zoonotic investigation team of icddr,b identified the way bats contaminate the shaved surface of the date palm trees (from where the sap is collected) using infrared camera.<sup>9</sup>

## Discussion

A combination of an 'event-based' and 'sentinel' surveillance system has been a successful strategy in Bangladesh for detecting recurrent outbreaks of Nipah

**Table 1: Clinical characteristics of Nipah cases in Bangladesh**

Clinical characteristic	Number (%)
Fever	196 (100)
Altered mental status	169 (86)
Sever weakness/lethargy	142 (72)
Headache	131 (67)
Acute respiratory distress syndrome	123 (63)
Cough	108 (55)
Vomiting	105 (54)
Myalgia	81 (41)
Convulsions	59 (30)

**Table 2: Risk factors identified through case control studies in Nipah outbreaks of Bangladesh**

Year	District	Risk factors	Odds Ratio	95% Confidence Interval	p
2001	Meherpur	Contact with a sick cow <sup>7</sup>	7.9	2.2 - 27.7	-
		Caring or living with a case <sup>7</sup>	4.8	1.23 - 18.8	-
2003	Naogaon	Close proximity with pig herds <sup>10</sup>	6.1	1.3 - 27.8	0.007
2004	Rajbari	Climbing trees <sup>13</sup>	8.2	1.25 - ∞	-
		Contact with Nipah patient <sup>13</sup>	21.4	2.78 - 966.1	-
2004	Faridpur	Touching a Nipah patient <sup>14</sup>	5.6	1.79 - 17.24	0.003
2005	Tangail	Drinking raw date palm juice <sup>8</sup>	7.9	1.6 - 38	<0.01
2007	Thakurgaon	Remaining in the same room with Nipah patient <sup>16</sup>	Undefined	-	<0.001
2007	Kushtia	Physical contact with a Nipah patient <sup>15</sup>	Undefined	-	<0.001
2008	Manikganj and Rajbari	Drinking raw date palm juice	18	2.2 - ∞	<0.005
2010	Faridpur	Drinking raw date palm juice	-	-	-
2011	Lalmonirhat	Drinking raw date palm juice	17	4 - 70	≤0.001

encephalitis. Multidisciplinary collaborative investigation of the outbreaks identified the clinical characteristics, risk factors and mode of transmission of this highly fatal zoonotic disease.

Over 50 species of *Pteropus* bats, the natural reservoir of Nipah virus, live in South and South-East Asian countries.<sup>10</sup> After the large outbreak of Nipah encephalitis in Malaysia, only three outbreaks have been reported from countries other than Bangladesh, one in Singapore and two

based surveillance system with a sentinel surveillance system for encephalitis has possibly increased the likelihood of identifying Nipah cases in Bangladesh in comparison to some other countries in the region, which lack a strong surveillance for encephalitis.

While more than 95% of the Nipah cases in Malaysia had a history of contact with pigs,<sup>11</sup> in only one of the 11 Bangladeshi outbreaks a close proximity to pig herds was identified as a risk factor. Identification of the drinking of raw date palm sap, a unique cultural practice

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