Foundation of Research: Overview of Regional Epidemiology of Nipah Virus

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Institute of Epidemiology, Disease Control and Research
Do we really understand Epidemiology of Nipah virus??????
Global Picture

• 1998-1999: Malaysia
  – Human febrile encephalitis,
  – high mortality
  – New virus discovered

• 1999: Singapore
  – Outbreak in abattoir workers
  – Pigs imported from Malaysia

• Since 2001 – Bangladesh, India
Nipah: World’s outbreak

- Reported from 4 countries of the world
- Bangladesh is the only country reporting Nipah almost every year
- Are there no cases or cannot detect???
Malaysia Outbreak

- Introduced into pig farms by fruit bats
- Amongst pigs: spread by droplet infection.
- **Pigs act as an intermediate and amplifying host.**
- Transmitted to humans close contact with infected pigs.
- Most patients had contact with sick pigs or close physical contact with Nipah virus infected patients.
- Presented with encephalitis
- Initially thought Japanese encephalitis, but later identified as Nipah virus encephalitis
Nipah virus has been isolated from CSF of victims in Malaysia.

Infective virus has also been isolated from environmental samples of bat urine and partially-eaten fruit in Malaysia.
Malaysia Outbreak

• Outbreak caused panic and fear in Malaysia
• The primary control measure has been culling of pigs. In the 3 affected states, almost 900,000 pigs have been killed.
• Tremendous economic loss
• Transport of pigs within the country has been banned.
• Other control measures include educational efforts and national surveillance to detect any additional infected
Nipah in Singapore

- Workers in Singapore
- Developed a febrile illness caused by Nipah virus
- During March 1999 following close contact with imported pigs from Malaysia.
Nipah In India

2001: Shiliguri, Late January to Mid February
Out of 66 cases 45 has history of contact with Nipah patient

2007: Nadia, West Bengal, 11 to 28th April
30 cases reported with Fever with Respiratory distress and Neurological symptom

2018: Kerala, India, May, 2018
Outbreaks in Bangladesh

• The first outbreak of Nipah virus in 2001 in Meherpur district.

• Since then, outbreaks reported almost every year in selected districts of Bangladesh.
<table>
<thead>
<tr>
<th>Year</th>
<th>Districts</th>
<th>Number of outbreak cases</th>
<th>CFR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>Meherpur</td>
<td>13 cases 9 deaths</td>
<td>69</td>
</tr>
<tr>
<td>2003</td>
<td>Naogaon</td>
<td>12 cases 8 deaths</td>
<td>67</td>
</tr>
<tr>
<td>2004</td>
<td>Rajbari Faridpur Joypurhat Manikganj Naugaon</td>
<td>12 cases 10 deaths 35 cases 27 deaths 4 cases 4 deaths 5 cases 4 deaths 2 cases 2 deaths</td>
<td>83 77 100 80 100</td>
</tr>
<tr>
<td>2005</td>
<td>Tangail</td>
<td>12 cases 10 deaths</td>
<td>83</td>
</tr>
<tr>
<td>2007</td>
<td>Thakurgaon Kushtia</td>
<td>7 cases 3 deaths 8 cases 5 deaths</td>
<td>43 63</td>
</tr>
<tr>
<td>2008</td>
<td>Manikganj Rajbari</td>
<td>4 cases 4 deaths 6 cases 5 deaths</td>
<td>100 83</td>
</tr>
<tr>
<td>2010</td>
<td>Faridpur</td>
<td>8 cases 7 deaths</td>
<td>88</td>
</tr>
<tr>
<td>2011</td>
<td>Rajbari Dinajpur Rangpur (Tari) Lalmonirhat</td>
<td>2 cases 2 deaths 5 cases 4 deaths 8 cases 5 deaths 22 cases 20 deaths</td>
<td>100 80 63 91</td>
</tr>
<tr>
<td>2012</td>
<td>Joypurhat Rajshahi (Tari)</td>
<td>7 cases 6 deaths</td>
<td>86</td>
</tr>
</tbody>
</table>
Bangladesh Situation

- Nipah outbreaks recur in a specific region
- And specific time of year in Bangladesh.
- Seasonality of outbreaks is: December-March
Figure 1: Chronological distribution of outbreak of Nipah virus infection in South Asia, 2001-2008

The boundaries and name shown on this map do not imply any expression or any opinion what so ever on the part of World Health Organization concerning the legal status of any country, territory, city or area of its authorities or concerning the delimitation of its frontiers or boundaries.
Nipah virus transmission

Pigs: Amplification

Fruit bats

Close contact with infected animals

Human

Healthcare workers

Secondary Transmission

indirect transmission from bats

Date palm sap
infectious disease

Mahmudur Rahman, Apurba Chakraborty

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.1, 2 Pteropus bats are the zoonotic host of the virus and pigs are the likely amplifying host.2, 3 The virus was first identified in Nipah village of Malaysia in 1998,4-6 since then three other countries have reported human cases of Nipah virus infection, including Bangladesh.5-7 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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Risk factor identified through case control studies in Nipah outbreaks of Bangladesh

<table>
<thead>
<tr>
<th>Year</th>
<th>District</th>
<th>Risk factors</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>Meherpur</td>
<td>Contact with a sick cow&lt;sup&gt;7&lt;/sup&gt;</td>
<td>7.9</td>
<td>2.2 - 27.7</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Caring or living with a case&lt;sup&gt;7&lt;/sup&gt;</td>
<td>4.8</td>
<td>1.23 - 18.8</td>
<td>-</td>
</tr>
<tr>
<td>2003</td>
<td>Naogaon</td>
<td>Close proximity with pig herds&lt;sup&gt;10&lt;/sup&gt;</td>
<td>6.1</td>
<td>1.3 - 27.8</td>
<td>0.007</td>
</tr>
<tr>
<td>2004</td>
<td>Rajbari</td>
<td>Climbing trees&lt;sup&gt;13&lt;/sup&gt;</td>
<td>8.2</td>
<td>1.25 - ∞</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contact with Nipah patient&lt;sup&gt;13&lt;/sup&gt;</td>
<td>21.4</td>
<td>2.78 - 966.1</td>
<td>-</td>
</tr>
<tr>
<td>2004</td>
<td>Faridpur</td>
<td>Touching a Nipah patient&lt;sup&gt;14&lt;/sup&gt;</td>
<td>5.6</td>
<td>1.79 - 17.24</td>
<td>0.003</td>
</tr>
<tr>
<td>2005</td>
<td>Tangail</td>
<td>Drinking raw date palm juice&lt;sup&gt;8&lt;/sup&gt;</td>
<td>7.9</td>
<td>1.6 - 38</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>2007</td>
<td>Thakurgaon</td>
<td>Remaining in the same room with Nipah patient&lt;sup&gt;16&lt;/sup&gt;</td>
<td>Undefined</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2007</td>
<td>Kushtia</td>
<td>Physical contact with a Nipah patient&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Undefined</td>
<td>-</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2008</td>
<td>Manikganj and Rajbari</td>
<td>Drinking raw date palm juice</td>
<td>18</td>
<td>2.2 - ∞</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>2010</td>
<td>Faridpur</td>
<td>Drinking raw date palm juice</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2011</td>
<td>Lalmonirhat</td>
<td>Drinking raw date palm juice</td>
<td>17</td>
<td>4 - 70</td>
<td>≤0.001</td>
</tr>
</tbody>
</table>
Nipah Virus Transmission from Bats to Humans Associated with Drinking Traditional Liquor Made from Date Palm Sap, Bangladesh, 2011–2014


Nipah virus (NiV) is a paramyxovirus, and Pteropus spp. bats are the natural reservoir. From December 2010 through March 2014, hospital-based encephalitis surveillance in Bangladesh identified 18 clusters of NiV infection. The source of infection for case-patients in 3 clusters in 2 districts was unknown. A team of epidemiologists and anthropologists investigated these 3 clusters comprising 14 case-patients, 8 of whom died. Among the 14 case-patients, 8 drank fermented date palm sap (tant) regularly before their illness, and 6 provided care to a person infected with NiV. The process of preparing date palm trees for tant production was similar to the process of collecting date palm sap for fresh consumption. Enteroic excreta was reported found inside pots used to make tant. These findings suggest that drinking tant is a potential pathway of NiV transmission. Interventions that prevent but access to date palm sap might prevent tant-associated NiV infection.

Nipah virus (NiV) is a bat-borne emerging infection, and Pteropus spp. bats are the wildlife reservoir (1). NiV was discovered in an outbreak in Malaysia in 1998 that affected 283 persons and caused 109 deaths (case-fatality rate 39%) (2). Subsequently, outbreaks of NiV infection have occurred nearly every year in Bangladesh and occasionally in India (1,5–5). A total of 33 outbreaks of NiV encephalitis have been reported in Bangladesh and India during 2001–2014, and epidemiologic investigations implicated batborne and human-to-human transmission (6,7). During 2004–2012, a total of 157 NiV infections were reported in Bangladesh, and 22% of these occurred through human-to-human transmission (8).

Investigations of NiV-associated outbreaks in Bangladesh identified consumption of fresh date palm sap as the primary route of bat-to-human transmission (1,9). In Bengali culture, sap harvested from the date palm tree is commonly used for fresh consumption and fermentation (10,11). Moreover, in Asia, Australia, and Africa, fermented date palm sap is used to make alcoholic drinks, known as toddy, nari, or palm wine (12,13). In Bangladesh, date palm sap is typically collected in clay pots that are attached to the tree. A top section of the date palm tree bark is shaved, allowing the sap to ooz overnight into the collection pot (11). A previous NiV study reported that Pteropus spp. bats frequently feed on the shaved bark and often contaminate the sap with saliva, urine, and excreta (14). Pteropus spp. bats are also known to occasionally shed NiV in their secretions and excretions (15,16).

Since 2006, the Institute of Epidemiology, Disease Control, and Research (IEDCR) in Dhaka, Bangladesh, under the Ministry of Health and Family Welfare of Bangladesh, has collaborated with the International Centre for Diarrhoeal Diseases Research, Bangladesh (icddr,b), Dhaka, on hospital-based encephalitis surveillance in the areas where NiV-associated outbreaks have been reported (3). From December 2010 through March 2014, the surveillance identified 18 clusters of NiV infection, in 15 of these cases...
Exposures among first generation cases

Drinking raw date palm sap:

- All drank it one week before illness onset

None of them had a close physical contact with any encephalitis case
## Date palm sap transmission of NiV

### Epidemiological Evidence

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Cases Exposed (%)</th>
<th>Controls Exposed (%)</th>
<th>Odds Ratio</th>
<th>95% Confidence Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>Tangail</td>
<td>58</td>
<td>17</td>
<td>7.0</td>
<td>1.6, 31</td>
</tr>
<tr>
<td>2008</td>
<td>Manikgonj</td>
<td>100</td>
<td>25</td>
<td>18</td>
<td>2.2, Inf</td>
</tr>
<tr>
<td>2010</td>
<td>Faridpur</td>
<td>69</td>
<td>30</td>
<td>5.2</td>
<td>1.2, 26</td>
</tr>
<tr>
<td>2011</td>
<td>Lalmonirhat</td>
<td>68</td>
<td>11</td>
<td>17</td>
<td>4.0, 70</td>
</tr>
</tbody>
</table>

Slide: Stephen P Luby, MD
Nipah Virus Contamination of Hospital Surfaces during Outbreaks, Bangladesh, 2013–2014

Md Zakriul Hassan, M.S. Sazzad, Stephen P. Luby, Katharine Sturm-Ramirez, Mejbah Uddin Bhuiyan, Mohammed Ziaur Rahman, Md Muzahidul Islam, Ute Ströher, Sharmin Sultana, Mohammad Abdullah Heel Kafi, Peter Daszak, Mahmudur Rahman, Emily S. Gurlay

Nipah virus (NiV) has been transmitted from patient to caregivers in Bangladesh presumably through oral secretions. We aimed to detect whether NiV-infected patients contaminate hospital surfaces with the virus. During December 2013–April 2014, we collected 1 swab sample from 5 surfaces near NiV-infected patients and tested surface and oral swab samples by real-time reverse transcription PCR for NiV RNA. We identified 16 NiV patients; 12 cases were laboratory-confirmed and 4 probable. Of the 12 laboratory-confirmed cases, 10 showed NiV RNA in oral swab specimens. We obtained surface swab samples for 8 NiV patients; 5 had evidence of NiV RNA on ≥1 surface: 4 patients contaminated towels, 3 bed sheets, and 1 the bed rail. Patients with NiV RNA in oral swab samples were significantly more likely than other NiV patients to die. To reduce the risk for future transmission of NiV, infection control should target hospital surfaces.

Nipah virus (NiV) is a bat-borne paramyxovirus (1,2) that causes encephalitis in humans. NiV has caused outbreaks almost every year in Bangladesh since 2001; the case-fatality rate is >70% (3). The primary pathways of NiV transmission in Bangladesh are drinking raw date palm sap contaminated with excretions from Pteropus spp. fruit bats and human-to-human transmission through close contact with infected persons (4–7). Nearly one third of identified NiV patients in Bangladesh were infected through person-to-person transmission (8); most of these were family caregivers who provided hands-on care to NiV patients at home and in hospital (3,9,10).

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DOI: https://doi.org/10.3201/eid2401.161758

Transmission of NiV in hospital settings was first identified in 2001 during an outbreak in Siliguri, India, and in several outbreaks in Bangladesh since 2004 (6,9,11–13). In the outbreak in Siliguri, 66 persons were infected, and of the 66 for whom exposure was known, 45 (75%) acquired infection during their hospital stay (11 patients admitted for other illness, 25 hospital staff, and 8 persons who visited an infected patient) (11). In Bangladesh, during the 2010–2011 NiV outbreak, 2 hospital staff (1 physician, 1 hospital cleaner) were infected (12,13).

NiV RNA has repeatedly been identified in infected patients’ oral secretions (14,15), and epidemiologic evidence suggests that exposure to respiratory secretions is a likely route of NiV transmission from patient to caregiver (6). In 2004, during an NiV outbreak with person-to-person transmission in Bangladesh, NiV RNA was found on a hospital wall near where an NiV patient received care (6).

Hospital wards in Bangladesh are often overcrowded with patients, family caregivers, and visitors and have a median of 4 persons/10 m² of floor space (16). The floor is often soiled with bodily secretions, and a median of 5 uncovered coughs or sneezes per 10 m² per hour has been observed (16). Most wards have intermittent water supply, lack functioning handwashing stations, and have an inadequate number of toilets (16,17). Hospital staff and family caregivers can acquire infections through direct or indirect contact with contaminated fomites (18,19). Healthcare workers (i.e., doctors and nurses) have direct contact with patients; other staff, such as hospital cleaners, and visitors, who are not involved in patient care, might have contact only with hospital surfaces. Possible contamination of nearby hospital surfaces by NiV patients with infectious bodily secretions, coupled with a lack of infection control measures in low-income hospitals, puts healthcare workers, caregivers, visitors, and other patients in the ward at risk for NiV infection by contaminated hospital surfaces. Propagation of a highly fatal pathogen with the capacity for person-to-person transmission within resource-constrained healthcare settings increases the risk for broader outbreaks (11,20).
<table>
<thead>
<tr>
<th>Patient</th>
<th>Oral swab sample</th>
<th>Surface swab sample</th>
<th>Days after hospitalization collected and result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>1</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
</tr>
<tr>
<td>4</td>
<td>Pos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Pos</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
</tbody>
</table>

*Pos, positive; neg, negative. Blank cells indicate no sample collected.
Nipah Surveillance

➢ Hospital based active surveillance and hospital based passive surveillance in Nipah belt areas
➢ Event based surveillance
   ➢ Media Monitoring
   ➢ Hotline
   ➢ Informal reporting
Nipah surveillance hospitals

- Rangpur Medical College Hospital
- Rajshahi Medical College Hospital
- Faridpur Medical College Hospital
- Chittagong Medical College Hospital
- Khulna medical college Hospital
Activities at the surveillance site

1. Check cases of acute meningo-encephaltis daily in adult medicine and paediatrics units.
2. Collect serum and CSF (If possible) specimens from the patients presenting with acute meningo-encephalitis.
3. Make line list of all the cases of acute meningo-encephalitis in line list form
4. Identify a cluster of cases
5. Report cluster of cases to hospital supervisor and surveillance co-ordinator of assigned institute.
Definition of cluster

- Two or more suspect cases living within a 30 minute walk of each other who develop symptoms within 21 days of each other
Case control study

• Case: All probable and confirmed cases

• Neighborhood control selection

• Case : control  1:4

• Selection of proxies for deceased cases
A One Health Approach to NiV Surveillance and Control
Motivate people to stop drinking raw date palm juice
• Few interventions are tried to prevent date palm sap contamination
Question?