Epidemiological investigations during Nipah outbreak
Kozhikode and Malappuram districts, Kerala, India, 2018

ICMR-National Institute of Epidemiology, Chennai
ICMR-Regional Medical Research Centre-Port Blair
Directorate of Health Services, Kerala
Government Medical College, Kozhikode
• 20 May 2018: NiV outbreak declared in Kozhikode and Malappuram districts

• 2 Jun 2018: ICMR-NIE team joined response team at the request of Kerala State to
  – Conduct epidemiological investigations
  – Support for data analysis and management
Objectives of NiV investigation
Kozhikode and Malappuram districts, Kerala, India, 2018

1. Describe epidemiology of the outbreak
2. Identify possible source/s of infection of primary case
3. Determine factors responsible for person-to-person transmission of NiV
4. Estimate sero-prevalence of IgM and IgG antibodies against NiV among close contacts of laboratory confirmed NiV cases
• 23 cases reported
  – 18 confirmed; 5 probable (including index case)
  – 22 had acute neurological and/or respiratory symptoms
  – 16 of the 18 lab confirmed cases died (CFR=89%)
• 18 patients were positive for NiV RT-PCR at Manipal Centre for Virus Research
  – Confirmed at ICMR-National Institute of Virology, Pune
• Source of infection of primary case remained unknown
  – 21 had history of contact with confirmed/probable cases

Source: District Nipah control centre, Kozhikode
1. Describe epidemiology of NiV outbreak
Kozhikode and Malappuram districts, Kerala, India, 2018

• Case definitions
  – **Confirmed case:** RT-PCR positivity for NiV infection
  – **Probable case:** Occurrence of
    • Acute fever illness with new onset of altered mental status or seizure
    OR
    • Acute febrile illness with severe headache
    OR
    • Acute febrile illness with cough or shortness of breath in a resident of Kozhikode/ Malappuram districts, Kerala, since 3 May 2018
    AND
    • Epidemiological linkage with lab confirmed case
1. Describe epidemiology of NiV outbreak
Kozhikode and Malappuram districts, Kerala, India, 2018

• Interviewed families of case-patients, medical officers, health staff and local authorities to generate hypothesis

• Data analysis
  – Drew epidemic curves based on the time of onset of fever and by type of contact
  – Created spot map by plotting cases by their residence
Transmission of Nipah from primary case by date of exposure and location
Kozhikode and Malappuram districts, Kerala, India, 2018

Perambra Taluk Hospital

Balussery Taluk Hospital

Medical College

ICU

CT waiting room

Changaroth village

Casualty

Referral Person-Person transmission

Primary
Survived
Deceased
Female
Male
Probable
Incidence of Nipah cases (n=23) by date of onset
Kozhikode and Malappuram districts, Kerala, India, 2018

Date of onset

# cases

1-May
2-May
3-May
4-May
5-May
6-May
7-May
8-May
9-May
10-May
11-May
12-May
13-May
14-May
15-May
16-May
17-May
18-May
19-May
20-May
21-May
22-May
23-May
24-May
25-May
26-May
27-May
28-May
29-May
30-May
31-May
1-Jun
2-Jun
3-Jun
4-Jun
5-Jun

Outbreak declared
Nipah control measures implemented

Confirmed
Probable
Alive
Incidence of Nipah cases (n=23) by date of onset and by type of contact
Kozhikode and Malappuram districts, Kerala, India, 2018

Date of onset

# cases

0 1 2 3 4 5 6


Unknown
Family
Health worker
Inpatient
Care giver
Distribution of Nipah cases (n=23) by residence
Kozhikode and Malappuram districts, Kerala, India, 2018

Kozhikode District

Malappuram District
2. Identify possible sources of infection of primary case
Kozhikode and Malappuram districts, Kerala, India, 2018

- Conducted in-depth interviews of relatives/friends/colleagues of primary case to
  - Reconstruct circumstances of primary case two-weeks prior to the onset of illness
  - Understand the behavior of primary case that resulted in spillover event through an anthropological perspective
Health status, behaviours and possible sources based on interviews around primary case
Outbreak of Nipah, Kozhikode, Kerala, 2018

• 27 year male, mentally sound and socially responsible
• Diagnosed with peptic ulcer 3 years ago
• Burn injury on leg 6 weeks prior to onset of illness
• Possible sources:
  – Bats frequented arecanut, plantain and fruit trees at house
  – Consumes half eaten fruits
  – Handled plantain leaves (with bat excrement) to feed pet animals
  – Death of a pet rabbit
  – Intake of medicine from traditional healer for peptic ulcer prior to onset of illness (Unclear about the ingredients)

Unpublished data, not to be quoted
3. Determine factors responsible for person-to-person transmission of NiV: Unmatched case-control study
Kozhikode and Malappuram districts, Kerala, India, 2018

• Descriptive epidemiology suggested predominant person-to-person transmission
• Definition of case
  – Laboratory confirmed (RT-PCR positive) NiV case patient
• Definition of control
  – Hospital control: Person present in hospital between admission of first case and discharge of last case and does not meet the definition of “case”
  – Community control: Person present in the same community as cases and does not meet the definition of “case”
3. Determine factors responsible for person-to-person transmission of NiV: Unmatched case-control study
Kozhikode and Malappuram districts, Kerala, India, 2018

• Sampling
  – Cases: Selected all confirmed case-patients
  – Controls
    • Used list of 2600 contacts (District Nipah control centre) as sampling frame
    • Selected hospital and community controls separately by simple random sampling

• Sample size: 18 cases and 72 controls (1: 4)
  – Contact with case-patient as a risk factor; Odds Ratio of 5 (Gurley et al, 2007); 95% Confidence Interval; 80% power; 50% contact exposure
3. Determine factors responsible for person-to-person transmission of NiV: Unmatched case-control study
Kozhikode and Malappuram districts, Kerala, India, 2018

• Data collection
  – Interviewed cases and controls to collect information on demographic characteristics, symptoms, risk factors (type and frequency of contacts with lab confirmed case) using a standardized questionnaire
  – For deceased case-patient a close relative/friend was interviewed

• Data analysis
  – Calculated crude odds ratio (OR) and their 95% confidence intervals (CI)
Frequency of selected characteristics among Nipah cases and controls: Unmatched case-control study
Kozhikode and Malappuram districts, Kerala, 2018

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency of exposure</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (n=18)</td>
<td>Controls (n=72)</td>
<td></td>
</tr>
<tr>
<td></td>
<td># (%)</td>
<td># (%)</td>
<td></td>
</tr>
<tr>
<td>Age [years] Mean (Standard Deviation)</td>
<td>39.9 (15.5)</td>
<td>36.6 (11.6)</td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td>8 (44)</td>
<td>45 (63)</td>
<td></td>
</tr>
<tr>
<td>Type of house</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living in pucca house</td>
<td>17 (94)</td>
<td>63 (88)</td>
<td></td>
</tr>
<tr>
<td>Living in kutcha/semi-pucca house</td>
<td>1 (6)</td>
<td>9 (13)</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthcare worker</td>
<td>2 (11)</td>
<td>39 (54)</td>
<td></td>
</tr>
<tr>
<td>Non-healthcare work</td>
<td>12 (67)</td>
<td>19 (26)</td>
<td></td>
</tr>
<tr>
<td>Not earning</td>
<td>4 (22)</td>
<td>14 (19)</td>
<td></td>
</tr>
</tbody>
</table>

Unpublished data, not to be quoted

No statistically significant difference
Frequency of selected risk factors among Nipah cases and controls: Unmatched case-control study
Kozhikode and Malappuram districts, Kerala, 2018

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Frequency of exposure</th>
<th>Crude Odds ratio</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Total (%)</td>
<td>Controls</td>
</tr>
<tr>
<td>Contact with body fluids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saliva</td>
<td>15</td>
<td>16 (94)</td>
<td>35</td>
</tr>
<tr>
<td>Cough/Sneeze</td>
<td>6</td>
<td>17 (35)</td>
<td>26</td>
</tr>
<tr>
<td>Feces</td>
<td>0</td>
<td>17 (0)</td>
<td>2</td>
</tr>
<tr>
<td>Vomit</td>
<td>0</td>
<td>16 (0)</td>
<td>6</td>
</tr>
<tr>
<td>Patient contact circumstances</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contact with &gt;2 patients</td>
<td>6</td>
<td>18 (33)</td>
<td>25</td>
</tr>
<tr>
<td>Present in same room</td>
<td>16</td>
<td>18 (89)</td>
<td>46</td>
</tr>
<tr>
<td>Patient vomited while nearby</td>
<td>8</td>
<td>15 (53)</td>
<td>20</td>
</tr>
<tr>
<td>Contact duration &gt;24 hours in hospital</td>
<td>7</td>
<td>14 (50)</td>
<td>12</td>
</tr>
</tbody>
</table>

*Unpublished data, not to be quoted*
Odds of Nipah according to increasing gradients of duration of contact with Nipah patient in hospital: Unmatched case-control study
Kozhikode and Malappuram Districts, Kerala, India, 2018

<table>
<thead>
<tr>
<th>Duration of contact in hospital</th>
<th>Cases (n=14)</th>
<th>Controls (n=66)</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#  (%)</td>
<td>#  (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 hour</td>
<td>2  (14)</td>
<td>35  (80)</td>
<td>Ref</td>
<td>-</td>
</tr>
<tr>
<td>1-24 hours</td>
<td>5  (36)</td>
<td>19  (29)</td>
<td>4.49</td>
<td>0.80-36.11</td>
</tr>
<tr>
<td>&gt;24 hours</td>
<td>7  (50)</td>
<td>12  (18)</td>
<td>9.72</td>
<td>1.88-76.27</td>
</tr>
</tbody>
</table>

Chi square for linear trend=7.7; p=0.006

*Unpublished data, not to be quoted*
Limitations

• Proxy respondents for all cases, except two
  – Doubtful veracity of information about cases
• Interviews conducted after exposure to prevention messages that might have influenced participants’ response
• Possibility differential recall between cases and controls
• Possibility of differential response between hospital staff and community participants
4. Estimate sero-prevalence of NiV specific antibodies among close contacts of confirmed cases
Kozhikode and Malappuram districts, Kerala, 2018

• Rationale:
  – Occurrence of lab confirmed infection with mild febrile illness
• Needed a sample size of 300*
  – Community & hospital contacts of 165 each
• Ethics committee approval from ICMR-NIE and Govt. Medical College, Kozhikode
• Interviewed to collect socio-demographic details, type and frequency of contact and history of febrile illness
• 3 ml blood sample collected from each individual
  – Serum separated and transported to ICMR-NIV, Pune
  – Tested for NiV specific IgM and IgG antibodies

*Assumptions: Estimate 5%, precision ±2.5%, 95% CI
Sero-prevalence of NiV specific antibodies among close contacts of confirmed cases
Kozhikode and Malappuram districts, Kerala, 2018

• Surveyed 279 contacts
  – Health care workers=155,
  – Household/community contacts=124
• Three were sero-positive (1.1%, 95% CI: 0.2-3.1)
  – 2 Household contacts of NiV case, 1 health care worker
  – 2 IgM positive; 1 IgM and IgG positive
  – None had history of febrile illness after probable exposure

Unpublished data, not to be quoted
Conclusions

- Evidence for human to human transmission through body fluids of NiV case-patients
- Low prevalence of sub-clinical NiV infection among contacts
Potential areas for future research

NiV risk assessment surveys

• Need to develop NiV risk assessment tools
  • Identify animal sources
  • Document human risk behaviours
• Estimate number/spread of NiV cases using model
• Identify areas at NiV risk

Surveillance for possible Nipah presentation (s) in identified NiV risk areas [Community/Hospital/Event-based]

Public health system preparedness for NiV surveillance, investigation and response through one health approach
Thank you team