

Outbreak Investigation of Fatal Nipah Virus Encephalitis in Bangladesh

Original Article

Mohammad Ferdous Rahman Sarker^{1,*}, AKM Dawlat Khan², Sharmin Sultana³,
Mohammad Mostafizur Rahman⁴, Tahmina Shirin⁵

¹ Senior Scientific Officer, Institute of Epidemiology, Disease Control and Research (IEDCR), Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare (MoHFW), Dhaka, Bangladesh.

² a. Institute of Epidemiology, Disease Control and Research (IEDCR), Dhaka, Bangladesh. b. EcoHealth Alliance, New York, NY 10018.

³ Senior Scientific Officer, Department of Virology, Institute of Epidemiology, Disease Control and Research (IEDCR), Mohakhali, Dhaka, Bangladesh.

⁴ Senior Scientific Officer, Department of Medical Social Science, Institute of Epidemiology, Disease Control and Research (IEDCR), Mohakhali, Dhaka, Bangladesh.

⁵ Professor of Virology & Director, Institute of Epidemiology, Disease Control and Research (IEDCR), Mohakhali, Dhaka, Bangladesh.

*Corresponding author

Mohammad Ferdous Rahman Sarker,
Senior Scientific Officer and FETP, B Graduate (US CDC), Institute of Epidemiology, Disease Control and Research (IEDCR), Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare (MoHFW), Dhaka, Bangladesh.
Phone: +8801711463939,
Email: ferdous48@yahoo.com.

Article Information

Received: 15-04-2022;
Accepted: 13-06-2022;
Published: 09-07-2022.

Abstract

In Bangladesh, the first case of NiV was reported as encephalitis in 2001. On 16th February 2017, an encephalitis patient was admitted in RMCH, one of the sentinel sites of NiV surveillance platform of Bangladesh. Outbreak investigation team was formed to identify possible sources of infection and to explore other possible contexts that contributed to outbreak. Team conducted outbreak investigation along with epidemiological and anthropological assessment at Pabna district, Bangladesh. Both prospective and retrospective investigations were followed. Blood samples, nasal swabs and throat swabs were collected from suspected cases. The confirmed case was a 13-year old boy with the symptoms of unconsciousness along with fever, and with the history of drinking RDPS before illness. Gradual development of difficulty in breathing resulted in death on the 7th day of illness. 34 contacts were identified and all were found Nipah negative by RT-PCR & ELISA test. A bat-roost was found within 5 kilometers from the deceased house. We confirm a single case of Nipah and no contacts were infected. We suspect the source of NiV was RDPS.

Keywords: Outbreak Investigation; Nipah Virus Encephalitis; Bangladesh

Introduction

Nipah virus (NiV) is a highly pathogenic paramyxovirus of the Henipavirus genus [1,2]. NiV is one of the organisms to cause outbreaks needing rapid response due to its zoonotic as well as person-to-person transmission [3]. Consequently, NiV disease is on the World Health Organization (WHO) priority list for diseases with pandemic potential [4].

The first outbreak of NiV disease occurred in Sungai Nipah, Malaysia in 1995 [5]. The initial cases had fever, headache and lack of consciousness. In this outbreak, the primary transmission was by droplet infection from pigs to humans [6]. Fruit bats were the reservoir for NiV [7] and pigs became infected with NiV when they ate partially eaten fruit by the bats [8]. The primary risk factor was working on a pig farm [9].

In Bangladesh, the first case of NiV was reported as encephalitis in 2001 [10]. Since 2001 to 2021, 322 NiV cases were identified in Bangladesh and case fatality rate is 70.1% [11]. NiV outbreaks have been reported from 20 districts of Bangladesh and mostly in the winter season from December to May [12,13]. The biggest NiV outbreak identified in Faridpur in 2004 [14]. Unlike Malaysia, the most common route of infection is by consumption of raw date palm sap (RDPS) contaminated with bat urine or saliva [15]. Subsequently, person-to-person transmission is initiated by droplets [16].

Nipah virus transmission surveillance in Bangladesh was conducted jointly by the Institute of Epidemiology, Disease Control and Research (IEDCR) and International Centre for Diarrheal Disease Research, Bangladesh (icddr,b) with the technical support from Centers for Disease Control and Prevention, United States (US-CDC) since 2006. The objectives of this surveillance are

to detect outbreaks and associated risk factors for transmission of Nipah encephalitis. NiV disease is reportable in Bangladesh. On 16 February 2017, 13 year old boy who was admitted to Rajshahi Medical College Hospital (RMSH) with symptoms of unconsciousness, fever and history of drinking RDPS before illness. He was diagnosed as NiV disease and we investigated:

To identify any other primary or secondary cases of Nipah encephalitis in the community.

- To identify possible sources of the infection
- To investigate the clinical presentation of the case
- To explore the possible behavioural factors and socio-cultural contexts that contributed to the outbreak.

Methods

Team conducted the field investigation at Uttor Raghobpur (25 km North-East of Pabna city) village under Malonchi union (local government administrative unit), Sadar upazilla (sub-district) Pabna District between 18th February and 20th February, 2017 (Figure 1). Epidemiological, anthropological and laboratory assessment was done for the outbreak investigation. Both prospective (to identify other cases and line listing) and retrospective (to obtain information on identified case) outbreak investigation was followed. Clinical records of the deceased were reviewed and verbal autopsy was done by proxy interview. Focus group discussion (FGD) was conducted to identify community suspected encephalitis cases, clusters and contacts of NiV case. Face to face interview was performed with the identified suspected cases by semi- structured questionnaire to explore the exposure history and clinical features. Line list was prepared and blood samples, nasal swabs and throat swabs were also collected from the suspected cases for enzyme-linked immunosorbent assay (ELISA) and real time polymerase chain reaction (RT-PCR) testing of NiV.

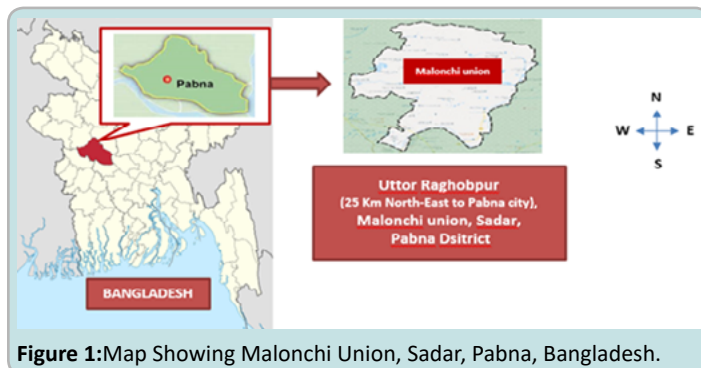


Figure 1: Map Showing Malonchi Union, Sadar, Pabna, Bangladesh.

Case definition of Nipah encephalitis in Bangladesh.

According to the National Guideline for Management, Prevention and Control of NiV including encephalitis of IEDCR, Directorate General of Health Services (DGHS)- “A person fulfilling both of the following criteria is defined as a suspected case:

1. Features of acute encephalitis as demonstrated by
 - a. Acute onset of fever AND b. Evidence of acute brain dysfunction as manifested by
 - i. Altered mental status OR
 - ii. New onset of seizure OR
 - iii. Any other neurological deficit

2. Epidemiological linkage
 - a. Drinking raw date palm sap OR
 - b. Occurring during Nipah season OR
 - c. Patient from Nipah endemic area” [17]

Moreover, cluster of encephalitis cases, was defined by two encephalitis cases within 21 days of each other and within half an hour walking distance from each other or in 2 km radius [17].

Case Definition for Suspected NiV Cases in this Outbreak:

Any person of any age and sex developing fever with any other symptoms according to the case definition of Nipah encephalitis based on NiV infection prevention and control guideline of DGHS [17], or those who had a history of drinking RDPS from a common source, or history of drinking RDPS with development of fever between 28 January to 20 February 2017 in the deceased’s village.

Contacts of Confirmed NiV Case:

For this study, those who (health care workers, care givers, family members, relatives, neighbours, persons in burial process etc.) directly touched the infected patient were direct contacts. Indirect contacts were those who stayed with the infected patient for more than 15 minutes within 3 feet of the patient.

Patient Consent and Sources of Data:

Informed consents were obtained from contacts and proxy respondents and assent were taken from children. Preliminary information was collected from the corresponding surveillance site’s Field Assistant (FA), and from the local Health Assistant (HA) of Malonchi Union, Pabna. Investigation was conducted with open discussion among relatives and neighbours of deceased, local community people and the member of that union.

For epidemiological investigation, deceased’s parents, grandmother and grandfather were interviewed by semi structured questionnaire. Detailed history of the deceased were taken like demographics, clinical features, exposure history and behavioural pattern, and doctor’s prescription and documents were collected for death review.

For anthropological investigation, the team explored the common source of infection, behavioural factors and socio-cultural contexts from observation and group discussions with community.

Laboratory:

Twenty-four throat and 24 nasal swabs samples were collected from suspected Nipah encephalitis cases for test real time polymerase chain reaction (RT-PCR) testing. Twenty-four serum samples were collected and tested by RT-PCR for NiV nucleic acid and enzyme-linked immunosorbent assay (ELISA) for the detection of IgM antibody. RDPS was not collected for testing because there is no facility to test NiV in food.

Ethical Considerations:

We sought informed oral consent from adult respondents and guardians and assent from children respondents 11–17 years of age. This field investigation was exempted from review by an independent human subjects committee since it was an emergency response investigation. The investigation was conducted in response to an outbreak and was approved by and conducted in collaboration with the Ministry of Health and Family Welfare (MoHFW).

Results

On 16th February 2017 at around 8 o'clock in the morning, an encephalitis patient was admitted to the medicine ward in RMSH, a sentinel site of NiV surveillance platform in Bangladesh. The case was a 13-year old boy with the symptoms of unconsciousness along with fever, and with the history of drinking RDPS before illness. Surveillance team collected his throat swab, nasal swab and blood sample on 16th February 2017. The collected sample was sent to IEDCR, Dhaka for laboratory testing. The case was confirmed as Nipah encephalitis by the laboratory test but unfortunately the patient died after collection of sample. An outbreak investigation team was formed by IEDCR and icddr,b, including an epidemiologist, medical technologist and anthropologist to investigate the outbreak.

Case

Clinical Features

The case developed mild fever, vomiting and headache on 10th February, 2017 and subsequently progressed to generalized weakness, difficulty in breathing and became unconscious on 15th February, 2017(Figure 2).

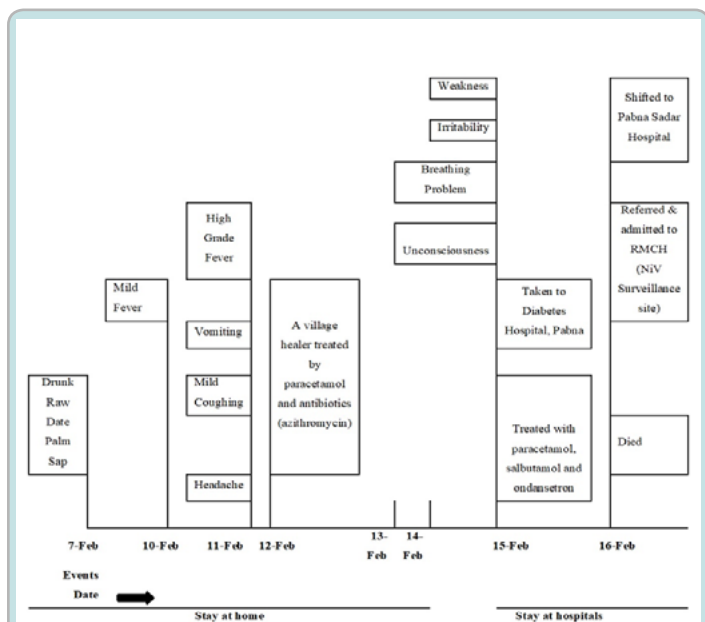


Figure-2: Chronological Events of the Deceased due to Nipah Virus Disease, Bangladesh, 2017.

Illness History of the Deceased

According to the statement of proxies of deceased, the case was apparently healthy before falling ill on 10 February 2017. After drinking about 250 ml of raw RDPS on 7th February 2017, he suddenly became feverish on 10th February 2017. He went to school the next day and developed high-grade fever (>39°C) and headache upon returning home. Then he had several episodes of vomiting and mild cough on 11th February. There was no history of neck rigidity or loose motion. A village traditional healer treated him with paracetamol and azithromycin for next three days (12th -14th February). However, his symptoms aggravated on 15th February and his father took him to Diabetes Hospital, Sadar, Pabna, where he underwent several medical examinations and was prescribed with paracetamol, salbutamol and ondansetron.

On that evening, he became irritable, developed difficulty in breathing and became unconscious at that night. He was brought to Pabna Sadar Hospital around 2 am on 16th February, from there he was referred to RMCH, one of the NiV surveillance platform. He was admitted to RMCH at 8.30 am on 16th February (Figure 2). He was diagnosed as a patient of Nipah encephalitis as he had history of consumption of RDPS before his illness. He expired around 1.30 pm on the same day. The Nipah surveillance team of RMCH collected his throat and nasal swab, and blood and sent it to IEDCR for laboratory investigation.

Exposure History of the Deceased

The deceased was fond of RDPS. There were plenty of date trees near by his household, which had regularly shaved bark during the winter season. RDPS was collected by the deceased from these trees during early mornings approximately every 2-3 days. He brought RDPS home to drink and share with other members of the family, his father, mother and younger brother. According to his parents' statement, he drank 250 milliliters of RDPS on 7th February at home. However, his neighbours noticed that he used to take date palm sap (DPS) several times a day, even directly from the clay pot hung on the date tree with a straw. He also ate raw fruits, sometimes without washing with water. Father and grandfather of the deceased noticed large fruit bats flying to nearby trees almost every night. They also reported that there was a bat-roost within 5-6 kilometers from their household.

Contacts

Thirty-four (34) direct and indirect contacts from the community and health care facilities were interviewed. There were 14 healthcare worker contacts and 20 community member contacts. Of the 34 contacts, 24 were male and 10 were female. Mean age of males were 25 years (age range: 4 - 65 year of age) and females were 31 years (age range: 9 - 57 year of age). Out of 34 contacts, 14 persons had a history of fever within the last month and 7 persons had a history of taking RDPS from the same source as that of the deceased. Fourteen people who had history of fever within the last month underwent a general examination. No abnormalities were found. We followed up all contacts for 12 days none had symptoms.

Table-1: Exposure and events of Nipah contacts, Bangladesh, 2017 (N=34).

Exposures/Events (Including multiple exposure events)	Number of contact persons						
	Day of illness						
	*D-1	D-2	D-3	D-4	D-5	D-6	D-7
Staying with case in house (home)	7	4	4				
Staying with case in a vehicle					4	5	5
Staying with case in hospital						3	4
Feeding the case (food & medicine)	1	2	2	4	4	2	3
Caring the case	2	2				3	
Treatment of case						8	6
Burial process							8

*D=Day

Table-2: Characteristics of Nipah contacts, Bangladesh, 2017 (N=34).

Variable	Number (N)	Percentage (%)
Male	24	70.6
Female	10	29.4
H/O Fever Last Month	14	41.2
H/O Drinking RDPS	7	20.6
Symptoms During Monitoring	0	0

Anthropological Findings

Many date trees and fruit trees were observed in the community nearby the deceased's household. Invariably every household in the community had date trees on their premises. The DPS was also available in the community. Almost all people of every household drank RDPS. In that community there were 17 sap harvesters who collect DPS from the date tree. They drink RDPS with their family, sell RDPS to the community and make molasses too. There were also bamboo clumps and fruit trees in household premises. According to the community people, fruit bats frequently came to those trees at night. Small bats were seen sometimes inside their houses. We also found a bat roost within 5 km radius of the deceased house (Figure 3).



Figure-3: Bat roost in a 5 km radius away from the center of the deceased's house, Malonchi Union, Sadar, Pabna.

Laboratory Results

Nasal swab, throat swab and blood samples were collected from 24 suspected cases tested to detect NiV nucleic acid & IgM by RT PCR and ELISA respectively. No NiV nucleic acid nor IgM were detected in any of the samples.

Discussion

NiV infection mostly occurs during December and May in the north-western and central region of Bangladesh. Our outbreak occurred within the same season and region [15]. A study in Bangladesh showed that out of 158 NiV infected patients, mostly were young males, which coincides with our findings [13]. From my professional experience, young male are the main harvesters of RDPS and often drink RDPS. Clinical features of the deceased developed within 3 days after the drinking RDPS which is within the incubation period, 2-12 days, of NiV [17]. Symptoms of this case were fever, vomiting, headache, mild cough, difficulty breathing and gradual development of unconsciousness similar to other studies on NiV infected patients [18,19]. In our current

study, the deceased had breathing difficulties. Whereas several other studies found that NiV cases with breathing difficulty are associated with a larger number of secondary cases [20,21], we did not identify any secondary cases in our outbreak investigation. However, early detection and subsequent intervention can reduce the chances of human-to-human NiV transmission [22]. Local health authority had limited experience in investigating NiV Nipah Virus Disease (NVD) and requested assistance for this investigation from IEDCR staffs.

Transmission of NiV is by ingestion of RDPS, inhalation of Droplet from infected person and eating half-eaten fruits by bats [23]. In this outbreak, contacts were potentially exposed when they drank RDPS and had close contacts with the case. We suspect that some of the contacts had immunity to NiV or didn't inhaled the infective dose. The R-naught (RO) of NVD is 0.4, thus there would be few secondary cases among the 34 contacts [24].

Nipah antibodies was found in fruit bats of Bangladesh [10]. In 2005, drinking RDPS was first identified as a risk factor for NiV at Tangail, Bangladesh [12]. Bats lick the RDPS that is collected in the clay pots hung on the date palm trees [25]. The case in this report drank RDPS directly from hung clay pot at date tree which might be have been contaminated with NiV. Thus the case was probably infected with NiV by drinking contaminated RDPS or eating contaminated fruits which is similar to previous other study findings [12,26].

Conclusion

In this Nipah encephalitis outbreak investigation, we found one primary case with history of RDPS consumption. He died within seven (7) days of illness. Nipah virus encephalitis has a fatality rate of 70% in Bangladesh. Fortunately, no contacts developed any symptoms related to Nipah virus disease. Awareness programs for RDPS collectors and the community along with the expansion of sentinel sites in the Nipah belt are imperative for early case detection. Moreover, distribution of material on Nipah infection prevention to local health authorities can decrease delays in

References

1. Chua K, Bellini W, Rota P, Harcourt B, Tamin A, Lam S, et al. Nipah virus: a recently emergent deadly paramyxovirus. 2000;288(5470):1432-5.
2. Eaton BT, Broder CC, Middleton D, Wang L-FJNRM. Hendra and Nipah viruses: different and dangerous. 2006;4(1):23-35.
3. Luby SP. The pandemic potential of Nipah virus. Antiviral research. 2013 Oct 1;100(1):38-43.
4. WHO (2018) WHO: Nipah Virus Infection. World Health Organization. Available at <http://www.who.int/csr/disease/nipah/en/> [cited 2022 Jan 1].
5. Chua KB. Nipah virus outbreak in Malaysia. Journal of Clinical Virology. 2003;26(3):265-75.
6. Luby SP, Gurley ES. Epidemiology of henipavirus disease in humans. Henipavirus. 2012:25-40.
7. Yadav PD, Raut CG, Shete AM, Mishra AC, Towner JS, Nichol ST, et al. Detection of Nipah virus RNA in fruit bat (*Pteropus giganteus*) from India. The American journal of tropical medicine and hygiene. 2012 Sep 5;87(3):576.
8. Ang BS, Lim TC, Wang L. Nipah virus infection. Journal of clinical microbiology. 2018 May 25;56(6):e01875-17.

9. Enserink M. New virus fingered in Malaysian epidemic. *Science* 1999; 284: 407-10
10. Hsu VP, Hossain MJ, Parashar UD, Ali MM, Ksiazek TG, Kuzmin I, et al. Nipah virus encephalitis reemergence, Bangladesh. 2004;10(12):2082.
11. Institute of Epidemiology, Disease Control and Research. Surveillance 2021, Nipah Virus Transmission in Bangladesh [Internet]. Dhaka (BD): Institute of Epidemiology, Disease Control and Research.; [cited 2021 Jan 30]. <<https://iedcr.gov.bd/surveillances/93c87e70-9c22-4f21-9506-a1161ecf404f>>
12. Luby SP, Rahman M, Hossain MJ, Blum LS, Husain MM, Gurley E, et al. Foodborne transmission of Nipah virus, Bangladesh. 2006;12(12):1888.
13. Nikolay B, Salje H, Hossain MJ, Khan AD, Sazzad HM, Rahman M, et al. Transmission of Nipah virus—14 years of investigations in Bangladesh. 2019;380(19):1804-14.
14. Gurley ES, Montgomery JM, Hossain MJ, Bell M, Azad AK, Islam MR, Molla MA, Carroll DS, Ksiazek TG, Rota PA, Lowe L. Person-to-person transmission of Nipah virus in a Bangladeshi community. *Emerging infectious diseases*. 2007 Jul;13(7):1031.
15. Rahman M, Chakraborty A. Nipah virus outbreaks in Bangladesh: a deadly infectious disease. *WHO South-East Asia Journal of Public Health*. 2012;1(2):208.
16. Epstein JH, Anthony SJ, Islam A, Kilpatrick AM, Khan SA, Balkey MD, Ross N, Smith I, Zambrana-Torrel C, Tao Y, Islam A. Nipah virus dynamics in bats and implications for spillover to humans. *Proceedings of the National Academy of Sciences*. 2020 Nov 17;117(46):29190-201.
17. DGHS DGoHS. National Guideline for Management, Prevention and control of Nipah Virus infection. August 20, 2020.
18. Nahar N, Sultana R, Gurley ES, Hossain MJ, Luby SPJE. Date palm sap collection: exploring opportunities to prevent Nipah transmission. 2010;7(2):196-203.
19. Islam MM, Rahman MM. Nipah virus Infection: A fatal Emerging disease. *Northern International Medical College Journal*. 2016 Sep 19;7(2):146-8.
20. Harcourt BH, Lowe L, Tamin A, Liu X, Bankamp B, Bowden N, et al. Genetic characterization of Nipah virus, Bangladesh, 2004. 2005;11(10):1594.
21. Lo MK, Lowe L, Hummel KB, Sazzad HM, Gurley ES, Hossain MJ, et al. Characterization of Nipah virus from outbreaks in Bangladesh, 2008–2010. 2012;18(2):248.
22. Nipah virus (NiV): Content source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP), Viral Special Pathogens Branch (VSPB); [Available from: <https://www.cdc.gov/vhf/nipah/index.html>].
23. Clayton BA, Middleton D, Arkinstall R, Frazer L, Wang LF, Marsh GA. The nature of exposure drives transmission of Nipah viruses from Malaysia and Bangladesh in ferrets. *PLoS neglected tropical diseases*. 2016 Jun 24;10(6):e0004775.
24. Luby SP, Hossain MJ, Gurley ES, Ahmed BN, Banu S, Khan SU, Homaira N, Rota PA, Rollin PE, Comer JA, Kenah E. Recurrent zoonotic transmission of Nipah virus into humans, Bangladesh, 2001–2007. *Emerging infectious diseases*. 2009 Aug;15(8):1229.
25. Salah Uddin Khan M, Hossain J, Gurley ES, Nahar N, Sultana R, Luby SP. Use of infrared camera to understand bats' access to date palm sap: implications for preventing Nipah virus transmission. *Ecohealth*. 2010;7(4):517-25.
26. Hughes JM, Wilson ME, Luby SP, Gurley ES, Hossain MJ. Transmission of human infection with Nipah virus. *Clinical Infectious Diseases*. 2009;49(11):1743-8.