Original Article

Sero-prevalence of Nipah antibodies among close contacts of the index case during 2019 Ernakulam outbreak

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Abstract

Introduction: Nipah virus (NiV) infection is a fatal emerging zoonotic disease. Infection with NiV has a wide range of clinical spectrum which can range from asymptomatic cases to acute respiratory distress syndrome (ARDS). The index case of NiV infection of 2019 outbreak in Ernakulam district was a 23-year-old male who presented with features of encephalitis. This study was undertaken to address the subclinical or asymptomatic NiV infection amongst the close contacts of this index case by using NiV-specific Immunoglobulin IgM and IgG antibodies. The index case was first treated in a primary care center. He survived the infection and was discharged after a period of 108 days from the tertiary care facility where he was treated eventually. **Methods:** Serum samples from 49 close contacts of the index case were collected and tested for anti-NiVIgM and anti-NiVIgG antibodies. The contacts included health care workers including those from the primary care facility, family members, and his friends. **Results:** Most common type of exposure included physical contact (59.2%), followed by exposure to body fluids (22.4%). **Conclusion:** None of the 49 contacts tested positive for anti-NiV human IgM and anti-NiVIgG antibodies. There were no subclinical cases amongst the close contacts of Nipah index case during the 2019 Kerala outbreak.

Keywords: Asymptomatic Nipah, Nipah IgM and IgG antibodies, Nipah outbreak India, subclinical Nipah infection

Introduction

Nipah virus (NiV) encephalitis is a highly fatal zoonotic disease which is identified as a major public health concern by World Health Organization. The disease is primarily transmitted from animals. Other routes of transmission include human to human by close contact and droplet infection. Although the number of outbreaks reported worldwide has been low, the extend of impact in terms of mortality and severity has been very high.[1]

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The virus was first identified during an outbreak among pig farmers in Malaysia during 1998. In India, first NiV outbreak was reported in Siliguri district (West Bengal) in 2001, followed by the second outbreak in Nadia district (West Bengal) in the year 2007.[1] The first outbreak reported 68% mortality while the second outbreak had 100% mortality.[2] The 2018 outbreak in Kozhikode had 91% case fatality.[3] The usual case fatality is about 61%.[4] Human infections can range from asymptomatic infection to acute respiratory infection and fatal encephalitis.[5,6] Although NiV is known to cause subclinical infections, the extend of these infections among the close contacts differ during outbreaks. In the 2007, West Bengal outbreak out of the 34 asymptomatic contacts, 1 was positive for IgG anti-NiV and negative for IgM anti-NiV and did not report any major illness in the past.[1] Malaysian NiV outbreak reported 1% to 15% subclinical cases.[7]

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The Singapore outbreak reported 4.6% sero-prevalence of NiV antibodies among asymptomatic contacts,[5] whereas a case control study reported a sero-prevalence of 11% (antibodies) among asymptomatic Nipahcontacts.[6] As per unpublished data from National Institute of Virology, Pune, India. The NiV strain responsible for the current (2019) outbreak in Ernakulam was similar to the Bangladesh strain of NiV_B responsible for the Kozhikode (Kerala, South India) outbreak in 2018. Three subclinical cases were identified with anti-NiV human IgM and IgG positivity among the contacts of Nipah positive cases in the Kozhikode (Kerala) outbreak of 2018.[8] NiV infection is an emerging infectious disease with significant gaps in the epidemiological aspects. Clinical symptoms in NiV infection begin with fever, headache, and/or cough.[5] Since these symptoms are common in most viral diseases, patients with these symptoms most often seek treatment from a primary care facility/physician at the onset, making them vulnerable to exposure to highly virulent Nipah infection. Therefore, knowledge regarding the dynamics of person to person transmission of Nipah will help plan preventive strategies and strengthen infection control practices especially in resource poor settings. Hence, this study was undertaken to assess the status of anti-NiV human Immunoglobulin IgM and anti-NiVIgG antibodies amongst the close contacts of 2019 index case, so as to address the presence or absence of subclinical (asymptomatic) Nipah infection during the outbreak.

Materials and Methods

NiV infection was confirmed in a 23-year-old male residing in Ernakulam District of Kerala state (India) in June 2019. The index case was initially taken to a primary care facility were the doctor suspected encephalitis, hence he was referred to a higher center for further management. The case was confirmed to be NiV infection by Real Time Polymerase Chain Reaction at (ICMR-NIV) Pune (unpublished data, NIV Pune). He survived the infection and was discharged from the tertiary care hospital after a period of 108 days. Although fever surveillance was strengthened post confirmation of Nipah in the district, NiV infection was not confirmed in any other acute encephalitis syndrome (AES) cases reported from the district during that period. A descriptive cross-sectional study to assess the status of anti-NiV human Immunoglobulin IgM and anti-NiVIgG antibodies among the close contacts of this case was carried out in the month of September 2019 at Government Medical College Ernakulam, Kerala, India. The guidelines by Nipah Advisory group, Kerala State health services[9] which had experts from various fields of scientific medicine and representatives from institutions like ICMR-National Institute of Epidemiology, Chennai, India were followed to identify 51 close contacts of the index case. Ethics committee clearance was obtained from the Institutional ethics committee of Government Medical College, Ernakulam, before the commencement of this study. After taking written informed consent from the study participants, a semistructured questionnaire was used to collect data using the interview technique. Two health care workers (HCWs) refused to participate in the study; hence, they were excluded from the study. Therefore, only 49 participants were included. Venous blood (3 ml) was collected under aseptic precautions in Serum Separator Gel vacutainer tube from the close contacts enrolled in the study either at their residence or work place. The collected blood samples were carried in cold chain to the designated laboratory at Government Medical College, Ernakulam. The blood samples were then centrifuged for the separation of serum. The serum samples were then transported maintaining the cold chain for serological analysis to (ICMR-NIV) Pune. Sera were screened for the presence of anti-NiV human IgM and IgG antibodies using indigenously developed Enzyme-linked Immunosorbent assay (ELISA) (ICMR-NIV, unpublished data). The data were entered in Microsoft Excel 2007 version and the same software was used for analysis of the data.

Results

Demographic and other parameters relevant to the exposure from the 49 close contacts of the Nipah case were collected and analyzed. The mean age of the study population was 29.4 years (SD ± 12.9). Of the total 49 close contacts, 24 (48.9%) were males and 25 were females (51.1%). Only three out of the total study subjects had comorbidities which included Diabetes mellitus, Bronchial asthma, and Hypertension. The mean duration between last exposure and the sample collection was 89 days (SD ± 13.4). More than half (26, 53.1%) of the close contacts were HCWs. The index case was initially treated at a primary care facility where a doctor and 2 nurses were his close contacts; other health care workers included doctors, nurses, nursing assistants and cleaning staff of the tertiary care facility where he was treated eventually. Rest of the contacts were 5 (10.2%) family members, 17 classmates (34.7%), and one fellow patient (2%). The index case had travelled and resided with these classmates in a hotel for few days during the early stages of his illness (when he had only slight headache and malaise). Physical contact like touching the patient, supporting the patient, feeding the patients, etc., were the most common type of exposure (55%) [Table 1]. None of the 49 samples tested were positive for anti-NiV human IgM and IgG antibodies. Hence, it could be inferred that there were no subclinical infection among the close contacts during this (2019) Nipah outbreak.

Discussion

The sample size was small as only one case of Nipah infection was reported in 2019; hence, the close contacts as per definition

Table 1: Distribution of close contacts of Nipah Index case by type of exposure

Type of exposure	Frequency	Percentage
Close physical contact for >30 min	27	55.1%
*Contact with blood/any other body fluid	11	22.4%
Contact with Fomites	6	12.2%
**Close contact ≤30 min	5	10.2%
Total	49	100%

*This type of exposure was present in health workers during procedures like drawing blood for investigation, Intra Venous infusion, Lumbar puncture. **Includes Medical rounds

were limited to 51 in number. The index case came into contact with majority of them during the first week of his illness. During this period the patient had fever, malaise, and disorientation which were due to encephalitis, but minimal or no respiratory symptoms like cough or vomiting. This could be the probable reason for non-transmission of the infection to his close contacts. The HCWs who handled body fluids during procedures like lumbar puncture and venepuncture had practiced personal protective equipment (PPEs) including coveralls, double surgical gloves, N-95 masks, and eye safety goggles. The study among contacts of Nipah patients in the Kozhikode (India) outbreak (2018) revealed three subclinical cases. Two of them had both anti-NiV human IgM and IgG antibodies and one had only anti-NiV human IgM antibody.[8] The Kozhikode study also highlighted the fact that subclinical infections were higher among close contacts with a history of exposure to body fluids of NiV patients than among those with only physical contact.[8] During the 2019 outbreak, all HCWs were trained in using PPEs; hence, it seems they were not directly exposed to the patient's body fluid. Paucity of case control and population-based studies (during the outbreak) was sighted as a reason for the difficulty in interpretation of the result in a contact who tested positive for anti-NiV IgG antibodies during the Siliguri NiV outbreak in 2001.[2] The strain responsible for the current NiV outbreak resembled the (Bangladesh strain) NiV_B which caused the Kozhikode, Kerala outbreak in 2018 (ICMR-NIV, India unpublished data). This strain was found to be more pathogenic when compared with the Malaysian strain. Malaysian strains are known to cause less severe illness, low fatality rate, and higher prevalence of asymptomatic infection.[10] There is limited knowledge regarding the period/duration for which the anti-NiV human IgM/IgG antibodies persists in the sera of asymptomatic/subclinical cases. In the study done amongst the close contacts of 2018 NiV outbreak in Kozhikode Kerala, the blood samples were collected for testing of anti-NiV IgM and anti-NiV IgG antibodies detection between 49 and 63 days post exposure,[8] whereas in our study, it was collected after a mean duration of 89 days post exposure. In a study among 176 Nipah positive cases at Kuala Lumpur in Malaysia, all the cases tested positive for anti-NiV IgM by the 12th day of illness, and it persisted for at least 3 months in most patients and more than 7 months in a few. Anti-NiVIgG was reported to have been present in most cases throughout the study period of 8 months.[11] A follow-up study amongst survivors of NiV 2018 and 2019 outbreak indicated that asymptomatic Nipah cases had detectable anti-NiV IgG from 49th post onset disease (POD) to approximately 13 months of POD (Unpublished data, NIV Pune). Study by Nickolay *et al.* among 1863 asymptomatic Nipah contacts revealed no infection, therefore he reported that asymptomatic and mild NiV infections are rare.[12] This study also could not establish asymptomatic infection. A clinicoepidemiological study on the 2018 Kozhikode outbreak revealed that 19 out of the 23 patients contracted the disease from the index case in a hospital setting. The authors of the study had called for stringent infection control strategies to be implemented at all levels of health care delivery.[13] The 2019 Ernakulam outbreak had not shown any clinical/subclinical/asymptomatic infection among the close contacts. The index case in the study had been treated in a primary care facility initially. Lessons learned from the 2018 Nipah outbreak might have helped the health care setting preparedness to handle all potential infectious diseases from being transmitted to health care workers and patients. Hence, we conclude that this study will help understand the dynamics of person to person transmission of Nipah and the circumstances which prevent the disease from being transmitted to the close contacts; thereby emphasising the need to continue stringent infection control practices at all levels of health care delivery including the primary care level, which might be the first contact point in most of the Nipah cases, as they present with general symptoms common to all viral fevers at the onset of the disease.

Keypoints

a) In the 2019 NiV outbreak, the index case presented with features of encephalitis and no respiratory symptoms which might have prevented the transmission of infection among the close contacts.
b) Health care workers even at the primary care facility practiced adequate infection control measures which might be a result of experience gained from state wide infection control measures undertaken following the 2018 NiV outbreak in Kozhikode district of Kerala, India.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Author's contributions

The 1st (corresponding author) and the 2nd authors have contributed towards the research question and methodology part of the manuscript. The 3rd and the 4th authors were responsible for the Microbiological and technical aspects of the study. All four authors have contributed towards the discussion part of the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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