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Nipah Virus: An Emerging Threat

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Abstract

The constantly evolving microbial world has the potential for introduction of agents with unique epidemiological characteristics, that pose a great threat and challenge to mankind. Nipah virus (NiV) infection is a striking example of these threats in the recent times. It is a zoonotic virus, transmitted to humans, mainly from tissues and secretions of infected animals or humans. The illness varies from sub-clinical infections to even fatal encephalitis, and the mortality is also varying, with up to 100% mortality being reported in some outbreaks. Many outbreaks have been reported since the discovery of the NiV in 1999, with high concentrations of them being in the Asian continent. No specific treatment is available, and the vaccine development is also under process/undergoing animal trials. Personal protective measures currently hold the key in the prevention of NiV infection. The recent outbreak in Kerala in India highlights the need for operationalization of an effective surveillance and response system at all time. At the same time, it also calls for greater focus on research and development of novel and effective diagnostic, vaccination and treatment strategies against Nipah virus.

Keywords: Nipah; Emerging; Virus; India.

Introduction

The microbial world is very complex and constantly evolving from time to time. One or many dynamic changes can occur at any time in the organism's epidemiological characteristics which can be due to either any gradual change through the process of adaptation, or it can be an abrupt change as a result of sudden genetic exchange during reproduction or replication [1]. Due to these changes, any infectious organism can spread with increased incidence and can spread to new geographical areas or unexposed population segments [2].

A recent emerging threat of similar background is the Nipah Virus (NiV) and is a member of family Paramyxoviridae, belonging to Genus Henipavirus. The infection with NiV mainly causes Encephalitis [3].

Transmission and Clinical Picture

NiV is zoonotic virus, which is transmitted to humans via direct contact/exposure to secretions or tissues of a sick and infected animal. Majority of the cases have occurred from exposure to fruits bats and pigs. People infected with NiV have also been shown to transmit the virus in some of the outbreaks in the past [3,4]. Transmission through contaminated food has also been reported in the past [4].

The infection in humans causes a spectrum of illnesses which can range from even asymptomatic (sub-clinical) presentation to acute respiratory illness and even, fatal encephalitis [4]. The patient can present with neurological signs or respiratory signs or a complex of both of these. The average incubation period has been noted to be 5 to 14 days, after which the signs and symptoms start to appear [3]. Case fatality rate of 40-75% is reported, as it varies from outbreak to outbreak, depending on the regional capabilities of epidemiological surveillance and clinical management, and can even be higher than the above denoted range [4].

Past Outbreaks and Burden

NiV was first recognized and isolated in a very

large outbreak reported in Malaysia and Singapore from September 1998 to May 1999. The outbreak was mainly among the pig farmers, who reported handling of pigs prior to the illness [4,5] No human to human transmission was reported at that time. Mass culling of pigs had to be done to control the outbreak [6]. No fresh outbreaks have been reported in Malaysia since then. The NiV has been periodically identified in Bangladesh and parts of Eastern India since 2001. Regions with high risk of outbreak are countries with evidence of virus in the fruit bats of *Pteropus* species, like Cambodia, Philippines, Ghana, Thailand etc [4].

Two outbreaks have been reported in India in the past, during 2001 and 2007 [5]. The 2001 outbreak occurred in Siliguri in West Bengal in February 2001, where 66 cases were reported. Among these cases, 45 deaths were reported, thus, a case fatality rate of 68% [7]. The second outbreak occurred in Nadia, West Bengal in April 2007, where though only 5 cases were reported, they had a 100% case fatality rate [7,8]. (Table 1)

Recent Outbreak in Kerala, India

A recent outbreak occurred in Kerala in May 2018, which initially originated in Kozhikode district of Kerala State. Initially, three deaths were reported which were clustered in a single family [9]. Two of these confirmed cases had history of contact with the index case [10]. A fourth death was reported of a health care worker involved in treatment of the family members [9]. These sudden and unexplained deaths alerted the authorities viz. Ministry of Health and Family Welfare (MoHFW) and National Centre for Disease Control (NCDC), and the samples from the suspected patients (throat swabs, urine and blood) were sent for testing to National Institute of Virology (NIV), Pune. Three out of the suspected four were confirmed NiV positive by Real-time polymerase chain reaction (RT-PCR) and IgM-enzymelinked immunosorbent assay (ELISA) [9,10].

The authorities in consultation with experts developed a draft reporting format for collecting data on cases, suspects and contacts [11]. At the same time, field investigation team investigated into the probable mode of spread. Bats were found living in an abandoned water well in the house premises of the index case, and some bats were caught and sent for laboratory testing to NIV [9,10]. Advisories were also issued by the field team to all hospitals to follow Infection Prevention and Control (IPC) guidelines, and use of personal protective equipment (PPE) by healthcare workers while handling and sample collection of diagnosed and suspected cases [10].

By 23rd May, 2018, the infection had spread to Malappuram district in Kerala and three deaths were reported there, which were among the contacts of the index case [9,11,12]. Later, some of the suspected cases were also reported and investigated from the states of Goa, Telangana, Karnataka and Himachal Pradesh. All of these samples eventually tested out to be negative, which were tested out at NIV, Pune and Manipal Institute of Virus Research [9,13,14]. The WHO South-East Asia Region morbidity and mortality report for NiV reported 14 cases with 86% mortality (12 deaths) as on 24th May 2018 [7]. However, a press release later by the MoHFW put the tally of the Kerala outbreak at 19 reported cases, where 18 cases were lab confirmed. Out of these 19 reported cases, 17 cases had died, thus raising the mortality to 89.4% [13].

The pattern of emergence of cases was highly suggestive of human-to-human transmission in the later period of spread of the outbreak. Although the transmission was also confirmed from an established host of Fruit Bats, in whom the presence of Nipah virus was confirmed [15].

Current Prevention and Treatment Strategies

The spread of Nipah virus is mediated by numerous determinants and the control also depends on various factors. Thus, even an established and responsive health system does not guarantee complete protection against infections from NiV. This somehow explains the outbreak of Nipah in Kerala, where Kerala is among states with the best health indicators in India [16].

No specific protection measures viz. vaccine are available for the prevention or control of NiV. Also, the treatment measures available for cases presenting to health system are only supportive. Preventive measures should be instituted beforehand, and the health system

Table 1: NiV outbreaks in India: Morbidity and mortality in humans

Month and Year	Location	Number of Cases	Number of Deaths	Case Fatality Rate (%)
February 2001	Siliguri, West Bengal	66	45	68%
April 2007	Nadia, West Bengal	5	5	100%
May 2018	Kerala	14	12	86%

strengthening plays an important role in this. This is the main strategy to prevent NiV infection and transmission in humans. Establishment of an appropriate surveillance system is also necessary so that the NiV outbreaks are detected very quickly and appropriate and timely response and control measures are initiated [17]. The general public is advised to avoid any contact with bats, pigs and pig handlers. They are also advised to avoid eating any half-bitten fruits or any fruits that are dropped on the ground [14]. The general public is also cautioned to avoid consumption of raw date palm sap or toddy, and avoid entering into abandoned wells [18]. An increase in awareness among the general public and focus on surveillance plays an important role in early detection of cases and prevention of future outbreaks [19].

For those infected, the mainstay of treatment is symptomatic and supportive care [19]. Those who develop severe illness need to be immediately hospitalized and they may require ventilatory support [17]. Severe neurological complications also require intensive supportive care [9].

At the same time, strict implementation of standard infection prevention and control measures is also needed to prevent nosocomial infections in healthcare settings. Nipah virus is internationally classified as a Bio-Security Level-4 agent (BSL-4) agent and thus, should be handled in similar level of facilities only. Only of the specimen can be first inactivated during the collection, then even BSL-2 level facilities are sufficient enough to handle the agent/specimens [17,20,21]. Presently, only two BSL-4 laboratories are the testing laboratories for diagnosing NiV infection in India. One each is there in the public and private sector viz. National Institute of Virology (NIV), Pune and Manipal centre for Virus Research, Manipal, Karnataka [21].

The samples that can be collected for diagnosis of NiV infection are Throat swab (collected in viral transport medium), 10ml urine in universal sterile container, 5ml blood in plain vial, or 1ml CSF in a sterile container. All samples should be collected within 4-5 days of onset of illness, and should be transported under cold chain [21]. Majority of countries in the South-East Asia region are not equipped with facilities for controlling or diagnosing Nipah virus. But, laboratory capacity for diagnostic and research purposes has been developed by India, Thailand and Bangladesh, who are at an increased risk of outbreaks [17].

The way forward and Recommendations

Ribavarin has been shown to alleviate the symptoms of encephalitis like nausea, vomiting, convulsions etc. Hence, it may have a role in mortality reduction among patients with encephalitis and thus, needs further work-up and investigation in its complete biological action in Nipah cases [5,17].

Vaccines for the prevention and control of Nipah virus are under development. Hey have shown promising results in infected animals by protecting against infections or severe disease manifestations. Hence, they hold the potential for development as a vaccine for humans in the later stages of development. A recombinant sub-unit formulation has been developed which has shown to be effective in cats, against the Nipah virus challenge. ALVAC Canarypox vectored Nipah F and G vaccine, appear to be a promising vaccination agent proven to be effective in the pigs [17,22,23].

Vaccine against Nipah Virus is a WHO priority for product development. As healthcare workers are and have been affected by NiV infection during the outbreaks. There is a heightened need for development of a vaccine strategy for the preventive use of healthcare workers [24]. There is also a need to develop better diagnostic tests for NiV detection to correctly identify all the infected patients in the various stages of the disease.

In order to respond quickly to any outbreak, mobile and wireless technologies can be assessed and roped in for the provision of services and collection of information. They can be used by the healthcare workers for case identification, tracing of possible contacts and accessing the laboratory data in real time, without any delay. These mobile health technologies can also be useful in educating the masses as well as the health care workers for dissemination of messages on precautions and personal protective measures [25,26,27].

Hence, strengthening of the appropriate surveillance systems, with roping in of mobile technology, and effective dissemination and implementation of control measures is the key in controlling an outbreak of NiV [28]. At the same time, it is recommended to focus on a priority basis, on the development of better diagnostic tests, effective treatment options and vaccine strategies against Nipah virus [24,28].

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