Deadly Nipah Outbreak in Kerala: Lessons Learned for the Future

The recent reemergence of Nipah virus belonging to the family *Paramyxoviridae* caused 17 case fatalities among the 19 infected patients (89% mortality) in Kozhikode (Calicut), a city in the state of Kerala, South India. It is extremely sad to note that Mrs. Lini Puthussery, a very committed young nurse who looked after the index patient, had to sacrifice her own life to the deadly illness. The outbreak has drawn immense global attention and underlines the need for adequate preparedness in the event of such episodes resurging in the future.

In the early hours of May 17 this year, a 28 year old male was shifted to the closed Multidisciplinary Intensive Care Unit (ICU) of Baby Memorial Hospital, Kozhikode, with clinical features suggestive of encephalitis. In the ensuing hours, the patient had developed certain unusual clinical signs including features of myoclonic jerks and significant autonomic response (severe tachycardia and high blood pressure). The patient's condition further progressed to myocarditis and circulatory failure. A detailed history by the ICU team revealed that the patient's younger brother had died exactly 12 days before, with similar symptoms. There was a history of ongoing fever for three more members in the same family at the same time. The ICU doctors requested the relatives to bring all three of them and get them admitted to the hospital immediately. In the same evening, two of the three admitted relatives also developed features suggestive of encephalitis along with segmental myoclonus, severe adrenergic response, ptosis, and segmental sweating. The possibility of a new viral syndrome was actively thought about in view of unusual unique clinical features, the unexpected rapid deterioration, and clustering of the cases. The case was discussed in detail with the director of Maniple Centre for Virus Research (MCVR) in the same evening and, as per his direction, the blood, urine, cerebrospinal fluid, and throat swab of the patients were sent to virus center on the same night via the attenders. It was bit of a communication challenge to convince and motivate the relatives regarding the urgent need to take the specimens (in three-layered safe containers) to the Manipal center which is almost 300 km away to the north of Calicut. On the next day morning, a detailed bedside discussion was carried out with the neurology and internal medicine team regarding the unique encephalitis, and the rare possibility of Nipah viral infection versus a toxic etiology was considered in the differential diagnosis. The first patient died in the same afternoon, and a pathological autopsy was carried out and the specimens were sent to MCVR and the regional toxicology laboratory. The challenge here again was to convince the relatives. The deceased happened to belong to the Muslim community who were strongly against any kind of dissection or disruption of human body during that ongoing Ramadan month. However, their consent was finally obtained after discussing and convincing via religious and political leaders. The reverse transcriptase-polymerase chain reaction done at the MCVR initially reported the diagnosis of an unusual highly infectious virus, which was subsequently confirmed as Nipah after cross checking with the National Institute of Virology, Pune.

After the initial Nipah virus outbreak in Malaysia in 1998–1999, the spread had occurred to Singapore, and further epidemics have occurred later in Bangladesh (sporadic between 2001 and 2008) and India (at Siliguri in 2001 and at Nadia in 2007, both in West Bengal). The Indian outbreaks occurred in the villages adjoining Bangladesh.[1-6] The Malaysian outbreak was found to have occurred via exposure to infected pigs which had consumed bat-eaten fruits or exposed to bats' urine.[2] Humans also get infected by consuming bat-eaten fruits or exposure to bats' urine or via human-to-human transmission.[7] The last Nipah outbreak was reported in the Philippines in the year 2014, probably via infected horses.[8] The incubation period in humans ranged from 4 days to 2 months, with more than 90% occurring at 2 weeks or less.[2]

After confirming the diagnosis, the next major challenge with the Kozhikode outbreak was that, unlike all the previous outbreaks, the current one had occurred in a densely populated area with a highly moving and intermingling population. There was no previous experience in tackling such health emergencies. Intensive measures were initiated by the state with the help of central government health authorities including the National Centre for Disease Control, National Institute of Epidemiology, Indian Council of Medical Research (ICMR), and experts from AIIMS, New Delhi. The target was active contact tracing and quarantining. Strong support and co-operation by the public ensured the success of all such measures. The state government also promoted the association and co-operation between private and public medical facilities. Strict isolation precautions were followed at the treatment centers and stringent measures for the prevention of droplet spread were initiated. At the community level, a special task force was set up to re ensure early suspicion and detection followed by isolation, treatment, and surveillance of confirmed cases. A single center for the treatment of suspected or confirmed cases was soon identified, with the Government Medical College, Calicut, being the point of care. Relevant health education was frequently provided via social, printed, and visual media. The social, political, and religious leaders were actively involved in facilitating the entire process. Taking active measures to restrict the movement of people in

the affected areas was also a crucial strategy and challenge in the isolation process. Movement of people and visits to the epicenter areas were strongly discouraged. Gathering of people was highly discouraged at least for 12 days after the death of last Nipah patient (since the known average incubation period was mostly within 12 days). All social and political gatherings were postponed including marriages and religious functions. Holiday was declared for all educational institutions in the two affected districts during the above period. Although the first case was diagnosed on May 18, the containment could be achieved with a span of 12 days, with the last case reported on May 30. The Kerala government has finally announced the state as free from Nipah infection on July 1, 2018. Postoutbreak surveillance for detection and prevention of a potential further outbreak is still going on.

Vomiting, high fever, agitation, and encephalitis characterized the clinical presentation of Nipah virus in the Kozhikode outbreak. Further complications, which are documented, include encephalitis with viral bronchopneumonia/acute respiratory distress syndrome (ARDS) in seven patients (36.84%), encephalitis with viral bronchopneumonia/ARDS with myocarditis in five patients (26.31%), encephalitis with myocarditis in four patients (21.05%), viral bronchopneumonia with ARDS in one patient (5.2%), viral bronchopneumonia with ARDS and myocarditis in one patient (5.2%), and only prodromal symptoms in one patient (5.2%).

Bat is the natural reservoir of Nipah.[9] The continued degradation and fragmentation of the natural habitats of bats has resulted in an increased overlap of bat, domestic animals, and human ecologies, which has created increased opportunities for emergence of bat-borne zoonotic diseases. Design of forest management strategies that preserve bats' roosting and foraging landscapes and prevention of viral spillover from bats to humans require a complete understanding of the ecological narrative, linking of bat habitat with human and livestock activity to explain when, where, and why a virus emerges.

The ICMR has finally confirmed fruit bats to be the source of the Kerala outbreak after isolating the virus from them.[10]

We, as critical care community, are immensely proud of the commendable contribution and the persistent enthusiasm shown by the Kozhikode ICU team resulting in early suspicion and early detection helping in the complete curtailment of the deadly epidemic in a span of 12 days. The episode underlines the need and importance of a meticulous history taking, excellent communication skills, and a multidisciplinary team interaction in such scenarios. The above success also exemplifies how well-organized and committed health-care interventions endorsed by government as well as nongovernment agencies, with complete indulgence of public, could achieve the desired targets within a short period of time.

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