Epidemiological Trends of Zoonotic Diseases in India: A Focus on Crimean-Congo Hemorrhagic Fever, Kyasanur Forest Disease, and Nipah Virus Disease

Deepak Y. Patil[1], Anita M. Shete[1], Rima R. Sahay[1], Sreelekshmy Mohandas[1], Pragya D. Yadav*

[1]Maximum Containment Laboratory, Microbial Containment Complex, ICMR-National Institute of Virology, Sus-Pashan Road, Pune, Maharashtra, Pin 411021, India

***Corresponding author**
Dr. Pragya D. Yadav
Scientist 'F' & Group Leader
Maximum Containment Laboratory, Microbial Containment Complex
ICMR-National Institute of Virology
E mail ID: hellopragya@gmail.com

Abstract

In recent decades, numerous emerging and re-emerging diseases have extended their reach to diverse global regions, collectively contributing to around 25% of annual global mortality. Over the past decade, highly contagious viruses such as Crimean-Congo Hemorrhagic Fever, Nipah Virus, and Kyasanur Forest Disease have emerged, causing severe outbreaks in various regions of India. However, it is evident that these viruses have now re-emerged in newer areas, resulting in significant morbidity and mortality among the human population. Given the changing epidemiological landscape, there is a good chance that these viruses will continue to appear in new places in the future. In light of this context, we present a comprehensive account of the incidence, prevalence, and the growing trend of these viruses appearing in various geographical locations throughout India.

Keywords: Crimean Congo Hemorrhagic Fever, Kyasanur forest disease, Nipah, India

Introduction

Being one of the world's most densely populated nations, India grapples with a multitude of infectious diseases, creating significant public health challenges. Among the prevalent infectious diseases reported in India are Malaria, Cholera, Hepatitis, Tuberculosis, Rabies, Dengue, Plague, Chikungunya, Japanese Encephalitis, Typhoid, HIV, Influenza, and Diarrhoeal illnesses.[1] However, the last two decades has been truly a menace to the public health of India. During this period, India has witnessed many outbreaks of deadly viral disease viz., Avian Influenza H5N1 (2006)[2]; Chikungunya (2006-2023)[3]; pandemic influenza (2009)[4]; Crimean Congo hemorrhagic fever (CCHF) (2011-2023)[5-17], Kyasanur Forest disease (KFD) (2014, 2016, 2017-2023)[19-32]; Nipah virus (2001, 2007 & 2018, 2019, 2021, 2023)[37-51]; Zika virus (2016, 2017, 2018, 2021, 2022, 2023)[52-56]; and SARS-CoV-2 (2020-2023)[57].

Among these, CCHF, KFD, and Nipah viruses stand out as the most significant and highly contagious emerging viral infections in India during the 21st century.[5-51] They have triggered periodic outbreaks in various parts of the country, despite originally being endemic to specific regions. In this report, we shed light on the occurrence, prevalence, and emergence/re-emergence of these viruses in various parts of India.

Crimean Congo hemorrhagic fever (CCHF)

CCHF is a zoonotic illness caused by ticks that affects humans and animals. A nairovirus, which is a member of the Nairoviridae family, is the causal agent. Human infection can occurs via direct contact with the blood of infected people or cattle or by the bite of an infected Hyalomma tick. There have been reports of human to human transmission, especially when the virus is in its acute viremic phase and involves close interactions. According to international classification, the CCHF virus is considered highly infectious due to its high pathogenicity, established human to human transmission, and high case fatality rate. This deadly disease has been documented in Africa, Asia, Middle East, southern and eastern Europe,[7,9,17] and has significantly impacted human and animal health in India.[5-17]

The initial identification of CCHF in India was made in 2011 after a nosocomial outbreak in Ahmedabad, Gujarat State, by the ICMR-National Institute of Virology (NIV) in Pune. The development of novel molecular and serological assays for the diagnosis of CCHF was made possible by the establishment of a state-of-the-art Biosafety Level (BSL)-4 Laboratory at ICMR-NIV, Pune. These tools were essential for the rapid diagnosis of suspected CCHF cases as well as for

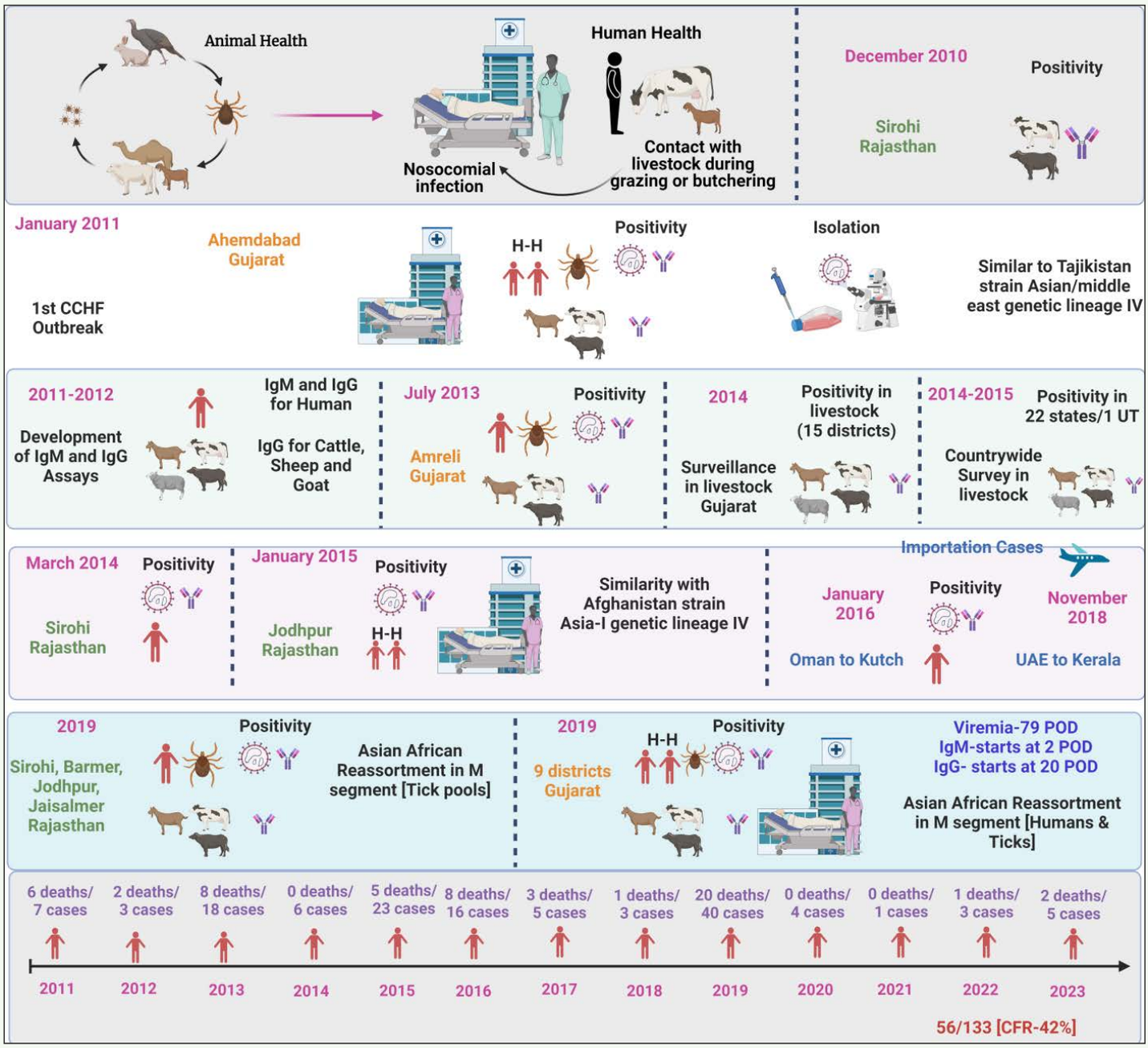

Figure 1: CCHF outbreaks in India – Outbreak investigations, surveillance, and R&D

monitoring populations of ticks, cattle, and humans. Numerous nosocomial and sporadic CCHF outbreaks were investigated and confirmed in fifteen districts of Gujarat State between 2011 and 2023.[5-17] Although anti-CCHF IgG antibodies were found in livestock in Rajasthan State in 2010,[5] the first human case of CCHF was reported in the Sirohi area of Rajasthan in 2014.[10] Subsequently, a nosocomial outbreak of CCHF was identified among healthcare workers in a private hospital in Jodhpur, Rajasthan, in 2015.[12] A nationwide serosurvey conducted by NIV, Pune revealed widespread seroprevalence of CCHF among sheep, goats, and cattle in 23 states and one union territory in India.[11] In recent years, two imported cases of CCHF were identified in individuals traveling from Oman13 and the UAE, and they were successfully managed in Gujarat and Kerala states in 2016 and 2018, respectively.

From 2011 to 2023, 138 cases of CCHF were confirmed, with 57 fatalities, accounting for a Case Fatality Rate (CFR) of 41.3%.[5-17] These CCHF cases were documented in 15 districts within Gujarat state, including Ahmedabad, Kutch, Patan, Surendranagar, Morbi, Jamnagar, Amreli, Aravali, Anand, Gandhinagar, Rajkot, Bhavnagar, Botad, Kheda, and Sabarkantha.

Additionally, CCHF cases were reported in 4 districts of Rajasthan state: Jodhpur, Jaisalmer, Barmer, and Sirohi. Since 2019, over 900 close contacts of CCHF cases have been monitored, and a very low sub-clinical infection rate of less than 0.3% was observed.

Many guidelines were developed for recognizing cases, diagnosing, putting isolation measures in place, and tracing contacts due to the high risk of CCHF in India as well as the possibility of the virus spreading through

animal trade and international travelers. The responsibility for managing sporadic CCHF outbreaks in India was shared among the Indian Council of Medical Research (ICMR), the Integrated Disease Surveillance programme (IDSP), and the National Centre for Vector Borne Diseases Control (NCVBDC). This collaborative effort enabled the timely detection, diagnosis, and efficient containment of CCHF outbreaks.

Following the larger outbreak of CCHF in 2019, a laboratory network equipped with BSL-3 facilities was established and staffs were trained across India for CCHF diagnosis, supported by an ICMR-funded project. Currently, seven active laboratories have the capacity to test for CCHF, including SMSMC, Jaipur; KGMU, Lucknow; ICMR-RMRC, Port Blair; AIIMS, Jodhpur; ICMR-NICED, Kolkata; ICMR-RMRC, Dibrugarh; and ICMR-NIRTH Jabalpur.

There are currently no licensed vaccines or approved treatments for CCHF, hence the primary strategy to treatment is supportive care. Although Ribavirin has displayed some efficacy in laboratory settings and has been employed during outbreaks, there is limited and uncertain evidence supporting its effectiveness.[18] In July 2023, Turkey initiated the first Phase-1 clinical trial for intravenous Ribavirin and Favipiravir as potential treatments.[19] Additionally, there is a pressing need for the development of monoclonal

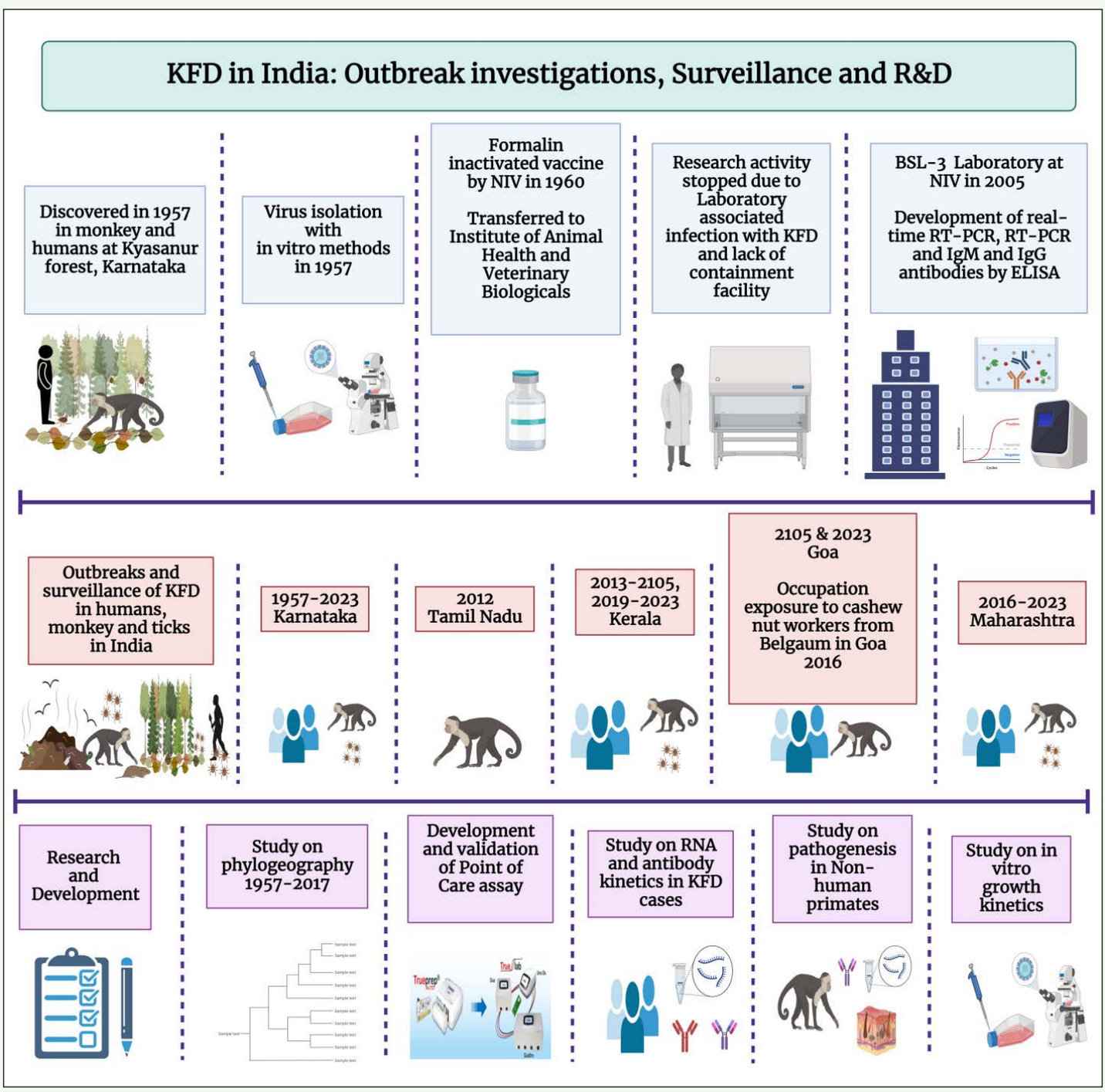

Figure 2: KFD outbreaks in India: Outbreak investigations, surveillance, and R&D

antibody therapies to address CCHF cases and individuals at high risk of infection.

A significant challenge in the quest for CCHF vaccines and therapeutics has been the absence of suitable and standardized animal models. The emergence of new animal models that are susceptible to CCHFV infection, such as IFNAR-/-mice, STAT-1 mice, and cynomolgus macaques, has enhanced the screening and validation of potential vaccines in preclinical studies.[19] Nonetheless, these models must be refined and standardized further, including the selection of appropriate viral strains, reagents, and challenge methods. This will better replicate clinical characteristics observed in humans, while bridging data on animal and human immunogenicity and facilitate the selection of vaccine candidates for human evaluation.

Kyasanur forest disease (KFD)

Kyasanur Forest Disease (KFD) was first discovered in 1957 following a study into a large number of monkey deaths in Karnataka's Shimoga district. The KFD virus, a member of the Flaviviridae family, causes the disease. Humans and monkeys are the main hosts that the virus primarily affects in its natural cycle, which is maintained in Haemaphysalis ticks, mammals, and birds. KFDV is transmitted to humans via tick nymph bites or contact with carcasses of deceased monkeys.[9,17]

Ever since its discovery, Kartaka State has had a number of outbreaks and occasional instances of KFD, mostly in five districts: Shimoga, Chikmagalur, Uttara Kannada, Dakshina Kannada, and Udupi. These areas have experienced an average of around 400 to 500 cases per year.[9,17]

Apparently from around 2012, KFD has been reported in new areas, involving either monkey deaths or human cases. These regions include the districts of Chamarajanagar in Karnataka State (2012), the Mudumalai Tiger Reserve in Tamil Nadu State (2012), the districts of Wayanad and Malappuram in Kerala State (2013–14, 2018), the state of Goa (2015–2023), and the state of Maharashtra (2016-2023).[20-32]

The mortality rate associated with KFDV infection is reported to range from 2% to 10%. Higher fatality rates have been observed in non-endemic areas, primarily due to a lack of awareness about the disease and lower levels of herd immunity to the virus. In Karnataka's KFD-endemic areas, a formalin-inactivated chick embryo tissue culture vaccination has been used since 1990. However, studies have indicated low vaccination coverage in the population and reduced vaccine effectiveness compared to initial reports.[33]
As a result, the use of the KFD vaccine has been discontinued, and ongoing efforts are focused on developing a new vaccine. Currently, supportive care is the main method of managing infected cases of KFD as there is no particular treatment for the disease.

Time-sensitive and affordable molecular and serological tests, such as nested RT-PCR and real-time RT-PCR, as well as KFD IgM and IgG ELISA, were developed for KFDV identification after a BSL-3 laboratory was established at ICMR-NIV in Pune.[21] These advances have greatly improved the screening for KFDV among human, monkey, and tick populations in various geographic locations across India. ICMR-NIV, Pune has taken significant steps in ecological, entomological, and virological research on KFD, shedding light on this enigmatic "monkey fever."

A number of variables, including deforestation, monkey migration, changes to agricultural land use methods, and changes in people's socioeconomic behavior, may have contributed to the disease's spread into new regions. Infected monkeys and rodents, along with ticks, contribute to the disease's expansion into new regions. Therefore, the KFD virus continues to spread through wildlife-tick-human interactions, and the Western Ghats' extensive densely forested areas provide the perfect environment for tick cycles to complete. While KFD is endemic to India,[9,17] it has the potential to spread to neighboring countries through animal transportation or the diverse migratory bird population.

Studies on the genome and phylogeography have shed light on the evolution of the virus and the areas connected to KFDV transmission dynamics. Recent KFDV isolates (from 2006-2017) displayed approximately a 3% difference compared to early strains from Karnataka.[34] Laboratory mice and Bonnet macaques have been extensively studied as animal models to understand KFD disease pathogenesis and progression. Rodent models exhibit neurological disease, while Bonnet macaques experience prolonged disease with relatively few fatalities. Studies on viremia, virus shedding in different secretions, antibody responses, and viral RNA loads in different organs have all benefited from the use of these animal models.[35-36]

In conclusion, KFD is a serious threat to public health, especially in India's Western Ghats. To manage and prevent future outbreaks and, ultimately, protect the health and well-being of at-risk communities, vigilance, research, and cooperative efforts are essential. This tick-borne viral disease, caused by KFDV, has demonstrated its potential to trigger periodic outbreaks of varying severity.

Nipah virus disease

Nipah virus (NiV), belonging to the paramyxovirus family, is a recently identified zoonotic virus capable of causing severe and fatal infections in humans. The first known case of NiV infection in humans was discovered in 1998–1999 during a major encephalitis outbreak in Malaysia.[58] The Nipah virus has been known to spread from animal to human and from human to human during a number of outbreaks. NiV can cause an extremely deadly respiratory and encephalitic disease in humans. From 1998 to 2023, cases of the disease were documented in a number of countries, including Singapore, Malaysia, Bangladesh, the Philippines, and India.[59]

During January and February of 2001, the Siliguri area of West Bengal in India experienced the first Nipah virus outbreak, which resulted in [45] deaths out of 66 cases (CFR 68%). The majority of the afflicted people had symptoms such as fever, headache, myalgia, vomiting, altered sensorium, acute respiratory distress, and convulsions. During that period, India was devoid of the diagnostic tests required to identify the Nipah outbreak and the containment facilities required to manage high-risk viruses.[37] In April 2007, the Nadia district of West Bengal had the second Nipah virus outbreak. This was an intra-familial outbreak, affecting all five family members, who unfortunately succumbed to the infection (CFR 100%).[38] In 2015, ICMR-NIV, Pune conducted a multi-site virological survey that established the presence of NiV in Pteropus giganteus bats in the Cooch Bihar district of West Bengal and the Dhubri district of Assam.[41]

During May 2018, the third Nipah virus outbreak occurred, resulting in 16 fatalities out of [18] confirmed cases (CFR 89%). The first Nipah outbreak in southern India was recorded in the Kerala state's Kozhikode district. This outbreak occurred far from the two earlier outbreaks in 2001 and 2007 in West Bengal, which is located in eastern India. Patients primarily presented with symptoms such as fever, cough, altered sensorium, acute respiratory distress syndrome, vomiting, headache, and signs of myocarditis.[40] During this outbreak, therapeutic monoclonal antibodies (m102.4), developed by the University of Queensland, Australia, were provided to India, and emergency use authorization was granted by the Drug Controller General of India in June 2018. Guidelines for the use of m102.4 monoclonal antibodies on Nipah cases were developed through global research collaboration in 2019.

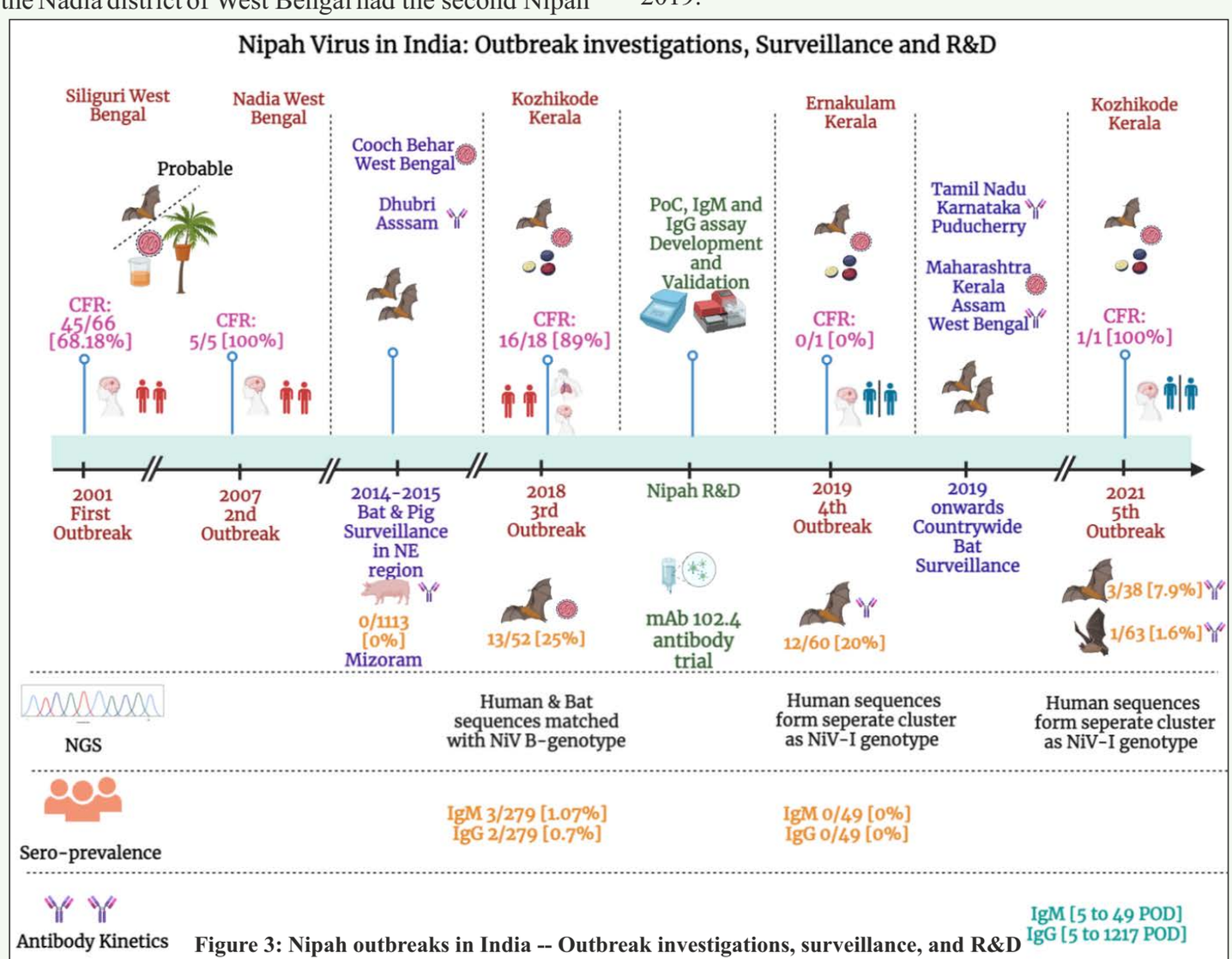

Figure 3: Nipah outbreaks in India -- Outbreak investigations, surveillance, and R&D

One significant development following the outbreak was the creation of a point of care (PoC) assay for NiV diagnosis. This PoC assay was standardized and employed in the field for Nipah diagnosis during the outbreaks in 2019 and 2021. NiV surveillance was made possible by the development of human IgM and IgG tests as well as an IgG screening assay for pigs and bats following the isolation of the virus. Only 3 out of 239 contacts (1.2%) tested positive for IgM and IgG during the 2018 outbreak, indicating an extremely low seroprevalence among close contacts.[40]

Only one case—who showed signs of fever and encephalitis-like symptoms—tested positive for the Nipah virus disease during the fourth outbreak that occurred in the Ernakulam district of Kerala in June 2019. During this outbreak, none of the patient's close contacts showed signs of seropositivity, and the patient survived with supportive treatment.46 Amidst the COVID-19 epidemic, the Kerala district of Kozhikode recorded the fifth Nipah outbreak in August-September 2021, which claimed one life (CFR 100%). Affected individual presented with fever and late-onset encephalitis.[51]

In all three of the outbreaks in 2018, 2019, and 2021, Pteropus medius bats were found to be the likely source of infection and transmission in the vicinity of the index case, based on positive results from real-time RT-PCR or IgG ELISA tests. The NiV sequences from the 2018 outbreak belonged to the B genotype, while sequences from the 2019 and 2021 outbreaks were identified as I (Indian) genotype. All of these human sequences were consistent with the bat sequences.[44,45,48]
The Pteropus species of fruit bats, also referred to as flying foxes, are identified as the Nipah virus's known reservoirs. Previous ICMR-NIV investigations in Nipah outbreak-affected areas have detected the virus in fruit bats from a number of locations, including Dubri in Assam, Myanaguri and Cooch Behar in West Bengal in 2015, Maharashtra in 2020, and Kozhikode, Kerala in 2018.[41,44,45] The paucity of information on the virus's presence among Pteropus bat species in the other parts of the country motivated the ICMR-NIV to initiate a nationwide survey. This survey has so far been carried out in fourteen states and two union territories, namely Kerala, Tamil Nadu, Karnataka, Telangana, Goa, Maharashtra, West Bengal, Gujarat, Punjab, Himachal Pradesh, Odisha, Bihar, Assam, Meghalaya, Chandigarh, and Puducherry. The presence of Nipah viral antibodies was detected in bats from seven states and one union territory,[52] suggesting evidence of virus circulation within the bat population. This study aims to identify areas at risk of spill-over and, as a result, facilitate the implementation of necessary precautionary measures and control strategies to prevent future outbreaks in the country.

In the most recent Nipah virus outbreak, the sixth occurrence, which was declared on September 13, 2023, in Kozhikode, Kerala, three out of five suspected cases were diagnosed as NiV positive by ICMR-NIV, Pune. Nipah virus was confirmed in six cases, resulting in two fatalities (CFR 33.33%). All close contacts and other suspected cases not epidemiologically linked were found to be negative for Nipah virus infection.[62] Further investigations are essential to delve into the underlying factors contributing to recurring spillover events in Kerala State. While bats in this region have tested positive for NiV RNA, the precise mode of transmission to the initial cases remains to be determined.

As of the now, there is no approved vaccine or therapies for Nipah virus infections. Since 2018, the Coalition for Epidemic Preparedness Innovations (CEPI) has supported the NiV vaccine development and continues to provide significant funding to scientific endeavors such as the creation of International Standards for NiV antibodies, assay development, and epidemiological research.[63] Numerous Nipah virus vaccine candidates are undergoing preclinical trials and clinical trials.[64,65]

Nipah virus is an extremely contagious and lethal virus. Because there is no specific treatment for Nipah virus infection, supportive care may enhance the patient's prognosis. Taking preventive measures is of paramount importance to prevent Nipah virus infection. This entails refraining from contact with bats and their excrement, consuming only well-cooked fruits and vegetables, and maintaining regular hand hygiene by washing hands with soap and water.

Current interventions and prospects

At present, there are no vaccines or antiviral drugs that are useful in treating Nipah virus disease and Crimean-Congo hemorrhagic fever (CCHF). Supportive care is the main strategy used to manage these diseases, and the main focus of current preventative efforts is increasing awareness in the affected areas. It is noteworthy that the WHO R&D Blueprint list of pandemic threats requiring immediate R&D initiatives includes both the CCHF and the Nipah virus. Recently KFD immunization campaigns have been discontinued due to a paucity of information regarding the immunogenicity of the currently available vaccine.[33] Cases of KFD are treated with supportive care because of the absence of antiviral treatment.

Reducing the chain of transmission, treating infectious diseases appropriately, and eventually saving lives all depend on accurate diagnosis. Given extensive scale of the outbreaks caused by these viruses, a more comprehensive examination of their areas of origin is necessary. Timely and affordable molecular and serological tests for the identification of CCHF, KFD,

and Nipah viruses have been established with the development of containment laboratories (BSL-3 & BSL-4 laboratories) at ICMR-NIV in Pune, India.

The implementation of these technologies has facilitated the identification of these diseases in various geographical locations across India, subsequently aiding in the application of effective control measures.

Furthermore, various training programmes have been organized for laboratories, healthcare officials, hospitals, and medical colleges, with a specific focus on biosafety, bio-risk mitigation, the transportation of infectious samples, and laboratory diagnosis of emerging and re-emerging viruses. This proactive approach has contributed to the development of emergency preparedness strategies to address significant public health challenges in India.

Acknowledgment
We acknowledge NIV for constant support.

Financial support & sponsorship
None.

Conflicts of Interest
None.

References

1. Kambrath SV, Deshmukh M. The burden of infectious diseases in India-An overview. International Journal of Current Research in Life Sciences. 2018; 7(06):2237-40.

2. Tosh C, Murugkar HV, Nagarajan S, Bhatia S, Pateriya AK, Behera P, et al. Outbreak of avian influenza virus H5N1 in India. The Veterinary Record. 2007; 161(8):279.

3. Translational Research Consortia (TRC) for Chikungunya Virus in India. Current status of chikungunya in India. Frontiers in Microbiology. 2021; 12:695173.

4. Khanna M, Kumar B, Gupta A, Kumar P. Pandemic influenza A H1N1 (2009) virus: lessons from the past and implications for the future. Indian Journal of Virology. 2012; 23:12-7.

5. Mourya DT, Yadav PD, Shete AM, Gurav YK, Raut CG, Jadi RS, et al. Detection, isolation and confirmation of Crimean-Congo hemorrhagic fever virus in human, ticks and animals in Ahmadabad, India, 2010–2011. PLoS Negl Trop Dis. 2012; 6:e1653.

6. Yadav PD, Raut CG, Mourya DT. Re-occurrence of Crimean-Congo haemorrhagic fever in Ahmedabad, Gujarat, India (2012): a fatal case report. The Indian journal of medical research. 2013; 138(6):1027.

7. Yadav PD, Raut CG, Patil DY, Majumdar T, Mourya DT. Crimean-Congo hemorrhagic fever: current scenario in India. Proceedings of the National Academy of Sciences, India Section B: Biological Sciences. 2014; 84:9-18.

8. Yadav PD, Gurav YK, Mistry M, Shete AM, Sarkale P, Deoshatwar AR, et al. Emergence of Crimean-Congo hemorrhagic fever in Amreli district of Gujarat state, India, June to July 2013. International Journal of Infectious Diseases. 2014; 18:97-100.

9. Mourya DT, Yadav PD, Patil DY. Highly infectious tick is borne viral diseases: Kyasanur forest disease and Crimean-Congo hemorrhagic fever in India. WHO South-East Asia J Public Health 2014; 3(1):8-21.

10. Makwana D, Yadav PD, Kelaiya A, Mourya DT. First confirmed case of Crimean-Congo hemorrhagic fever from Sirohi district in Rajasthan State, India. Indian J Med Res. 2015; 142:489–91.

11. Mourya DT, Yadav PD, Shete AM, Sathe PS, Sarkale PC, Pattnaik B, et al. Cross-sectional serosurvey of Crimean-Congo hemorrhagic fever virus IgG in livestock, India, 2013–2014. Emerg Infect Dis. 2015; 21:1837–9.

12. Yadav PD, Patil DY, Shete AM, Kokate P, Goyal P, Jadhav S, et al. Nosocomial infection of CCHF among health care workers in Rajasthan, India. BMC Infect Dis. 2016; 16:624.

13. Yadav PD, Thacker S, Patil DY, Jain R, Mourya DT. Crimean-Congo Hemorrhagic Fever in Migrant Worker Returning from Oman to India, 2016. Emerging infectious diseases. 2017; 23 (6), 1005.

14. Mourya DT, Yadav PD, Gurav YK, Pardeshi PG, Shete AM, Jain R, et al. Crimean Congo hemorrhagic fever serosurvey in humans for identifying high-risk populations and high-risk areas in the endemic state of Gujarat, India. BMC infectious diseases. 2019; 19(1):1-8.

15. Sahay RR, Dhandore S, Yadav PD, Chauhan A, Bhatt L, Garg V, et al. Detection of African genotype in Hyalomma tick pools during Crimean Congo hemorrhagic fever outbreak, Rajasthan, India, 2019. Virus research. 2020; 286:198046.

16. Tripathi S, Bhati R, Gopalakrishnan M, Bohra GK, Tiwari S, Panda S, et al. Clinical profile and outcome of patients with Crimean Congo haemorrhagic fever: a hospital based observational study from Rajasthan, India. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2020; 114(9):650-6.

17. Mourya DT, Yadav PD, Patil DY, Sahay RR. Experiences of Indian Council of Medical Research with tick-borne zoonotic infections; Kyasanur Forest disease and Crimean Congo hemorrhagic fever in India with one health focus. Indian J Med Res. 2021; 153(3):339.

18. Hawman DW, Feldmann H. Crimean–Congo haemorrhagic fever virus. Nature Reviews Microbiology. 2023 Mar 14:1-5.

19. ClinicalTrials.gov. UMIT-1 Trial Favipiravir & Ribavirin for the Treatment of CCHF (UMIT-1). Available from: https://classic.clinicaltrials.gov/ct2/show/NCT05940545. Accessed on October 16, 2023

20. Mehla R, Kumar SR, Yadav PD, Barde PV, Yergolkar PN, Erickson BR, et al. Recent ancestry of Kyasanur Forest disease virus. Emerg Infect Dis. 2009; 15(9):1431-7.

21. Mourya DT, Yadav PD, Mehla R, Barde PV, Yergolkar PN, Kumar SR, et al. Diagnosis of Kyasanur forest disease by nested RT-PCR, real-time RT-PCR and IgM capture ELISA. J Virol Methods. 2012; 186(1-2):49-54.

22. Mourya DT, Yadav PD, Sandhya VK, Reddy S. Spread of Kyasanur Forest disease, Bandipur Tiger Reserve, India, 2012-2013. Emerg Infect Dis. 2013; 19(9):1540-1.

23. Kasabi GS, Murhekar MV, Yadav PD, Raghunandan R, Kiran SK, Sandhya VK, et al. Kyasanur Forest disease, India, 2011-2012. Emerg Infect Dis. 2013; 19(2):278-81.

24. Yadav PD, Shete AM, Patil DY, Sandhya VK, Prakash KS, Surgihalli R, et al. Outbreak of Kyasanur Forest disease in Thirthahalli, Karnataka, India, 2014. Int J Infect Dis. 2014; 26:132-4.

25. Murhekar MV, Kasabi GS, Mehendale SM, Mourya DT, Yadav PD, Tandale BV. On the transmission pattern of Kyasanur Forest disease (KFD) in India. Infect Dis Poverty. 2015; 4:37.

26. Tandale BV, Balakrishnan A, Yadav PD, Marja N, Mourya DT. New focus of Kyasanur Forest disease virus activity in a tribal area in Kerala, India, 2014. Infect Dis Poverty. 2015; 4:12.

27. Awate P, Yadav PD, Patil DY, Shete AM, Kumar V, Kore P, et al. Outbreak of Kyasanur Forest disease (monkey fever) in Sindhudurg, Maharashtra State, India, 2016. J Infect. 2016; 72(6):759-761.

28. Patil DY, Yadav PD, Shete AM, Nuchina J, Meti R, Bhattad D, et al. Occupational exposure of cashew nut workers to Kyasanur Forest disease in Goa, India. Int J Infect Dis. 2017; 61:67-69.

29. Sadanandane C, Gokhale MD, Elango A, Yadav PD, Mourya DT, Jambulingam P. Prevalence and spatial distribution of Ixodid tick populations in the forest fringes of Western Ghats reported with human cases of Kyasanur forest disease and monkey deaths in South India. Exp Appl Acarol. 2018; 75(1):135-142.

30. Munivenkatappa A, Sahay RR, Yadav PD, Viswanathan R, Mourya DT. Clinical & epidemiological significance of Kyasanur forest disease. Indian J Med Res. 2018; 148(2):145-150.

31. Yadav PD, Sahay RR, Mourya DT. Detection of Kyasanur forest disease in newer areas of Sindhudurg district of Maharashtra State. Indian J Med Res. 2018; 148(4):453-455.

32. Gurav YK, Yadav PD, Gokhale MD, Chiplunkar TR, Vishwanathan R, Patil DY, et al. Kyasanur Forest Disease Prevalence in Western Ghats Proven and Confirmed by Recent Outbreak in Maharashtra, India, 2016. Vector Borne Zoonotic Dis. 2018; 18(3):164-172.

33. Kasabi GS, Murhekar MV, Sandhya VK, Raghunandan R, Kiran SK, Channabasappa GH, et al. Coverage and effectiveness of Kyasanur forest disease (KFD) vaccine in Karnataka, South India, 2005–10. PLoS neglected tropical diseases. 2013; 7(1):e2025.

34. Yadav PD, Patil S, Jadhav SM, Nyayanit DA, Kumar V, Jain S, et al. Phylogeography of Kyasanur Forest Disease virus in India (1957–2017) reveals evolution and spread in the Western Ghats region. Scientific reports. 2020; 10(1):1966.

35. Sawatsky B, McAuley AJ, Holbrook MR, Bente DA. Comparative pathogenesis of Alkhumra hemorrhagic fever and Kyasanur forest disease viruses in a mouse model. PLoS neglected tropical diseases. 2014; 8(6):e2934.

36. Patil DR, Yadav PD, Shete A, Chaubal G, Mohandas S, Sahay RR, et al. Study of Kyasanur forest disease viremia, antibody kinetics, and virus infection in target organs of Macaca radiata. Sci Rep. 2020; 10(1):12561.

37. Chadha MS, Comer JA, Lowe L, Rota PA, Rollin PE, Bellini WJ, et al. Nipah-virus associated encephalitis outbreak, Siliguri, India. Emerg Infect Dis. 2006; 12(2):235–240.

38. Arankalle VA, Bandyopadhyay BT, Ramdasi AY, Jadi R, Patil DR, Rahman M, et al. Genomic characterization of Nipah virus, West Bengal, India. Emerg Infect. Dis. 2011; 17(5):907–909.

39. 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. Am J Trop Med Hyg. 2012; 87(3):576-8.

40. Arunkumar G, Chandni R, Mourya DT, Singh SK, Sadanandan R, Sudan P, et al. Outbreak Investigation of Nipah Virus Disease in Kerala, India, 2018. J Infect Dis. 2019; 219(12):1867-1878.

41. Yadav PD, Sudeep A, Gokhale M, Pawar S, Shete A, Patil DY, et al. Circulation of Nipah virus in Pteropus giganteus bats in northeast region of India, 2015. Indian J Med Res. 2018; 147(3):318-320.

42. Kumar CPG, Sugunan AP, Yadav PD, Kurup KK, Aarathee R, Murhekar MV et al. Infections among Contacts of Patients with Nipah Virus, India. Emerg Infect Dis. 2019; 25(5):1007-1010.

43. Mourya D, Yadav PD, Rout M, Pattnaik B, Shete A, Patil DY. Absence of Nipah virus antibodies in pigs in Mizoram State, North East India. Indian J Med Res. 2019; 149(5):677-679.

44. Yadav PD, Shete AM, Kumar GA, Sarkale P, Sahay RR, Radhakrishnan C, et al. Nipah Virus Sequences from Humans and Bats during Nipah Outbreak, Kerala, India, 2018. Emerg Infect Dis. 2019; 25(5):1003-1006.

45. Mourya DT, Yadav PD, Sudeep AB, Gokhale MD, Gupta N, Gangakhedkar RR, et al. Spatial Association Between a Nipah Virus Outbreak in India and Nipah Virus Infection in Pteropus Bats. Clin Infect Dis. 2019; 69(2):378-379.

46. Sahay RR, Yadav PD, Gupta N, Shete AM, Radhakrishnan C, Mohan G, et al. Experimental learnings from the Nipah virus outbreaks in Kerala towards containment of infectious public health emergencies in India. Epidemiol Infect. 2020; 148:e90.

47. Gokhale MD, Sreelekshmy M, Sudeep AB, Shete A, Jain R, Yadav PD. Detection of possible Nipah virus infection in Rousettus leschenaultii and Pipistrellus bats in Maharashtra, India. Journal of Infection and Public Health. 2021; 14(8): 1010-1012.

48. Sudeep AB, Yadav PD, Gokhale MD, Balasubramanian R, Gupta N, Shete A, et al. Detection of Nipah virus in Pteropus medius in 2019 outbreak from Ernakulam district, Kerala, India. BMC Infect Dis. 2021; 21(1):162.

49. Shete AM, Radhakrishnan C, Pardeshi PG, Yadav PD, Jain R, Sahay RR, et al. Antibody response in symptomatic & asymptomatic Nipah virus cases from Kerala, India. Indian Journal of Medical Research. 2021; 154(3):533-5.

50. Yadav PD, Majumdar T, Gupta N, Kumar MA, Shete A, Pardeshi P, et al. Standardization & validation of Truenat™ point-of-care test for rapid diagnosis of Nipah. The Indian Journal of Medical Research. 2021; 154(4):645.

51. Yadav PD, Sahay RR, Balakrishnan A, Mohandas S, Radhakrishnan C, Gokhale MD, et al. Nipah virus outbreak in Kerala State, India amidst of COVID-19 pandemic. Frontiers in Public Health. 2022; 10:14.

52. Gokhale M, Sudeep AB, Mathapati B, Balasubramanian R, Ullas PT, Mohandas S, et al. Serosurvey for Nipah virus in bat population of southern part of India. Comparative Immunology, Microbiology and Infectious Diseases. 2022; 85:101800.

53. Shete AM, Jain R, Mohandas S, Pardeshi P, Yadav PD, Gupta N, et al. Development of Nipah virus-specific IgM & IgG ELISA for screening human serum samples. The Indian Journal of Medical Research. 2022; 156(3):429.

54. Gupta N, Potdar V, Yadav PD, Patil DY, Sapkal GN. Preparedness of public health-care system for Zika virus outbreak: An Indian perspective. J Infect Public Health. 2020: 13(7): 949-955.

55. Malhotra B, Gupta V, Sharma P, Singh R, Sharma H, Vyas M, et al. Clinico-epidemiological and genomic profile of first Zika Virus outbreak in India at Jaipur city of Rajasthan state. J Infect Public Health. 2020; 13(2020) 1920-1926.

56. Yadav PD, Niyas VK, Arjun R, Sahay RR, Shete AM, Sapkal GN, et al. Detection of Zika virus disease in Thiruvananthapuram, Kerala, India 2021 during the second wave of COVID-19 pandemic. Journal of Medical Virology. 2022; 94(6):2346.

57. Gurav YK, Alagarasu K, Yadav PD, Sapkal G, Gokhale M, Parashar D, et al. First case of Zika virus infection during an outbreak of chikungunya in a rural region of Maharashtra state, India. Transactions of The Royal Society of Tropical Medicine and Hygiene. 2022; 116(10):974-7.

58. Yadav PD, Kaur H, Gupta N, Sahay RR, Sapkal GN, Shete AM, et al. Zika a vector borne disease detected in newer states of India amidst the COVID-19 pandemic. Frontiers in Microbiology. 2022:1852.

59. Markov PV, Ghafari M, Beer M, Lythgoe K, Simmonds P, Stilianakis NI, et al. The evolution of SARS-CoV-2. Nature Reviews Microbiology. 2023; 21(6):361-79.

60. Chua KB, Goh KJ, Wong KT, Kamarulzaman A, Tan PS, Ksiazek TG, et al. Fatal encephalitis due to Nipah virus among pig-farmers in Malaysia. Lancet. 1999; 354(9186):1257–1259.

61. Gavi. Seven things you need to know about Nipah virus. Available from: https://www.gavi.org/vaccineswork/seven-things-you-need-know-about-nipah-virus. Accessed on October 16, 2023.

62. World Health Organization. Nipah Virus Infection – India. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON490#:~:text=Between%2012%20and%2015%20September,the%20Kozhikode%20district%20of%20Kerala. Accessed on October 16, 2023.

63. CEPI. Targeting diseases with epidemic and pandemic potential. Available from: https://cepi.net/research_dev/priority-diseases/. Accessed on October 16, 2023.

64. Johnson K, Vu M, Freiberg AN. Recent advances in combating Nipah virus. Faculty Reviews. 2021;10.

65. de Wit E, Feldmann F, Cronin J, Goldin K, Mercado-Hernandez R, Williamson BN, Meade-White K, Okumura A, Callison J, Weatherman S, Rosenke R. Distinct VSV-based Nipah virus vaccines expressing either glycoprotein G or fusion protein F provide homologous and heterologous protection in a nonhuman primate model. EBioMedicine. 2023 Jan 1;87.