Review

Emerging and re-emerging viral infections in India

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Keywords

Nipah • KFD • CCHF • Zika • COVID-19

Summary

The number of outbreaks have progressively increased since many years in India. In this era of globalization and rapid international travel, any infectious disease in one country can become a potential threat to the entire globe. Outbreaks of Nipah, Zika, Crimean-Congo Haemorrhagic Fever and Kyasanur Forest Disease have been reported since a decade and now we are facing COVID-19 pandemic. One of the challenges in the prevention of these outbreaks is that as the cases decrease, the felt need declines, the public demand decreases and the mitigation responses get overshadowed by the need of emergency responses elsewhere. The One Health approach is a movement to promote alliance between medicine field, veterinary medicine and environmental sciences to upgrade the health of humans, animals, and ecosystem. The data in this article is compiled from different websites and publications of World Health Organization (WHO), Centre for Disease Control and Prevention (CDC), Integrated Disease Surveillance Programme (IDSP), grey literature and media. There is an urgent need for better surveillance and disease burden assessments in the country and to gain detailed insights into vector biology, factors of environment influencing the diseases, mapping of endemic areas, strengthen intersectoral coordination, infection control practices, and ensure use of Personal Protective Equipment's (PPE) and availability of drugs and vaccines to handle the outbreaks in a better way.

Introduction

Man is in a continuous battle with emerging and re-emerging diseases. In past, the incidence of these diseases in humans has increased and threatens to increase in future. The number of reported outbreaks have progressively increased from 553 in 2008 to 1,611 in 2018 [1] (Fig. 1).

Infectious diseases do not respect international borders. Especially in this era of globalization and rapid international travel, any infectious disease in one country can become a potential threat to the entire globe. India being a country with massive population and extreme geo-climatic diversity, faces a persistent threat of viral infections of public health importance.

The emerging diseases are threat to community as it increases morbidity and mortality and even increases bioterrorism potential. The categorization of bioterrorist agents have been done as A, B and C based on priority of agents posing risk and ease with which they can be disseminated [2].

One of the challenges in the prevention of outbreak is that as the cases decrease, the fear declines, the public demand decrease and the mitigation responses get overshadowed by the need of emergency responses elsewhere. And it is known that if a pathogen is not eliminated, it may become endemic. Low socio-economic status, impoverished environment, lack of affordability and accessibility all contribute towards risk of infectious disease outbreaks. Poor surveillance system and lack of understanding of the diverse epidemiological factors necessary for the emergence make control and prevention of these outbreaks challenging.

It has been almost a decade since the first PHEIC (Public Health Emergency of International Concern) was declared. WHO has declared six PHEIC till date-Swine flu in 2009, Polio in 2014, Ebola and Zika in 2016, Kivu Ebola in 2019 and the ongoing 2019-20 coronavirus pandemic [3, 4]. In the last decade, various viral diseases have had a serious health impact in India. The objective of the current narrative review is to explore the various characters of emerging infectious disease seen in recent past in India.

Methods

The current narrative article reviews some recent viral outbreaks that have occurred in India. The data is compiled from World Health Organization (WHO), Centre for Disease Control and Prevention (CDC), Integrated Disease Surveillance Programme (IDSP), grey literature and media. Two of the authors were engaged in writing the review article, two in conceptualizing and investigating the data and two in validation. Two of them were occupied in finding the resources and one author did the data curation (Tab. I). The database used are scopus, Pubmed and Google scholar.

NIPAH

The recent outbreak of Nipah in Kerala India had sent panic ripples across the world. Nipah virus outbreak was

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Fig. 1. Line graph showing number of reported outbreaks from 2008 to 2018 (source: IDSP, original to the manuscript).

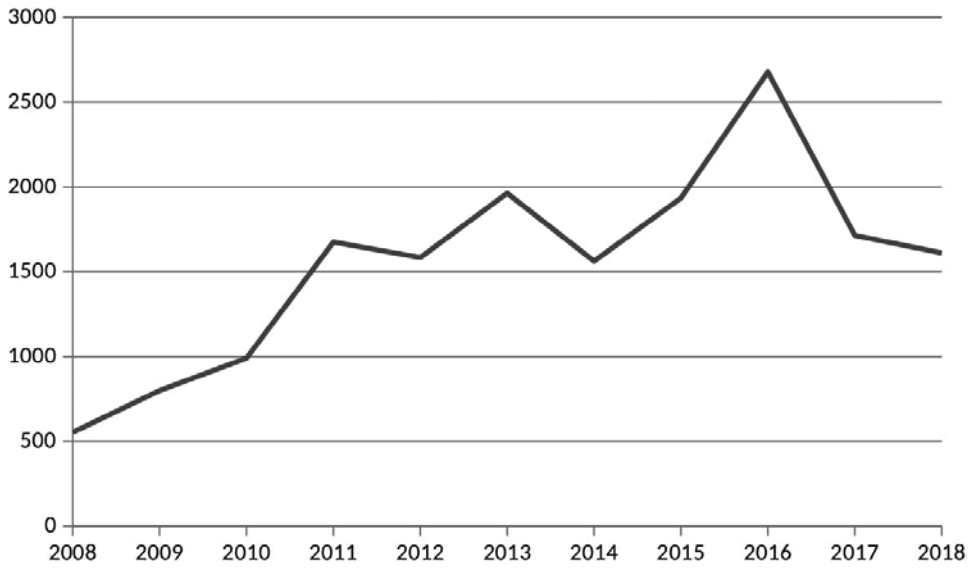
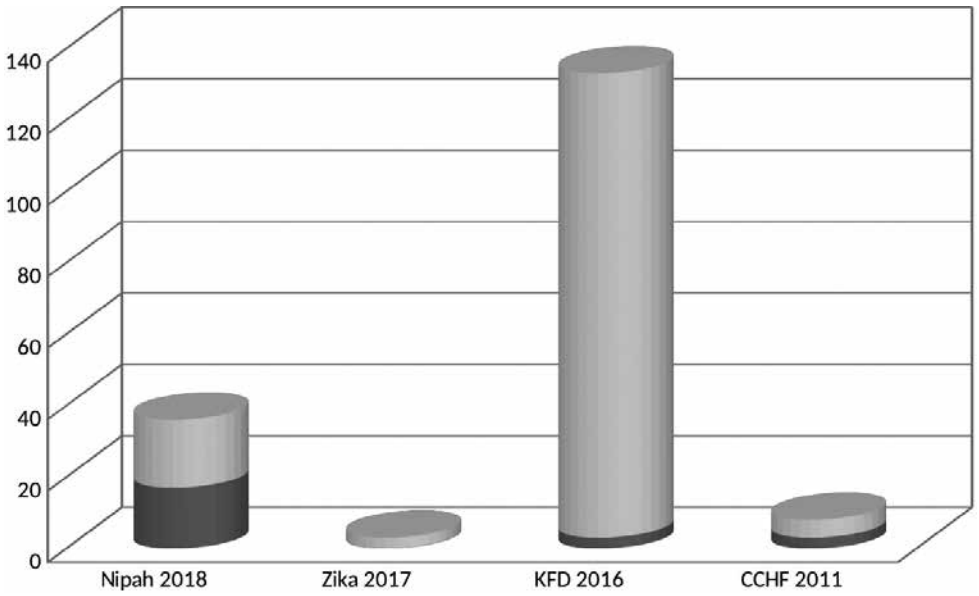


Fig. 2. Graph depicting cases confirmed and died in the reported outbreaks(source: IDSP, original to the manuscript).



reported on 17th July 2018 in Kozhikode and Malappuram districts of Kerala state. A total of 19 cases were seen of which 17 died [5] (Fig. 2).

The causative agent is Nipah virus (family Paramyxoviridae) and host being pigs and bats. Nipah virus emerged as a new virus 21 years ago i.e. in 1998 in Malaysia which caused morbidity and deaths and demolished the pig-farming industry in Malaysia. This virus caused outbreaks in Bangladesh and Siliguri, India in 2001 where bats of the Pteropodidae family were incriminated as potential reservoirs [6].

Nipah virus outbreak should be suspected in relevant epidemiological settings, considering history of travel or contact with pigs or bats in patients presenting with acute encephalitis. If an outbreak is suspected, the animal premises should be quarantined instantly.

Nipah is classified as category C of bioterrorism potential which includes emerging pathogens that could be engineered for mass dissemination, are easily produced and disseminated, and have capacity for high morbidity and mortality rates [7].

Tab. I. Details of some viral outbreaks in India.

	CCHF outbreak	KFD outbreak	Zika outbreak	Nipah virus outbreak	COVID-19 outbreak
Year and place of outbreak	2011, 2012, 2013 - Gujarat 2014 - Gujarat and Rajasthan 2015 - Gujarat, Rajasthan and Uttar Pradesh 2019 - Gujarat and Rajasthan	1957 - Karnataka 2012-2013 - Karnataka, Tamil Nadu, Kerala 2014 - Karnataka 2015 - North Goa 2016 - Maharashtra 2017 - Goa and Maharashtra	2017 - Gujarat	2001, 2007 - West Bengal 2018- Kerala	2019-2020 Asia (China, Japan, India, Malaysia, Thailand, Indonesia, South Korea and many other countries), Europe, Middle East, North Africa
Causative agent (family)	Nairovirus (Bunyaviridae)	KFD virus (Flaviviridae)	Zika virus (Flaviviridae)	Nipah virus (Paramyxoviridae)	Novel Corona virus (Coronaviridae)
Host	Range of domestic animals (cattle, sheep and goats)	Rodents, shrews, and monkeys	Monkeys and Humans	Pigs and bats	Most likely to be of zoonotic origin
Mode of transmission	Tick bite, human to human spread by contact with infectious blood or body fluids	Tick bite, contact with an infected animal, no person-to-person transmission	Bite of infected Aedes mosquito, from mother to fetus during pregnancy, through sexual contact, transfusion of blood and blood products	Direct contact with bodily fluids of infected bats or pigs, contaminated foods, directly from human-to-human through close contact with secretions and excretions	Person to person contact through small droplets from the nose or mouth which are spread when a person with COVID-19 coughs or exhales
Symptoms					
• General symptoms	Fever, chills, severe headache, sore eyes, neck pain, myalgia, arthralgia, petechial rash	High fever, frontal headache, , vomiting, muscle stiffness, tremors	Fever, rash, itching, headache, joint and muscle pain, lower back pain	Fever, headache, , resp. illness, myalgia, vomiting	Fever, difficulty in breathing tiredness, and dry cough aches and pains, nasal congestion, runny nose, sore throat, diarrhoea
• Haemorrhagic	+	+	-	-	-
• Ocular complications	Photophobia	Photophobia	Conjunctivitis	-	-
• Neurological complications	-	Encephalitis	Microcephaly	Encephalitis, drowsiness, mental confusion	-
Incubation period	Infection with tick bite: 1-3 days Infection with infected blood or tissue: 5-6 days	3 to 8 days	3 to 12 days	4 to 14 days	1 to 14 days
Case fatality rate	As per literature: 30-50% As per the outbreaks: 2011-66.6% 2012-50% 2013-38.8% 2014-75% 2015 (up to March) - 50%	As per literature: 3-5% As per the outbreaks: 1999 to 2017 - 2.42%	As per literature: 8.3% As per the outbreak: 2017-0%	As per literature: 40-75% As per the outbreaks: 2001-68% 2007-100% 2018-89%	Estimated to be 3-4% but exact CFR will require some time to be deciphered
High risk groups	Contact with livestock Agricultural workers Slaughterhouse workers Veterinarians	People living/working in and around forest areas of endemic regions	Travellers	Family and caregiver of Nipah virus infected patients	Older persons and persons with pre-existing medical conditions (such as high blood pressure, heart disease, lung disease, cancer or diabetes)

Tab. I. Details of some viral outbreaks in India.

	CCHF outbreak	KFD outbreak	Zika outbreak	Nipah virus outbreak	COVID-19 outbreak
Immuno prophylaxis	No	Yes (formalin inactivated tissue culture vaccine)	No	No	No
Vaccine efficacy	-	60-65%	-	-	-
Chemo Prophylaxis	No proven role of Ribavirin as chemoprophylaxis	No specific treatment	No specific treatment	No specific treatment	Hydroxy-chloroquine for high risk population
Biosafety level	Level 4	Level 4	Level 2	Level 4	Level 2
Classifi cation of infective microorganisms by risk group	Risk group 4	Risk group 4	Risk group 3	Risk group 4	Risk group 4
Critical steps in containment	Robust surveillance system Entomological studies undertaken Tick vector control measures Health education	Human, monkey and tick surveillance Awareness regarding use of PPE Vaccination campaigns Routine IEC activities Spraying of insecticides Inter-sectoral coordination	Robust surveillance system International airports and ports displayed information for travellers Inter-Ministerial Task Force set up Tracking for clustering of acute febrile illness in the community	House to house active case search and contact tracing Infection control protocol strengthened Isolation, quarantine medical camps for awareness	Country knockdown Cluster Containment Strategy Robust surveillance system House to house active case search and contact tracing Isolation, quarantine Travel advisories Buffer stock of Personal Protective Equipment (PPE) Inter-Ministerial coordination Expanding laboratory capacity Deployment of Rapid Response Teams (RRT)
One health concept applied	+	+	+	+	+

Source: IDSP, WHO, CDC, MOHFW.

ZIKA

The Zika outbreak has captivated a global audience. It is transmitted by mosquito vector and possibly by sexual transmission [8]. On 15th May 2017, Ministry of Health and Family Welfare reported 3 laboratory confirmed cases of Zika in Bapunagar, Ahmedabad, Gujarat [9] (Fig. 2).

Zika virus was first isolated in 1947 in Uganda from a rhesus macaque. The first outbreak of Zika virus disease has been reported from the Island of Yap, Western Pacific region of WHO in 2007. Zika is one of the four PHEIC and is unique as it is incriminated in causing congenital anomalies [10].

The agent is Zika virus *(family* Flaviviridae) and host are monkeys and humans. There is scientific agreement that the Zika virus can cause microcephaly, Guillain–Barré syndrome (GBS) and other congenital brain deformities [11]. In adult cases it is not severe but it can have an impact on foetal development and lead to severe neurodevelopmental abnormalities.

KYASANUR FOREST DISEASE (KFD)/ MONKEY FEVER

KFD was reported in 2016 in Sindhuburg, Maharashtra, India where 488 suspected cases, 130 confirmed cases and 3 deaths occurred [12] (Fig. 2).

It was first discovered in 1957 in Kyasanur forest of Shimoga district, Karnataka, India. KFD is a public health problem along the belts of Western Ghats of India. Deforestation results in occupation of shrubs which gives a favourable environment to rodents and birds. And these rodents act as hosts for the growing larvae and nymphs which increases hosts, reservoirs and vector interaction [13]. To control the tick population, forest floor is treated with gamma-hexachlorocyclohexane. Tick repellents like N, N-diethyl-meta-toluamide (DEET) and dimethyl phthalate (DMP) oil can be used to avoid tick bites. The first vaccine for this was made by Indian Council of Medical Research (ICMR) that is Russian spring-summer encephalitis virus (RSSEV) because of the nearly antigenic resemblance between KFD virus and RSSEV [14].

Karnataka state government is following KFD

vaccination policy in endemic areas. The vaccine is formalin inactivated tissue culture vaccine. It is recommended for age group of 5-75 years with a dose of 1ml for age above 6 years and 0.5 ml below 6. There are 3 scheduled doses at 0,1,6 months [15].

CRIMEAN-CONGO HAEMORRHAGIC FEVER (CCHF)

First case of CCHF in India was diagnosed in 2011 and again the disease re-emerged in 2019 in Gujarat and Rajasthan. 5 cases of the disease including 3 deaths in Gujarat were reported [16] (Fig. 2).

It was first described in Crimea in 1944. In 1956 the pathogen causing Crimean haemorrhagic fever was found to be the same as that responsible for an illness recognized in Congo, and so it was named as Crimean–Congo haemorrhagic fever [17]. It is a serious threat for community as well as for health workers mainly in countries with poor resources. CCHF and dengue share initial clinical features and so it is difficult to diagnose. The agent for CCHF is Nairovirus (family Bunyaviridae) and host being a range of domestic animals like cattle, sheep and goats. Patients with CCHF face bleeding from multiple sites as the disease progresses. Several case reports recommend that Ribavirin is effective for treating CCHF infections [18]. This is the only antiviral known to have some effect on the viruses causing viral haemorrhagic fever. Health care professionals should strictly follow barrier nursing care for undiagnosed haemorrhagic fever patients so that nosocomial transmission can be prevented [19]. Tick control measures should be used for the tick host and habitat. Insecticidal formulations like 0.5% Dichlorovos, 1% Carbaryl or 3-5% Malathion can be used on domestic animals to get free from ticks [20].

CHANDIPURA VIRUS

The epidemic of Chandipura virus started in June, 2003. In Andhra Pradesh, 329 children (9 months and 14 years) developed encephalitis, and the number of deaths were 183. The suffering children complained of vomiting, abdominal pain, symptoms like Japanese encephalitis virus. Chandipura virus was first isolated in 1965 in a village in Maharashtra, India. It is a member of family Rhabdoviridae and is transmitted by vectors such as mosquitoes, ticks and sand flies. There is no specific treatment available and symptomatic treatment is done [21].

JAPANESE ENCEPHALITIS

In Asia, the major cause of viral encephalitis is Japanese encephalitis virus. This flavivirus, is possessed by the same genus as dengue and yellow fever. The first case of Japanese encephalitis viral disease (JE) was registered in 1871 in Japan. As the vector population increases in rainy season, JE transmission becomes more intense. Approximately 1 in 250 cases results in severe clinical illness. Safe and effective JE vaccines are available to prevent this disease [22].

CORONAVIRUS DISEASE (COVID-19)

An unprecedented outbreak of Corona virus in Wuhan City, China emerged in December 2019. The second wave has also started in India in 2021. Hospital isolation of confirmed cases, contact tracing and home quarantine of contacts is ongoing [23, 24].

Discussion

To target the agent, host and environment triad in a better way, a concept named One Health approach arrived. The One Health approach is a movement to promote alliance between medicine field, veterinary medicine and environmental sciences to upgrade the health of humans, animals, and ecosystem. It is to educate and refine health outcomes. This concept of one health is for well being of human, animal and plants through a collaborative universal approach [25].

In November 2004 Integrated Disease Surveillance Project (IDSP) with financial help from World Bank commenced disease surveillance system for epidemic prone diseases to strengthen decentralized laboratory based Information Technology, to detect and respond to outbreaks in early phase with the help of Rapid Response Teams (RRTs). It presents weekly update on outbreaks in the country [26].

Diagnosis of these viruses is possible but is too expensive for a cost-effective commercial or routine use. VRC (Viral Research Centre) was redesignated as National Institute of Virology (NIV) Pune. It is identified today as WHO Collaborating Center for arboviruses and haemorrhagic fever reference. The centre studies about viral diseases, investigates outbreaks and provides diagnosis for viral diseases and development of indigenous diagnostic tests. Vaccination has played a crucial role in reducing morbidity and mortality from infectious diseases such as in case of Small pox. Vaccines are precious means to fight infections and even represents the much wanted achievement. But a vaccine takes time to come in public due to its side effects and manufacturing problems, lack of experimental animal models, faster developing, producing and licensing issues. Therefore a new or alternative approach in vaccine development is required to face pandemic situations [27].

The Department of Health Research (DHR), MOHFW, Government of India, in 2013 made a vision to establish and strengthen the network of laboratories across the country namely Viral Research and Diagnostic Laboratory Network (VRDLN). There is a network of about 100 laboratories in India with the objectives to create infrastructure and identify viruses, for capacity building, to develop diagnostics, trainings and meetings of health officials and professionals and for research [28].

The most essential aspects of prevention of viral outbreaks lies in surveillance of agent, host and environment. WHO since long has a mandate for promoting and supervising surveillance activities which has been emphasized further in recent times as evident from International Health Regulations (IHR) and pandemics of Public

Health Emergency of International Concern (PHEIC). An important limitation of the current review is that only the recorded data could be included in this review. There could be many other outbreaks which could have missed detection or underreported. Thus an essential recommendation is the need for a better surveillance and disease burden assessments in the country.

Conclusions

The past events strengthen the fact that infectious diseases will continue to emerge. If not controlled effectively, they will take a devastating toll on human life. There is an urgent need for better surveillance and disease burden assessments in the country. It is also required to gain detailed insights into vector biology, environmental factors, mapping of endemic areas, strengthen intersectoral coordination, infection control practices, and ensure use of Personal Protective Equipment's (PPE) and availability of drugs and vaccines to handle the outbreaks in a better way [29].

Ethics

Ethics permission from IEC committee of the institution AIIMS Jodhpur was not sort as it is a review article and secondary data is used.

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Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

Mamta Patel: Writing- Original draft preparation. Akhil Dhanesh Goel: Writing, supervision. Pankaj Bhardwaj: Validation, visualization. Nitin Joshi: Conceptualizing. Nitesh Kumar: Conceptualizing, finding resources. Manoj Kumar Gupta: Validation, investigating data. Vidhi Jain: Finding resources, investigating data, Suman Saurabh: Data curation. Kamlesh Patel: Investigating data.

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