Journal of Pharmaceutical Research International

33(10): 82-93, 2021; Article no.JPRI.65362
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Novel and Re-emerging Zoonotic Viral Diseases in India during Last Two Decades: An Overview

Priyanka Venugopal[1], Damal Kandadai Sriram[2] and Melvin George[1*]

[1]Clinical Research, Hindu Mission Hospital, 103, GST Road, West Tambaram, Chennai-600045, India.
[2]Diabetology and Endocrinology, Hindu Mission Hospital, 103, GST Road, West Tambaram, Chennai-600045, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author PV designed the concept, managed the literature searches and wrote the manuscript. Author DKS supervised and approved the manuscript. Author MG designed the concept of the manuscript supervised and approved the final manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i1031236
Editor(s):
(1) Dr. Sawadogo Wamtinga Richard, Scientific Research and Innovation, Burkina Faso.
(2) Dr. Paola Angelini, University of Perugia, Italy.
(3) Dr. Alyautdin Renad N, Scientific Centre for Expert Evaluation of Medicinal Products, Russia.
Reviewers:
(1) Rakesh Yonzone, Ubkv,India.
(2) Lucinda Choules, USA.
(3) Abu Hasan Sarkar, Tomo Riba Institute of Health and Medical Sciences (TRIHMS), India.
(4) Ehsan Gharib mombeni, Shahid Chamran University of Ahvaz, Iran.
(5) Nezihe GÖKHAN, Malatya Turgut Özal University, Turkey.
Complete Peer review History: http://www.sdiarticle4.com/review-history/65362

Mini-review Article

Received 08 December 2020
Accepted 12 February 2021
Published 13 March 2021

ABSTRACT

Zoonotic diseases or zoonosis is an infectious disease caused by the transmission of pathogens from animals to humans. Depending on the pathogens, these diseases can be bacterial, viral, or parasitic and the route of transmission of the pathogens can be via reservoirs including birds, bats, pigs, and mosquitoes, eventually infecting humans. Spread among humans arises primarily through person-person contact and fomites, causing major outbreaks (epidemics and pandemics). Some of the major zoonotic outbreaks include plague, influenza, West Nile fever, brucellosis, and rabies. This review focuses on zoonotic viral outbreaks in India over the past 20 years highlighting the spread and severity of the disease, measures to control the infection and prevention, treatment and management of the infectious diseases. New or emerging and re-emerging viral diseases such as

**Corresponding author: E-mail: drmelvingeorge@hindumissionhospital.org;*

coronavirus, Japanese encephalitis, dengue and chikungunya are discussed. These outbreaks have been reported to cause high morbidity and mortality, in addition, pose a major risk to the health security, safety, and economy of the country. Insufficient knowledge of emerging diseases is a major challenge for producing effective anti-viral drugs and vaccines. Understanding the etiology and spread of the disease is essential for preventive measures and the development of efficient treatment strategies.

Keywords: Zoonoses; vaccines; viruses; mortality.

1. INTRODUCTION

Zoonotic diseases, also known as “zoonoses”, as simply defined by the Centers for Disease Control and Prevention (CDC), are caused by germs that spread among animals and people. Transmission of these harmful germs/microorganisms like viruses, bacteria, fungi, or parasites can cause various illnesses, ranging from mild to severe including fatalities in susceptible humans. Transmission can occur via direct/indirect contact, vector-borne, food-borne, or water-borne. Infectious diseases of zoonotic origin pose a greater danger to public health, security and economic growth, causing major epidemics or pandemics and withstanding their emergence is a priority. However, the mechanism by which they originate is still unexplored. This review focuses on zoonotic viral disease outbreaks in the last 20 years in India, from the perspective of the route of transmission of pathogens and a special mention on the most recent outbreaks such as Nipah, Zika, and (Severe Acute Respiratory Syndrome Coronavirus 2) SARS-COV-2 viruses.

2. HISTORY OF VIRAL EPIDEMICS AND PANDEMICS IN INDIA OVER THE PAST 2 DECADES

India has and continues to witness various outbreaks, affecting public health, security, and the economy. The timeline for the various viral outbreaks in the last 20 years is represented in Fig. 1. These outbreaks are classified as emerging and re-emerging viral infections. The new or emerging diseases pose a major threat to society due to the lack of knowledge about their origin, etiology, and epidemiology. Some examples include Nipah and Zika virus. Re-emerging diseases are those which recur at a later period after an epidemic has been controlled or declined. The reappearance may be due to a collapse in the health care management or development of new strains or mutations in the strains of the causative pathogens. Dengue and Chikungunya are examples of such re-emerging zoonotic viral diseases [1]. Among the Nine (9) zoonotic diseases highlighted in this review, except for SARS and SARS-CoV2, all the outbreaks were categorized as re-emerging diseases.

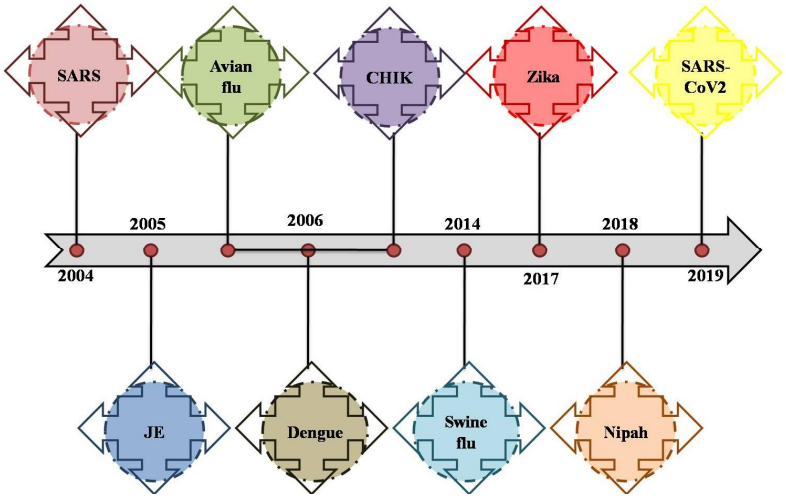

Fig. 1. Timeline for viral epidemics and pandemics in India in the past 20 years

Zoonotic spillover or zoonoses is referred to the transmission of a pathogen from a vertebrate animal to a human [2]. This process is controlled by important factors such as environment, pathogen, and host. A disease outbreak (epidemic or pandemic) arises as a result of human-human transmission, following zoonotic spillover. Moreover, the transmission cycle can be of bat origin, vector-borne, birds' origin and airborne. The route of transmission of all 9 viral diseases is illustrated in Fig. 2.

3. VECTOR-BORNE DISEASE

3.1 Japanese Encephalitis

Japanese encephalitis is a vector-borne viral disease caused by the Japanese Encephalitis Virus (JEV). It was first reported in 1955 in south India with an estimated 65 cases. Thereafter, from 1978 till 2007, the outbreak was reported in Gorakhpur, Uttar Pradesh, India. In 2007, an estimated 1,03,389 cases were reported throughout the country, out of which 33729 deaths were also observed [3]. It was the longest and most severe outbreak in 30 years [4]. It is transmitted by varying species of the *Culex* mosquitoes breeding in the immediate vicinity with pigs, ducks, and bats, eventually affecting humans in the rural areas. The disease symptoms include fever, diarrhea, vomiting, and weakness, and in some cases seizures and tremors [5]. Fig. 3 illustrates the JEV disease statistics reported from 2010 till August 2020.

3.2 Dengue

Dengue is a vector-borne disease caused by *Aedes* mosquitoes and belonging to the *Flaviviridae* family. About 100 million new cases are reported every year globally. Over the past 4 decades, dengue fever outbreaks have been reported in many different parts of India. The first epidemic in India was reported in Madras(1780) and in the East-coast of India(1963-1964) [6]. A huge outbreak occurred in 2003 which reported 12,754 confirmed cases and 215 deaths [7]. The epidemic during the period 2006-2012 reported 20,474 cases and 132 deaths. Symptoms include fever, headache, rash, muscle and joint pain and in severe cases Haemorrhagic Fever and Shock Syndrome (DHF and DSS). The statistics of dengue over the last decade in India is represented in Fig. 4.

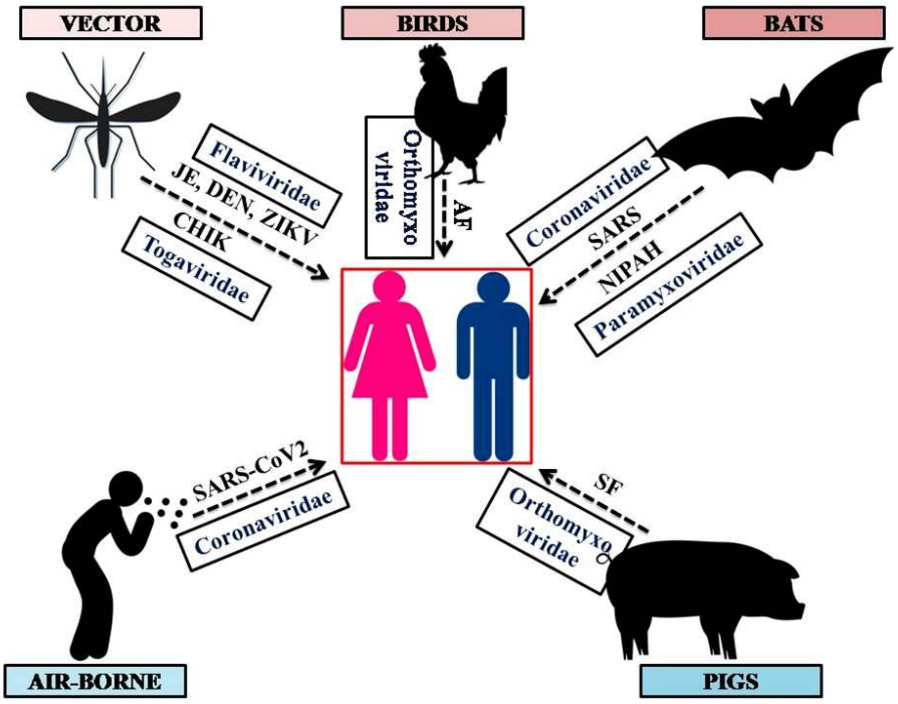

Fig. 2. Transmission of zoonotic viral diseases

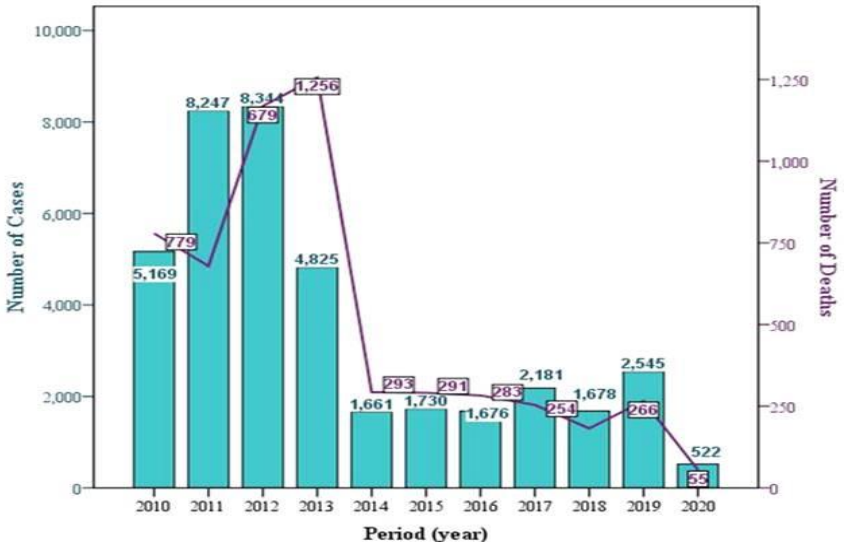

Fig. 3. Number of confirmed cases and deaths for Japanese encephalitis from 2010 till august 2020 (National Vector Borne Disease Control Programme database) in India

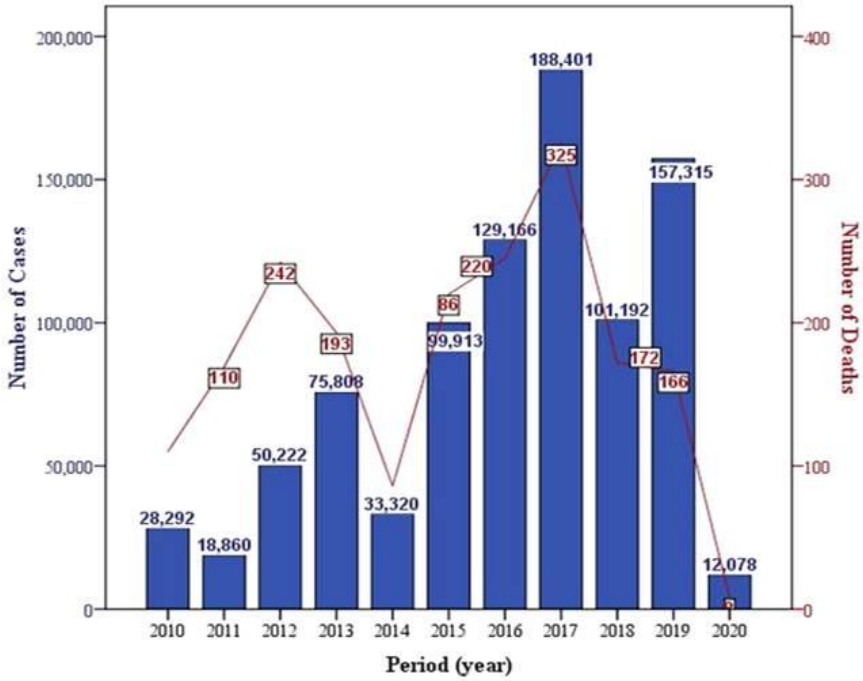

Fig. 4. Dengue disease statistics expressing number of confirmed cases and deaths in the last 10 years in India, obtained from the National Vector Borne Disease Control Programme database

3.3 Chikungunya

Chikungunya is a re-emerging viral disease that first occurred in India in 1973; however, the major outbreak happened in 2006, where the affected rate increased from 37.5% to 45%. During this period, around 1.39 million people were affected in over 10 states in India [8]. Major outbreaks of Chikungunya fever have been reported in various parts of South India [9-11]

and about 1.8 lakh cases have been reported since December 2005, where Andhra Pradesh was the first and one of the worst affected states in south India with an estimated 80,000 cases. Chikungunya is a vector-borne disease transmitted to humans by the bite of infected *A. aegypti* mosquitoes, causing symptoms similar to the dengue virus. These include sudden onset of fever, chills, joint pain with or without swelling, rashes, headache, vomiting, and muscle weakness [12]. Large numbers of cases are reported annually in different parts of India, however, to date there have been no deaths recorded that were directly caused by the Chikungunya virus. Fig. 5 illustrates the confirmed Chikungunya cases from 2010 till July 2020 reported in India, according to the National Vector Borne Disease Control Programme (NVBDCP) database.

3.4 Zika Virus

Zika virus infection (ZIKV) is a vector-borne disease caused by the bite infected of *Aedes* mosquito. Other non-vector modes of transmission include sexual intercourse, trans-placental route, breast milk, and blood transfusion [13,14]. The incubation period of the virus was found to be 3 to 12 days. The first case of ZIKV was reported in Nigeria in 1954, followed by sporadic cases in other parts of Africa in the next 3 decades. The first major ZIKV outbreak occurred in 2007 in Yap Island, followed by French Polynesia and Brazil in 2013-2014 and 2015-2016, respectively. India reported 4 cases in 2016-2017 from Gujarat and Tamil Nadu. The outbreak returned in 2018 in Rajasthan and Madhya Pradesh [15]. According to the National Centre for Disease Control, 157 confirmed cases were reported as of November 2018. ZIKV infection has also been reported in 63 pregnant women, causing congenital birth defects in the fetus. ZIKV is often misdiagnosed for dengue and chikungunya due to their similarities, as they all belong to the family of *Flaviviridae* [16,17]. The symptoms include low-grade fever, headache, muscle and joint pain, nausea, vomiting, and general malaise. However, the distinguishing features of this illness comprise pink eye or inflammation of the conjunctiva, a skin rash with red spots on the face, neck, trunk, and upper arms which can spread to the palms or soles, and sensitivity to light [18]. ZIKV has been reported to be a major public health issue due to two associated dreaded complications, namely, Guillain-Barre Syndrome (GBS) and congenital defects such as microcephaly [19-24]. ZIKV associated GBS and microcephaly was reported in outbreaks of French Polynesia (2014) and Brazil (2015), respectively. However, during the outbreak in India, the associated complications were not observed in any ZIKV affected patients [18].

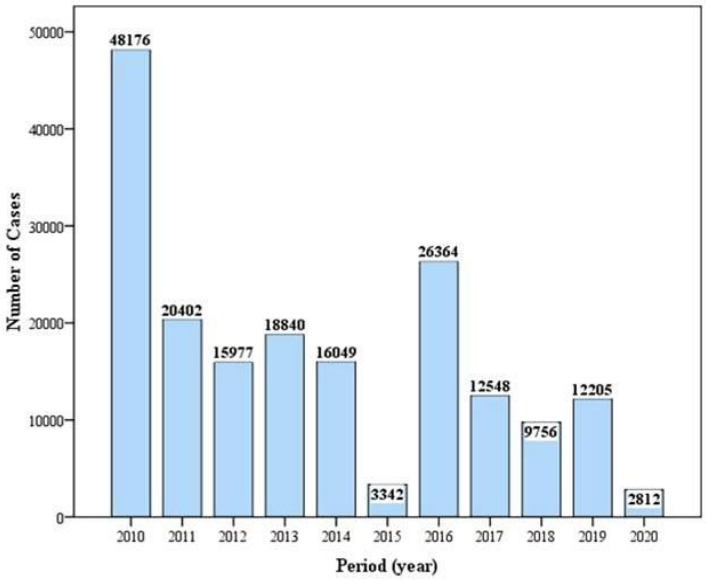

Fig. 5. Chikungunya virus infection statistics in India from 2010 till july 2020, according to National Vector Borne Disease Control Programme database

4. BIRDS

4.1 Avian Flu

Bird flu or avian influenza (H5N1) is caused by influenza type A virus which was first reported in Italy centuries ago. Wild aquatic birds such as ducks and geese are infected by the virus, which is present in their saliva, feces, and mucus, spread easily between birds. Poultry or domestic birds such as chickens and turkeys are more susceptible to these infections causing rapid spread of the virus, eventually resulting in epidemics. The spread of the virus from birds to humans is via direct contact, contaminated surfaces or inhalation. The severity of the disease can range from mild illness to highly communicable and fatal, hence, these are referred to as "highly pathogenic avian influenza" (HPAI) virus [25]. H5N1 outbreak in India affected 14 states since 2006, predominantly in Eastern and North-Eastern states of India [26].

5. BATS

5.1 Severe Acquired Respiratory Syndrome (SARS)

An outbreak of this respiratory illness started in Guangdong, China, characterized by a severe form of pneumonia caused by typical or mostly, atypical organisms. The disease spread rapidly among household and healthcare providers, crossing boundaries and affecting about 8098 people across various parts of China, Singapore, Canada, Vietnam, the United States of America, and the UK from November 2002 to July 2003 [27]. Moreover, in India, W.H.O reported a total of 3 probable SARS cases, one each from West Bengal, Karnataka, and Gujarat during that period. Tamil Nadu reported only 1 probable case of SARS in 2003 [28]. SARS infection is characterized by influenza-like symptoms for 3-7 days (after an asymptomatic period of 4-7days) which comprises fever, malaise, headache, chills, anorexia, and fatigue [27]. The transmission of the virus was reported via bats to civets and then to humans, with the first infected human reported in Guangdong province, South China (2002) [29].

5.2 Nipah Virus

Nipah virus (NiV) is one of the emerging zoonotic viral diseases, belonging to the family of Paramyxoviridae. The outbreak was first reported in West Bengal, India, in 2001 and again in 2007. The third outbreak occurred on 19th May 2018 in Kozhikode, Kerala, India. Fig. 6 illustrates the resurgence of the outbreak in India. The outbreak was localized between the Kozhikode and Malappuram districts of Kerala. A total of 18 confirmed cases and 17 deaths were reported in Kerala as of 17th July 2018. The virus was transmitted via fruit bats belonging to Pteropus, which was then passed on to pigs and humans. The incubation period of the virus in humans was 6 to 14 days. The outbreak was found to be associated with the ingestion of fresh date palm sap contaminated by infected fruit bats. Symptoms of the infection included high-grade fever, shortness of breath or respiratory distress syndrome, altered sensorium, myalgia, headache, vomiting, cough, and seizures.
Moreover, the virus caused encephalitis and pneumonia, thereby leading to coma or even death in infected individuals [30]. The outbreak was brought under control by the end of July 2018. [31]. The health measures adopted for containing the infection included isolation of infected individuals, contact tracing, and implementation of infection control practices in hospitals [32].

6. SARS-COV2

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as COVID-19 as the name suggests was first reported in December 2019 in Wuhan city, China. The disease then widely spread to other parts of the country [33]. The first case of COVID-19 in India was reported on 30th January 2020 in Kerala, a medical student who had traveled from Wuhan, China, which then spread to other parts of the country such as Mumbai, New Delhi, Chennai, Karnataka, and Andhra Pradesh. Later, on 11th March 2020, W.H.O declared the disease as a pandemic. Transmission of the disease is primarily via direct person-person contact, through fomites and droplets of respiratory secretions from the infected person. The incubation period of the virus ranges from 1 to 14 days. Shedding of the virus in pre-symptomatic individuals during the incubation period has also been reported as a possible route of transmission in some cases [34,35]. Initial symptoms include fever, cough, and shortness of breath, followed by saturation of oxygen in the blood (93%) and above 50% lung infiltrates within 24-48 hours for severe cases and in geriatric patients with pre-existing chronic systemic illness.

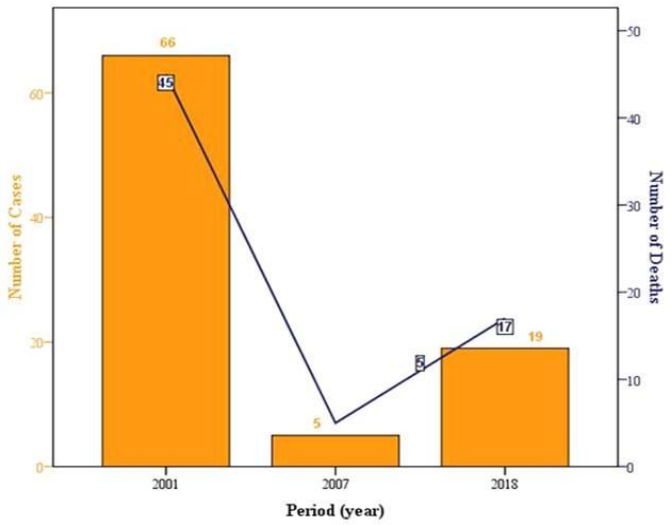

Fig. 6. Resurgence of Nipah virus outbreak in India

A total of 67, 57,131 confirmed cases and 1,04,555 deaths have been reported in India as of October 2020. The number of cases/day reached the peak on 17th September 2020 with 97,894 cases marking the largest single-day record in the world. Individuals who are ≥70 years of age and/or those with co-morbidities such as respiratory illness, cardiovascular disease, diabetes, and cancer are at high risk of COVID-19. Moreover, these risk factors increase the severity of the disease and risk of death [36]. The government has implemented strict regulations including social distancing, lockdown, and frequent hand sanitization in order to contain the spread of the virus. There are no specific treatments or drugs identified yet for this disease, however, circumstantially certain drugs are being used at present for treating the disease, namely, Hydroxychloroquine, Chloroquine, Remdesivir, and so on [37,38].

7. PIGS

7.1 Swine Flu

Swine flu or H1N1 is a common infection that affects pigs throughout the world. People working in pig farms or those who come in close proximity with the infected pigs usually develop H1N1 [39]. The disease broke out first in April 2009 in Mexico and then spread throughout the world, [40,41] causing respiratory distress ranging from mild flu symptoms to severe pneumonia, bronchitis, and death [42]. By June 2009, the outbreak had spread across 74 countries affecting 30,000 people globally [43]. The first case in India was reported in May 2009 in Hyderabad and the outbreak caused 981 deaths in 2009 and 1763 deaths in 2010 [42].

The pandemic affected over 214 countries globally, reaching the post-pandemic stage on August 10, 2010 [5]. This was followed by a decline in the disease activity across the six W.H.O member states, especially in India where the deaths had reduced to 75 in 2011 [43]. Meanwhile, a rapid increase in mortality was observed in 2012 and 2013, with 405 and 699 deaths, respectively. India recorded 837 confirmed cases and 218 deaths in 2014. As the temperature was found to affect the virus, a higher number of cases and deaths were reported in the winter season every year, particularly during the 2015 winter. An epidemic was declared in Rajasthan on 12th February 2015 [44].

8. CASE FATALITY RATIO FOR ZOONOTIC DISEASES

It has been reported that infectious diseases pose a major risk to health security and about 15.8% of all deaths worldwide are caused by infectious diseases. In addition, they account for 43.7% of deaths in low-income countries [45]. These infectious diseases are predominantly zoonotic in origin and most of the emerging or new and re-emerging zoonotic diseases had lead to major outbreaks globally [46]. According to the Centers for Disease Control and Prevention

(CDC), the case-fatality ratio (CFR), also known as the case-fatality rate is defined as the proportion of cause-specific deaths among incident cases. CFR is a measure of the severity of an existing condition or disease. Of the 9 zoonotic viral diseases discussed in this review, globally, the highest CFR was estimated for avian flu and Nipah virus disease and the lowest CFR was estimated for swine flu, dengue, and SARS-CoV2. Table 1 represents the CFR for the 9 zoonotic infections. CFR was not reported for chikungunya and Zika virus disease as disease-specific deaths have not been reported.

9. PREVENTION OR CONTROL OF EMERGING AND RE-EMERGING VIRAL DISEASES

Zoonotic diseases, particularly re-emerging diseases have significant damaging effects on public health, economy, security, and stability globally [47]. In order to take control of such outbreaks, the development of vaccines is critical, wherein they reduce morbidity and mortality, eventually eradicating the disease [48]. However, until effective and safe vaccines are developed, other measures including social distancing, quarantine, and anti-viral drugs are recommended in order to reduce the spread of the disease. Anti-viral medications prescribed treatment for viral diseases, although effective in treating the disease (inhibiting the development of virus) but not eradicating them. Anti-viral drugs including ribavirin, Remdesvir and Zanamivir are prescribed for SARS, SARS-CoV2, and swine flu, respectively [38]. For the remaining diseases, fluids and pain relievers such as acetaminophen are provided as treatment, as there are no FDA approved antiviral medications yet. Table 2 lists the anti-viral drugs approved by FDA and provided as treatment for zoonotic viral infections, as well as drugs under investigation. Vaccines are under development in pre-clinical and phase I-III clinical trials for all the viral diseases, except chikungunya and avian flu virus, as the former is short-lived and rarely fatal, whereas the latter has not been reported in humans in India. Table 3 describes the list of vaccines approved by the FDA and those in various phases of clinical trials. Vaccines in phase III trials are listed for SARS-CoV2, whereas for the remaining diseases only those in phase I and II trials are listed as no vaccines have progressed to phase III trials.

10. CHALLENGES FOR VACCINE DEVELOPMENT

Over the past 2 decades, emerging and re-emerging outbreaks have occurred in India, affecting public health, safety, and the economy. Some major outbreaks have caused significantly high mortality, thereby demanding the development of vaccines to limit the spread of the infections. Vaccines are particularly essential for diseases where alternative treatment options do not exist. Understanding the immune response to the pathogen is the most critical part of vaccine development. Another major challenge is the lack of basic biological information including antigenic variability and lack of an appropriate antigen delivery system. Extensive pre-clinical and clinical research is required to gain detailed knowledge on the replication and pathogenesis of the virus to help minimize the challenges. The most predominant challenge, however, is the decline in incident cases, for example, Nipah and Zika infections. Preventing zoonotic spillover of pathogens to humans may help in containing the virus within the wild-life reservoir, thereby reducing the spread. This can be achieved using self-disseminating vaccines [49].

Table 1. Global case fatality ratio for the zoonotic viral diseases

Virus	Case fatality ratio
SARS	14-15%
Japanese encephalitis	30%
Avian flu	60%
Dengue	2-5%
Chikungunya	No direct deaths reported
Swine flu	1-4%
Zika	No direct deaths reported
Nipah	40-75%
SARS-CoV2	2.76%

Table 2. Antiviral medications for the zoonotic diseases approved by FDA and under investigation

Virus	FDA approved drugs	Clinical trials
SARS	Ribavirin	Lopinavir+Ritonivir Methylprednisolone Alferon (low dose oral)
Japanese encephalitis	No approved anti-viral drugs	IV-immunoglobulin (IVIG)
Avian flu	Oseltamivir (Tamiflu) Zanamivir (Relenza)	Peramivir
Dengue	No approved anti-viral drugs	Ivermectin Celgosvir Balapiravir
Chikungunya	No approved anti-viral drugs	Methotrexate
Swine flu	Oseltamivir (Tamiflu) Zanamivir (Relenza)	Peramivir
Zika	No approved anti-viral drugs	Tyzivumab ZIKV-IG (IV)
Nipah	No approved anti-viral drugs	Ribavirin
SARS-CoV2	Remdesivir	Lopinavir/Ritonivir+Hydroxychloroquine Ivermectin+Doxycyclin Hydroxychloroquine+Azithromycin Favipiravir Nitazoxanide+Ribavirin+Ivermectin

Table 3. Vaccines approved and under clinical trials for the zoonotic viral diseases

Virus	FDA approved vaccines	Clinical trials
SARS	No approved vaccines	VRC-SRSDNA015-00-VP
Japanese encephalitis	Ixiaro, JE-VAX, IMOJEV	Live attenuated SA 14-14-2
Avian flu	Fluzone	Orniflu IVACFLU-A/H5N1 VAX161C
Dengue	Dengvaxia	Vaxfectin
Chikungunya	No approved vaccines	MV-CHIK CHIK001
Swine flu	No approved vaccines	Cell-derived A/HA vaccine CR6261 FLU-IGIV ASO3
Zika	No approved vaccines	ZPIV ZikaVac VRC705 VLA1601
Nipah	No approved vaccines	HeV-SG-V NIPARAB
SARS-CoV2	No approved vaccines	Gam-COVID-Vac CoronaVac RUTI vaccine BCG vaccine Ad5nCoV AZD1222 mRNA-1273

11. CONCLUSION

This review article highlights the importance of understanding emerging and re-emerging zoonotic viral disease outbreaks in India, threatening the socio-economical and health security of the country. Understanding the epidemiology of the viruses to identify candidate zoonotic reservoirs and routes of transmission are critical. Extensive, precise, and timely measures have to be taken to avoid novel and re-emerging diseases.

CONSENT

It's not applicable.

ETHICAL APPROVAL

It's not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kumar S, Swain S, Preetha GS, Singh BS, Aggarwal D. Zoonotic diseases in India. Indian J Community Med. 2020;45(Suppl 1):S1.
2. Plowright RK, Parrish CR, McCallum H, et al. Pathways to zoonotic spillover. Nat Rev Microbiol. 2017;15(8):502- 10.
3. Tiwari S, Singh RK, Tiwari R, Dhole TN. Japanese encephalitis: A review of the Indian perspective. Braz J Infect Dis. 2012;16(6):564-73.
4. Parida M, Dash PK, Tripathi NK. Japanese encephalitis outbreak, India, 2005. Emerg Infect Dis. 2006;12(9):1427.
5. Kulkarni R, Sapkal GN, Kaushal H, Mourya DT. Japanese encephalitis: A brief review on Indian perspectives. Open Virol J. 2018;12:121.
6. Gupta N, Srivastava S, Jain A, Chaturvedi U. Dengue in India. Indian J Med Res. 2012;136(3):373-90.
7. Singh B. Dengue outbreak in 2006: Failure of public health system? Indian J Community Med. 2007;32(2): 99.
8. Mavalankar D, Shastri P, Bandyopadhyay T, Parmar J, Ramani KV. Increased mortality rate associated with chikungunya epidemic, Ahmedabad, India. Emerging infectious diseases. 2008;14(3):412.
9. Enserink M. Massive outbreak draws fresh attention to little-known virus. Science 2006;311:1085.
10. CDC. Chikungunya Fever in India. Travelers' Health Outbreak Notice April 21; 2006.
Available:http://www.cdc.gov/travel
11. Chikungunya and Dengue in the South West Indian Ocean. Epidemic and Pandemic Alert and Response (EPR); 2006
Available:http://www.who.int/csr/don/2006
12. Ravi V. Re-emergence of chikungunya virus in India. Indian J Med Microbiol. 2006;24(2):83.
13. Foy BD, Kobylinski KC, Chilson Foy JL, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis. 2011;17(5):880-2.
14. Besnard M, Lastere S, Teissier A, Cao-Lormeau V, Musso D. Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. Euro Surveill. 2014;19(13).
15. Singh R, Gupta V, Malhotra B, et al. Cluster containment strategy: Addressing zika virus outbreak in Rajasthan, India. BMJ Glob Health. 2019;4(5):e001383.
16. Faye O, Freire CCM, Iamarino A, et al. Molecular evolution of ZiV during Its emergence in the 20th century. PLoS Negl Trop Dis. 2014;8:e2636.
17. Kuno G, Chang GJ, Tsuchiya R, Karabatsos N, Cropp BC. Phylogeny of the genus Flavivirus. J Virol. 1998;72:73–83.
18. Gupta N, Kodan P, Baruah K, Soneja M, Biswas A. Zika virus in India: Past, present and future. QJM; 2019.
19. Shanshan Wu, Yu Zeng, Alexander Lerner, Bo Gao, Meng Law. Nervous system injury and neuroimaging of zika virus infection. Front Neurol. 2018;9:227.
20. Souza BS, Sampaio GL, Pereira CS, et al. Zika virus infection induces mitosis abnormalities and apoptotic cell death of human neural progenitor cells. Sci Rep. 2016; 6:39775.
21. Garcez PP, Nascimento JM, de Vasconcelos JM, Madeiro da Costa R, Delvecchio R, Trindade P. Zika virus disrupts molecular fingerprinting of human neurospheres. Sci Rep. 2017;7:40780.
22. Jampol LM, Goldstein DA. Zika virus infection and the eye. JAMA Ophthalmol. 2016:1–8.

23. Ventura CV, Maia M, Bravo-Filho V, Góis AL, Belfort R. Zika virus in Brazil and macular atrophy in a child with microcephaly. Lancet. 2016;387:228.
24. Zin AA, Tsui I, Rossetto J, et al. Screening criteria for ophthalmic manifestations of congenital Zika virus infection. JAMA Pediatr. 2017;171(9):847-54.
25. Broor S. Recent avian influenza outbreaks: A pandemic in the waiting. Indian J Med Microbiol. 2005;23(2):72.
26. Sridevi R, Krishnamoorthy P, Suresh KP and Rahman H. Epidemiology of avian influenza in India. J Vet Sci Technol. 2014.
27. Mehta SR, Sashindran VK, Kumar K, Gupta A. Severe acute respiratory syndrome: An update. Med J Armed Forces India. 2007;63(1):52-5.
28. Agarwal SP. Severe acute respiratory syndrome (SARS): An opportunity to improve public health systems. Natl Med J India. 2003;16(4):183-185.
29. SARS (Severe Acute Respiratory Syndrome) [Internet]. World Health Organization. World Health Organization; 2012.
Available:https://www.who.int/ith/diseases/sars/en/
30. Goh KJ, Tan CT, Chew NK, et al. Clinical features of Nipah virus encephalitis among pig farmers in Malaysia. N Engl J Med. 2000;342(17):1229-35.
31. Thomas B, Chandran P, Lilabi MP, et al. Nipah virus infection in Kozhikode, Kerala, South India, in 2018: Epidemiology of an outbreak of an emerging disease. Indian J Community Med. 2019;44(4):383.
32. Arunkumar G, Chandni R, Mourya DT, Singh SK, Sadanandan R, Sudan P, Bhargava B. Outbreak investigation of Nipah virus disease in Kerala, India, 2018. J Infect Dis. 2019;219(12):1867-78.
33. Kumar SU, Kumar DT, Christopher BP, Doss C. The Rise and Impact of COVID-19 in India. Front Med. 2020;7:250.
34. Mazumder A, Arora M, Bharadiya V, et al. SARS-CoV-2 epidemic in India: Epidemiological features and in silico analysis of the effect of interventions. F1000Res. 2020;9.
35. Chekani-Azar S, Gharib Mombeni E, Birhan M, Yousefi M. CRISPR/Cas9 gene editing technology and its application to the coronavirus disease (COVID-19), a review. Journal of World's Poultry Research. 2020;10(1):1-9.
36. Jordan RE, Adab P, Cheng KK. Covid-19: Risk factors for severe disease and death. BMJ. 2020;368:m1198.
37. Paital B, Das K, Parida SK. Inter nation social lockdown versus medical care against COVID-19, a mild environmental insight with special reference to India. Sci Total Environ. 2020:138914.
38. Gharib Mombeni E, Yousefi M, Chekani-Azar S, Abousenna MS, Armin K, Shavandi F, Emami E, Bahrami Y. Recent drugs and vaccines candidates to tackle COVID-19. J Life Sci Biomed. 2020;10(6):70-9.
39. Jilani TN, Jamil RT, Siddiqui AH. H1N1 influenza (swine flu). Stat Pearls [Internet]; 2020.
Available:https://www.ncbi.nlm.nih.gov/books/NBK513241/
40. Cheng AC, Kotsimbos T, Reynolds A, et al. Clinical and epidemiological profile of patients with severe H1N1/09 pandemic influenza in Australia and New Zealand: An observational cohort study. BMJ open. 2011;1(1).
41. Novel swine-origin influenza A (H1N1) virus investigation team. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. N Engl J Med. 2009;360(25):2605-15.
42. Kshatriya RM, Khara NV, Ganjiwale J, Lote SD, Patel SN, Paliwal RP. Lessons learnt from the Indian H1N1 (swine flu) epidemic: Predictors of outcome based on epidemiological and clinical profile. J Family Med Prim Care. 2018;7(6):1506.
43. Choudhry A, Singh S, Khare S, et al. Emergence of pandemic 2009 influenza A H1N1, India. Indian J Med Res. 2012;135(4):534.
44. Malhotra B, Singh R, Sharma P, et al. Epidemiological and clinical profile of influenza A (H1N1) 2009 virus infections during 2015 epidemic in Rajasthan. Indian J Med Res. 2016;144(6):918.
45. Wang H, Naghavi M, Allen C, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: A systematic analysis for the Global burden of disease study 2015. The Lancet. 2016;388(10053):1459-544.
46. Salyer SJ, Silver R, Simone K, Behravesh CB. Prioritizing zoonoses for global health capacity building—themes from One Health zoonotic disease workshops in 7

countries, 2014–2016. Emerg Infect Dis. 2017;23(Suppl 1):S55.
47. Abebe GM. Emerging and re-emerging viral diseases: The case of coronavirus disease-19 (COVID-19). Int J Virol AIDS. 2020;7:067.
48. Trovato M, Sartorius R, D'Apice L, Manco R, De Berardinis P. Viral emerging diseases: Challenges in developing vaccination strategies. Front Immunol. 2020;11.
49. Afrough B, Dowall S, Hewson R. Emerging viruses and current strategies for vaccine intervention. Clin Exp Immunol. 2019;196(2):157-66.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/65362