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A review on emerging and reemerging viral diseases

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Abstract
The incidence of emerging infectious diseases in humans has increased within the recent, past or threatens to increase in the near future. Over 30 new infectious agents have been detected worldwide in the last three decades. Developing countries such as India suffer disproportionately from the burden of infectious diseases given the confluence of existing environmental, socioeconomic, and demographic factors. In the recent past, India has seen outbreaks of eight organisms of emerging and re-emerging diseases in various parts of the country, six of these are of zoonotic origin. The numbers of emerging and re-emerging outbreaks epidemics are higher in viral diseases. Just as an example is Ebola virus, Nipah virus, Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), Corona virus, Dengue virus. Constant awareness and pursuance of effective strategies for controlling infectious diseases and disease emergence thus remain crucial. Recent interact in emerging virus disease has focused on first, how the interplay of climate, environment and human societal pressures can trigger emergence. Second, how viruses can transmit between an established reservoir species and a new host species and determine pathogenicity. And third, the aspects of these processes after opportunities for therapy and prevention. This review presents current updates on contemporary emerging and reemerging viral disease and highlights the scope, dynamics, and its advances in infectious management based on the clinical perceptions.

Keywords: ebola virus disease, h1n1 influenza, nipah virus, dengue virus, corona virus

Introduction

The emergence of novel human pathogens and reemergence of several diseases is of particular concerns in the current decade [1]. In recent years there has been increasing attention paid to the changing patterns of infectious diseases. The factors that lead to increases in the rates of these so-called 'emerging infectious diseases' (EIDs) has focused primarily on the role of human activities, such as land use changes, population growth, increased contacts with wild animal reservoirs and the degradation of health care resources. It is estimated that the majority – some estimates place it as high as 75%, of these emerging diseases are derived from animals [2]. At a basic level, emerging infections can be defined as those diseases whose incidence has been found to be increased within recent decades or which have threatened to increase in the future. Several factors underlie the emergence of such diseases, including increasing population, poverty and malnutrition, increased domestic and global connectivity, economic factors leading to population migration, social practices, and the prevalence of immunosuppressive diseases, unplanned urbanization, deforestation and change in agricultural practices such as mixed farming [1]. These spill over from their natural reservoirs either through direct contact or indirectly through close contact with domestic animals and subsequently into human populations. But the most important event in new disease emergence is genetic changes in the pathogen that make it possible to become established in a new host species, productively infect new individuals in the new hosts.

Respiratory viral infections, arboviral infections, bat-born viral infection and COVID-19 viral infections represent four major categories of emerging viral infections in India. The Middle East respiratory syndrome corona viruses (MERS-CoV) represent the pathogens posing severe threat in this category. Arthropod-borne viruses have consistently been the reason of emerging and re-emerging diseases in the Indian subcontinent, including Crimean-Congo hemorrhagic fever (CCHF), dengue, Chikungunya, and Japanese encephalitis. The major arboviral pathogens of humans belong to the three genera of Flavivirus, Alpha virus and Nair virus. Several bats-borne viruses have also come into prominent notice, best exemplified by Nipah viral disease, severe fever with thrombocytopenia virus (SFTV), as well as Ebola viral disease [3].

Table 1

Emerging Virus		Re-Emerging Virus	
2001	Nipah virus	1955	Yellow fever
2003	SARS Coronavirus	1992	Dengue
2004	Avian Influenza	2003	Ebola
2006	Influenza H5N1	2005	Chikungunya
2007	Polyoma like virus	2017	West Nile virus
2009	Influenza H1N1	2017	Human monkey pox
2011	Crimean Congo hemorrhagic Fever	2018	Rift valley fever

Dengue virus

Dengue virus (DENV) is a small single-stranded RNA virus comprising four distinct serotypes (DEN-1 to 4). These closely related serotypes of the dengue virus belong to the genus Flavivirus, family *Flaviviridae* [4]. It is a mosquito-borne disease and is primarily transmitted to humans by the female Aedes mosquito. The disease is mainly concentrated in tropical and subtropical regions, putting nearly a third of the human population, worldwide, at risk of infection [5]. Infection with DENV results in varying degrees of pathological conditions, ranging from mild asymptomatic

dengue fever (DF) to severe dengue hemorrhagic fever (DHF) and dengue shock syndrome [6].

Epidemiology

During the 19th century, dengue was considered a sporadic disease, causing epidemics at long intervals. Annually 100 million cases of dengue fever and half a million cases of dengue hemorrhagic fever (DHF) occur in the world with a case fatality in Asian countries by 0.5%–3.5% of those with DHF, 90% are children less than 15 years of age. The incidence of dengue is increased 30 fold between 1960 and 2010 [7]. In 1981 Cuban epidemic has been considered one of the most severe DHF epidemics to date in the Americas [8].

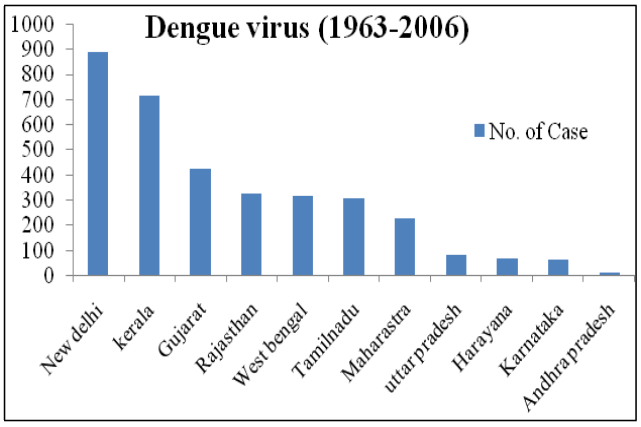

Fig 1: Epidemiology of Dengue [9]

Morphology

DENV is an envelope, single-stranded positive-sense RNA virus. The RNA genome consists of approximately 10,700 nucleotides and encodes a 3,411 amino acids long precursor polyprotein containing three structural proteins (capsid [C], precursor membrane [prM], and envelope [E]) and seven non-structural (NS) proteins (NS_1, NS_{2A}, NS_{2B}, NS_3, NS_{4A}, NS_{4B}, and NS_5). The structural proteins are components of the mature virus particle whereas the NS proteins are expressed only in the infected cell and are not packaged to detectable levels into mature particles. The structural proteins are not involved in replication of the viral genome [7].

Dengue virus transmission

A few hundred years ago, dengue was primarily a sylvatic disease. The sylvatic cycle is ecologically and evolutionarily-distinct from the human transmission cycle, causing sporadic outbreaks in humans. A sylvatic cycle that serves as an enzootic cycle involving female Aedes mosquito species of *A. aegypti* [10, 11].The mosquito becomes infected when it bites a person with DENVs in their blood. Dengue is transmitted by vectors and is not spread from one person to another person directly.

Symptoms of dengue virus

Symptoms usually begin four to six days after infection and last for up to 10 days. The symptoms may progress to massive bleeding, shock, and death. This is called dengue shock syndrome

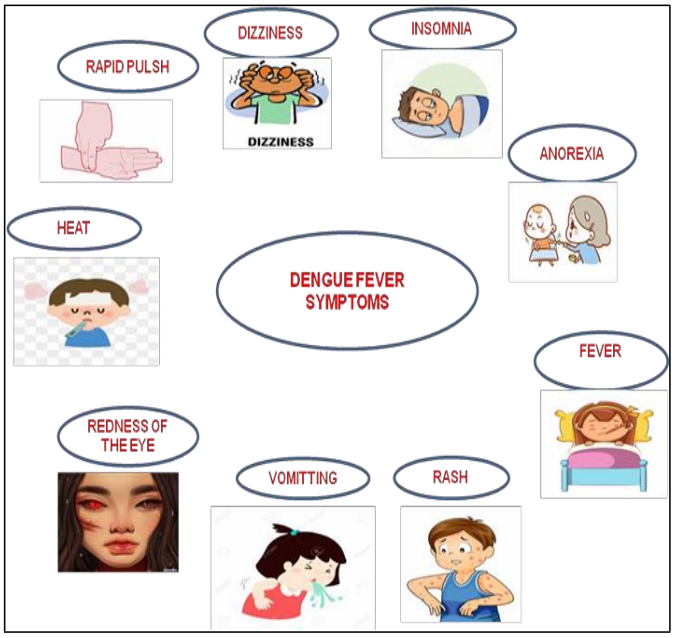

Fig 2: Dendue virus symptoms [12, 13]

Diagnosis

Laboratory diagnosis of dengue virus infection can be made by the detection of specific viral antigen, genomic sequence, or antibodies. At present, the three basic methods used by most laboratories for the diagnosis of dengue virus infection are viral isolation and characterization, detection of the genomic sequence by a nucleic acid amplification technology assay, and detection of dengue virus-specific antibodies [14]. Molecular diagnosis based on reverse transcription (RT)-PCR, such as one-step or nested RT-PCR, nucleic acid sequence-based amplification (NASBA), or real-time RT-PCR, has gradually replaced the virus isolation method as the new standard for the detection of dengue virus in acute-phase serum samples [15].

Treatments

There is no specific treatment for dengue fever. Fever reducers and painkillers can be taken to control the symptoms of muscle aches and pains, and fever [16].

- The best options to treat these symptoms are acetaminophen or paracetamol.
- NSAIDs (non-steroidal anti-inflammatory drugs), such as ibuprofen and aspirin should be avoided [17]. These anti-inflammatory drugs act by thinning the blood, and in a disease with risk of hemorrhage, blood thinners may exacerbate the prognosis.

The first dengue vaccine, Dengvaxia® (CYD-TDV) developed by Sanofi Pasteur was licensed in December 2015 and has now been approved by regulatory authorities in ~20 countries. The analysis showed that the subset of trial participants who were inferred to be seronegative at the time of first vaccination had a higher risk of more severe dengue and hospitalizations from dengue compared to unvaccinated participants [16]. After described in the WHO position paper on the Dengvaxia vaccine (September 2018) the live attenuated dengue vaccine CYD-TDV has been shown in clinical trials to be efficacious and safe in persons who have had a previous dengue virus infection [18].

Nipah virus

Nipah virus is a single-stranded RNA virus belonging to family *Paramyxoviridae* that has caused epidemics of respiratory illness and fatal encephalitis. The virus normally circulates among specific types of fruit bats. It can both spread between people and from other animals to people [19].

Epidemiology

Human NiV infection was first identified in Malaysia from 1998 to 1999. Eventually, the outbreak caused 283 symptomatic cases and 109 deaths. In March 1999, an outbreak (11 cases, one death) was reported from Singapore among slaughterhouse workers. The epidemiology of NiV is significantly different in Bangladesh. Since 2001, seasonal outbreaks of NiV have occurred in Bangladesh in the winter months [20]. There have been a total 639 human cases of NiV infection reported from Bangladesh (261 cases), India (85 cases), Singapore (11 cases), Philippines (17 cases) and Malaysia (265 cases), with a mortality rate of about 59% [14, 21, 22]. As reported in the Disease Outbreak News published on 31 May 2018, three deaths due to new infection were reported on 19 May from Kozhikode District, Kerala State As of 17 July 2018, a total of 19 Nipah virus cases, including 17 deaths, were reported from Kerala State [23].

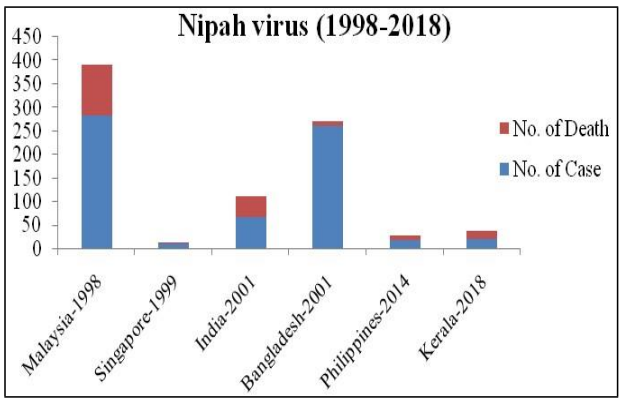

Fig 3: Nipah Virus Epidemiology

Morphology

The structure of NiV virus is a parallel, long, coiled-coil, tetrameric with a small helical cap as tethers of the viral polymerase to nucleocapsid and multimeric phosphoprotein. Nipah virus has a single-stranded, negative-sense RNA genome that is encapsidated by the nucleoprotein (N) and transcribed and replicated by the polymerase protein (L) The phosphoprotein (P) plays an essential role as a polymerase cofactor, enhancing polymerase processivity and allowing the encapsidation of the newly synthesized viral genomes and antigenomes [24].

Structure of NiV [25]

Nipah virus is an enveloped virus measuring 40 – 600 nm in size and pleomorphic. Nipah virus genome is non-segmented, single-stranded negative-sense RNA. The genome is 18.2 kb in length and contains six genes corresponding to six structural proteins. They are nucleocapsid (N), phosphoprotein (P), matrix protein (M), fusion protein (F), glycoprotein (G) and polymerase (L).

Nipah virus transmission

NiV is a zoonotic virus, and infects animals such as pigs and fruit bats. Infected fruit bats sheds virus in their saliva or urine or body secretions, and humans get infection by direct contact with these animals [26]. NiV infected people characterized by, prominent brainstem dysfunction, high fatality rates, and declining level of consciousness where infection causes by direct contact with pigs in livestock farm [27].

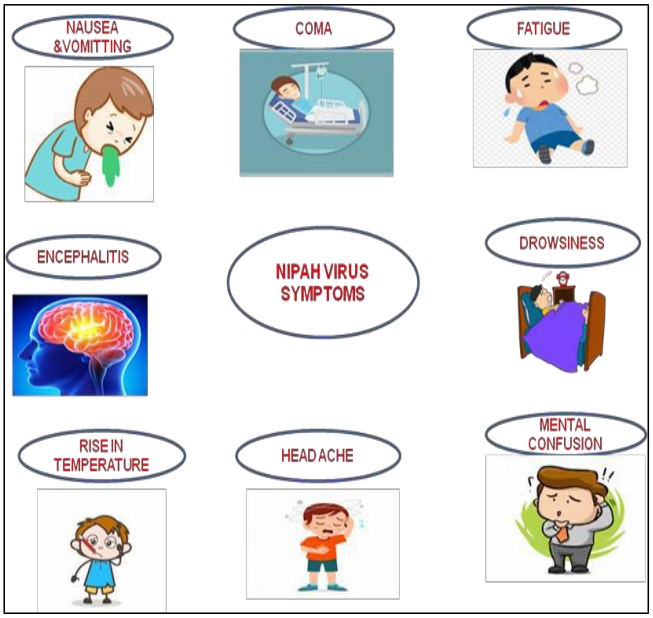

Fig 4: Nipah virus symptoms [28]

Diagnosis

Laboratory diagnostic tests of NiV encephalitis consist of detecting anti-NiV immunoglobulin M (IgM) and IgG antibody in the serum and cerebrospinal fluid (CSF), with or without viral isolation [20]. Most commonly used diagnostic method is enzyme-linked immunosorbent assay (ELISA) test, using monoclonal antibody-based antigen, for virus detection and for differentiating NiV from Hendra virus [14].

Treatments

No specific drug has been yet approved for the treatment. Limited work has been done to develop therapeutics against NiV infection. In preclinical studies, monoclonal antibodies have been used for treatment purposes. A monoclonal antibody targeting the viral G glycoprotein has been shown beneficial in a ferret model of the new disease. According to the U.S. Centers for Disease Control and Prevention (CDC), supportive care is the only current treatment for this viral infection [20, 14]. Ribavirin and acyclovir have been used to treat NiV infection during past outbreaks. The Malaysian outbreak, Ribavirin was given orally or intravenously to patients with NiV encephalitis. The mortality rate was reduced up to 36% when the infected patients were treated with Ribavirin. In Singapore outbreak, acyclovir was given to all NiV encephalitis patients and only one death reported due NiV infection, but the role of acyclovir drug is still unclear. In a recent *in vivo* study, Favipiravir (T- 705) antiviral showed promising results when tested on NiV infected golden hamsters. A study involving use of vaccine against NiV has shown promising results in hamster models [29].

Ebola virus

Ebola virus disease (EVD) is a deadly disease also known as Ebola hemorrhagic fever is an acute, severe and fatal

disease in humans caused by infection with a virus of the *Filoviridae* family, genus *Ebolavirus*. The Ebola virus is characterized by high lethality, high infectivity, and lack of effective treatment or prophylaxis. EVD can occur during any season and affect people of any race and age group [30]. The genus Ebolavirus consists of five species: EBOV, Sudan ebolavirus (SUDV), Tai forest ebolavirus (TAFV), Bundibugyo ebolavirus (BDBV) and Reston ebolavirus (RESTV) [31].

Epidemiology

The first cases of Ebola virus infection reported in Congo1976. There were 318 cases and 280 deaths, an 88% case fatality rate. Zaire ebolavirus was responsible for the outbreak that started in West Africa in 2014. Over 28,000 cases were reported in this outbreak, with over 11,000 deaths. An outbreak was announced in the Democratic Republic of the Congo in August 2018. As of 3 December 2019, 3313, including 2207 deaths have been reported in the North Kivu [32, 31]. A total of 18,464 suspected, probable and confirmed (11,699) cases with 6841 deaths have been reported 13th December 2014 in Liberia and Sierre. Limited transmission reported from the United States of America (4 cases, 1 death) and Mali (8 cases, 6 deaths) whereas, Nigeria (20 cases, 8 deaths), Senegal (1 case, 0 deaths) and Spain (1 case, 0 deaths) have been declared free of EVD [33].

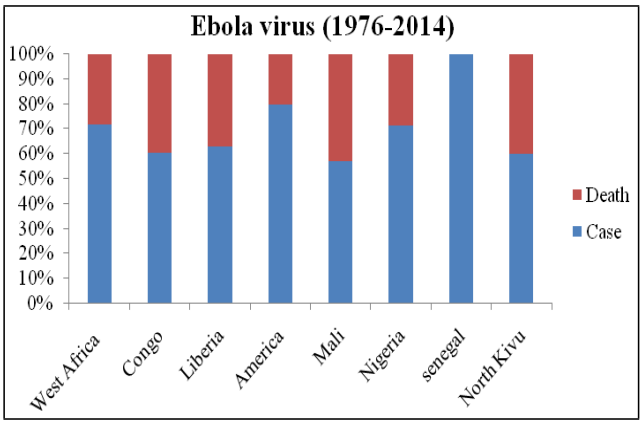

Fig 5: Ebola virus Epidemiology

Morphology

The Ebola virus is a highly virulent, single-stranded ribonucleic acid virus. The Ebola viruses exist as filamentous and polymorphic structures, often taking on different shapes. They may occur in long filaments or branched, U-shaped, 6-shaped or circular forms. Ebola viruses have a uniform diameter of 80 mm but vary considerably in length, with some as long as 14,000 mm. Structurally Ebola viruses consist of three layers: a surface glycoprotein layer, a lipid membrane envelope unit and an internal tubular helical nucleocapsid. The virus surface layer consists of glycoprotein spikes, each about 7–10nm long, spaced at about 10 NM intervals. The second layer, the lipid membrane, surrounds the internal helical nucleocapsid. This, in turn, houses the third layer, the negative-stranded viral genome, which controls viral replication in cells [34].

Structure of Ebola virus

Ebola Virus have a negative-sense, non-segmented single stranded linear RNA genome about 18-19 kb in size. Virus is generally approximately 80 nm in diameter, 970 nm long. They are tubular, and contain viral envelope, matrix, and nucleocapsid components. The virus generally appears in a long, filamentous. It encodes seven structural proteins: nucleoprotein (NP), polymerase cofactor (VP35), (VP40), GP, transcription activator (VP30), VP24, and RNA polymerase (L) [35, 36].

Ebola virus transmission

Ebola viruses are highly transmissible by direct contact with infected blood, secretions, tissues, organs, and other bodily fluids from dead or living infected persons. Ebola is not spread through the air or by water, or in general, by food [37]. The virus is thought to be initially acquired from infected animals such as bats and nonhuman primates, but has potential for human-to-human transmission.

Symptoms of Ebola virus:

Ebola virus is one of a group of viruses that cause a hemorrhagic fever syndrome [38]. Symptoms of Ebola virus infection are similar to those produced by other hemorrhagic fever viruses and include:

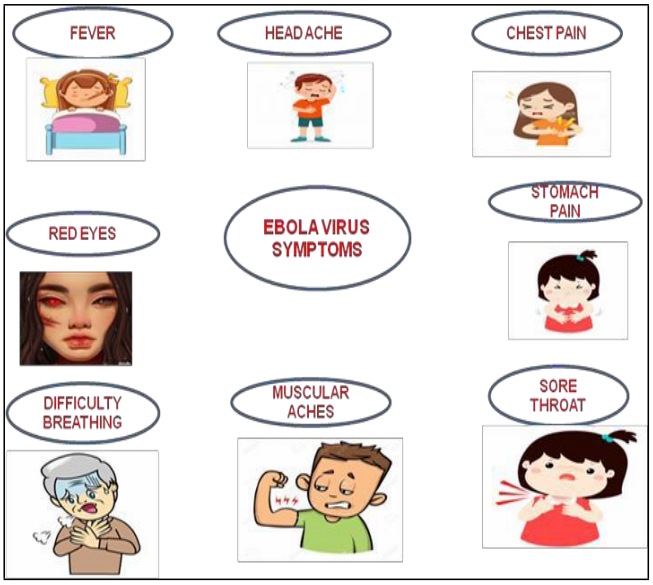

Fig 6: Ebola virus Symptoms [39]

Diagnosis

For early detection of Ebola virus is, detection of viral RNA or viral antigen are the recommended tests. Laboratory-confirmed cases must test positive for the presence of the Ebola virus, either by detection of virus RNA by RT-PCR, or by detection of Ebola antigen by a specific Antigen detection test, and/or by detection of Immunoglobulin M (IgM) antibodies directed against Ebola [40].

Treatments

Since 1976, no attempt was made to create the vaccine against the deadly disease until at present, when the localized problem has surrounded to become a global threat. The WHO declared that, considering the magnitude and severity of the current outbreak, it is ethical to use experimental drugs for treatment and prevention of EVD. Zmapp is a cocktail of monoclonal antibodies and is being used to treat some victims of the current EBOV outbreak. Unfortunately, there is a limited supply of ZMapp at this moment. The non-antibody based antiviral preparations, only the nucleoside analogue favipiravir has been tested

extensively in humans. Recently the drug gained approval in Japan for use in humans infected with novel and re-emerging influenza viruses [31]. Besides activity against influenza virus infection, this drug also has documented activity against a wide variety of RNA viruses including Ebolaviruses [41]. Favipiravir prevented death in mice infected with EBOV when treatment was started six days post infection. These results are promising, but need to be confirmed with a non-human primate model. BCX-4430 is also a nucleoside analogue with broad spectrum activity against RNA viruses and has proven to be effective against the Marburg virus in a non-human primate model and Ebola virus in a mouse model. Finally, TKM-Ebola and AVI-6002 are under development for the treatment of EVD and exert their action via gene silencing. Both drugs have proven to be effective in mouse and primate models, and some safety and pharmacokinetic data in humans are available for AVI-6002 [42].The CDC recommends the following medical treatments for Ebola-infected patients: Patients have mostly died from dehydration and electrolyte imbalance caused by vomiting and diarrhea. Rehydration by oral solution (ORS) or intravenous (IV) fluids, with daily electrolyte monitoring can prevent vascular collapse and maintain electrolyte balance [32].

Corona virus

Corona virus disease (COVID-19) is an infectious disease caused by a newly identified and named type of single-stranded, positive-sense RNA corona virus called SARS-CoV-2 that likely jumped from infecting only animal species to infecting humans that, in turn, developed person-to-person transmission that results in respiratory problems. The 2019 novel corona virus is related to SARS and MERS corona viruses [43]. SARS-CoV is thought to be an animal virus from an animal reservoir, perhaps bats, that spread to other animals (civet cats) and first infected humans in the Guangdong province of southern China. SARS-CoV is transmitted from person to person by close personal contact. It is thought to be transmitted most readily by respiratory droplets produced when an infected person coughs or sneezes [44]. The reservoir of MERS-CoV is thought to be dromedary camels, but the mechanism of transmission from camels to humans. Most reported cases involved direct human-to-human transmission in health care settings. Most reported cases have involved severe respiratory illness requiring hospitalization, with a case fatality rate of about 35%; however, at least 21% of patients had mild or no symptoms. Fever, chills, myalgia, and cough are common. Gastrointestinal symptoms (E.g. diarrhea, vomiting, abdominal pain) occur in about one third of patients [45].

Epidemiology

The corona virus COVID-19 is affecting 155 countries and territories around the world [46]. Wuhan Corona virus was first identified in the Chinese city of Wuhan in 2019. The virus has killed 4632 people and infected more than 80000 in China, according to the World Health Organization. SARS-CoV was identified in 2002 as the cause of an outbreak of severe acute respiratory syndrome (SARS). An epidemic of SARS affected 26 countries and resulted in more than 8000 cases in 2003 [44].

And the MERS was also identified in Saudi Arabia in 2012 as the cause of the Middle East respiratory syndrome. The WHO declared the COVID-19 outbreak a global health emergency [45].

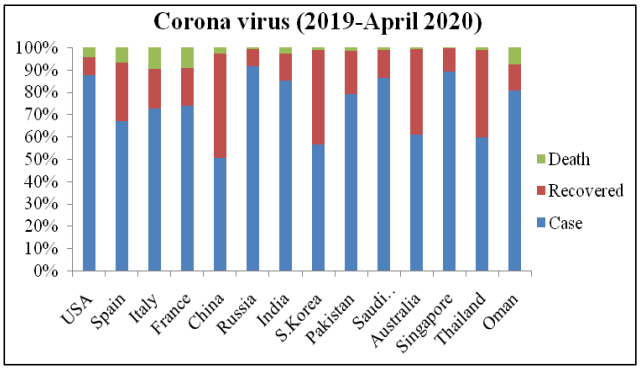

Fig 7: Corona virus Epidemiology

Morphology

Corona viruses (CoVs), enveloped, positive-sense RNA viruses, are characterized by the club-like spikes that project from their surface, an unusually large RNA genome, and a unique replication strategy. Corona virus virus particles contain four main structural proteins. These are the spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins, all of which are encoded within the 3′ end of the viral genome. The S protein (~150 KDa) utilizes an N-terminal signal sequence to gain access to the ER, and is heavily N-linked glycosylated. The M protein is the most abundant structural protein in the brain. It is a small (~25–30 kDa) protein with 3 transmembrane domains and is thought to give the virion its shape. The N protein constitutes the only protein present in the nucleocapsid. A fifth structural protein, the hem agglutinin-esterase (HE), is present in a subset of β-corona viruses [47].

Structure of corona virus

Corona viruses are spherical shape. The virus has a diameter of 75 to 160 nanometers, and the virus genome is a continuous linear single-stranded RNA, and the molecular weight is usually (5.5 to 6.1) $x10^6$. The corona virus genome encodes a spike protein (S), an envelope protein, a membrane protein, and a nucleoprotein in this order. Among them, spike protein is the most important surface membrane protein of the corona virus [48].

Corona virus transmission

COVID-19 cases were linked to a live animal market in Wuhan, China, suggesting that the virus was initially transmitted from animals to humans [45]. Commonly spread from person to person, usually via close contact, they could be physical contact or simply being near an infected person who cough sneezes or talks can expose infected respiratory droplets [49].

Symptoms of Corona virus

Signs and symptoms of COVID-19 may appear two to 14 days after exposure and can include:

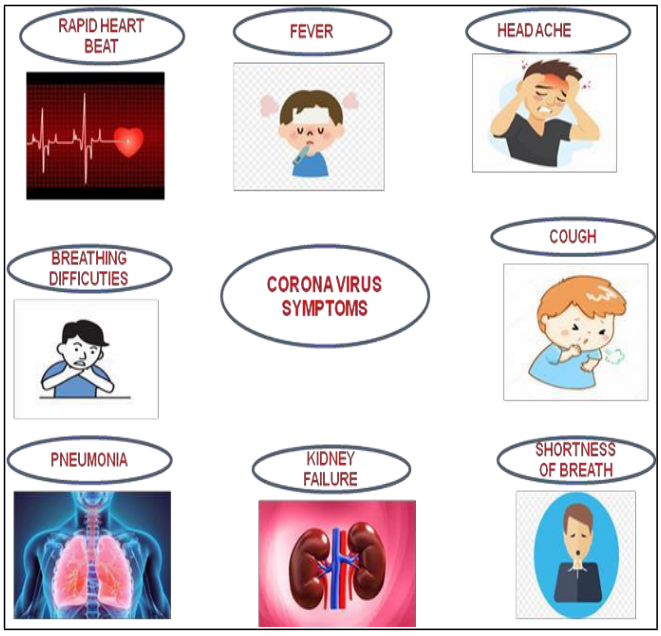

Fig 8: Corona virus symptoms [50]

Diagnosis

Laboratory tests are detection of proteins from the COVID-19 virus in respiratory specimens. FDA has approved about 20 different suppliers of various tests of blood or swab samples to quickly diagnose (from about 5-15 minutes) infected or uninfected people [43]. Molecular (e.g. PCR) testing of respiratory tract samples is the recommended method for the identification and laboratory confirmation of COVID-19 cases.

Treatment

Treatment of COVID-19 is supportive. No vaccine, antiviral drug, or other specific treatment is available. Over 175 treatment and vaccine clinical trials are currently registered, but data on effective therapy remains sparse. Current therapeutic strategies in practice for severe disease include antiviral agents (notablyremdesivir,), chloroquine derivatives, and immunomodulatory agents [43]. Currently, no antiviral medication is recommended to treat COVID-19. Treatment is directed at relieving symptoms and may include: Pain relievers (ibuprofen or acetaminophen), Cough syrup [45].

Conclusion

There is no antiviral therapy or vaccination available for viral infection, leaving only early detection and symptomatic treatment with fluid resuscitation essential for management of severe cases. The Future efforts need to focus on developing effective vaccines, drugs and therapies. However, the fact that the trials to develop such vaccines or treatments are still far away necessitates emergency preparedness for early detection and control.

Reference

1. Mourya DT, Yadav PD, Ullas PT, Bhardwaj SD, Sahay RR, Chadha MS, *et al*. Emerging/re-emerging viral diseases & new viruses on the Indian horizon. Indian Journal of Medical Research. 2019; 149:447-467.
2. Pekosz A, Glass GE. Emerging Viral Diseases. Md Med. 2008; 9(1):11-16.
3. Ho ZJM, Hwang YFJ, Lee JMV. Emerging and re-emerging infectious diseases: challenges and opportunities for militaries. Military Medical Research. 2014; 1(21):1-10.
4. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control: New Edition. Geneva: World Health Organization, 2009. https://www.ncbi.nlm.nih.gov/books/NBK143157/
5. Chen LH, Wilson ME. Transmission of dengue virus without a mosquito vector: nosocomial mucocutaneous transmission and other routes of transmission. Clin Infect Dis. 2004; 39(6):56-60.
6. Khetarpal N, Khanna I. Dengue Fever: Causes, Complications, and Vaccine Strategies. Journal of Immunology Research. 2016; 5:1-14.
7. Srinivas V, Srinivas VR. Dengue fever: a review article. Journal of Evolution of Medical and Dental Sciences, 4(29):5048-5058.
8. Guzman MG, Kouri G. Dengue: an update. The Lancet Infectious Disease. 2002; 2(1):33-42.
9. 2006 dengue outbreak in India- en.wikipedia.org
10. Tayade MR, Shinkar DM, Ptil PB, Saudagar RB. Emerging therapy for dengue. Int J Curr Pharm Res. 2018; 10(2):1-4.
11. Ahammad F, Rashid TRTA, Mohamed M, Tanbin S, Fuad FAA. Contemporary Strategies and Current Trends in Designing Antiviral Drugs against Dengue Fever via Targeting Host-Based Approaches. Microorganisms. 2019; 7(9):296.
12. Sapir DG, Schimmer B. Dengue fever: new paradigms for a changing epidemiology. Emerg Themes Epidemiol. 2005; 2(1):1-10.
13. Symptoms and treatment |Dengue |CDC www.cdc.gov
14. Aditi Shariff M. Nipah virus infection: A review. Epidemiol Infect. 2019; 147:e95.
15. Shu PY, Huang JH. Current advances in dengue diagnosis. Clin Diagn Lab Immunol. 2004; 11(4):642-650.
16. Dengue and severe dengue-www.who.int
17. Srinivasan R, Raju MD, Prasad SD, Rao ME. Study of diseases like malaria, chikungunya and Dengue caused by Mosquitoes in human kind. Int J of Pharmacy and Analytical Research. 2015; 4(2):94-99.
18. Rather IA, Parray HA, Lone JB, Paek WK, Lim J, Bajpai VK, *et al*. Prevention and Control Strategies to Counter Dengue Virus Infection. Front Cell Infect Microbiol, 2017, 7:336.
19. Nipah virus infection –https://en.m.wikipedia.org
20. Ambat AS, Zubair SM, Prasad N, Pundir P, Rajwar E, Patil DS, *et al*. Nipah Virus: A Review on Epidemiological Characteristics and Outbreaks to Inform Public Health Decision Making. J Infect Public Health. 2019; 12(5):634-639.
21. Singh RK, Dhama K, Chakraborty S, Tiwari R, Natesan S, Khandia R, *et al*. Nipah virus: epidemiology, pathology, immuno biology and advances in diagnosis, vaccine designing and control strategies – a comprehensive review. Veterinary Quarterly. 2019; 39(1):26-55.
22. Update: Outbreak of Nipah Virus -- Malaysia and Singapore, 1999, 48(16).
23. Nipah virus –India https://www.int
24. Bruhn JF, Barnett KC, Bibby J, Thomas JM, Keegan RM, Rigden DJ, *et al*. Crystal structure of the nipah virus phosphor protein tetramerization domain. J Virol.

2014; 88(1):758-762.
25. Reddy KR. Nipah Virus (NiV) Infection: An Emerging Zoonosis of Public Health Concern. J GMC N, 2018; 11(2).
26. Chattu VK, Kumar R, Kumary S, Kajal F, David JK. Nipah virus epidemic in southern India and emphasizing "One Health" approach to ensure global health security. J Family Med Prim Care. 2018; 7(2):275-283.
27. Gupta A. Clinical Research and Role of Dietary Supplement in the Treatment of Nipah Virus: Current Status. International Journal of Research in Clinical Medicine and Pharmacy Practice. 2018; 1(1):20-27.
28. Nipah virus infection (NIV) symptoms, transmission and treatment. www.medicinenet.com
29. Sharma V, Kaushik S, Kumar R, Yadav JP, Kaushik S. Emerging trends of Nipah virus: A review. Rev Med Virol. 2019; 29(1):e2010.
30. Liu WB, Li ZX, Du Y, Cao GW. Ebola virus disease: from epidemiology to prophylaxis. Mil Med Res. 2015; 2:7.
31. Goeijenbier M, Kampen JJV, Reusken CB, Koopmans MP, Gorp ECV. Ebola virus disease: a review on epidemiology, symptoms, treatment and pathogenesis. Neth J Med. 2014; 72(9):442-448.
32. Khalafallah MT, Aboshady OA, Moawed SA, Ramadan MS. Ebola virus disease: Essential clinical knowledge. Avicenna J Med. 2017; 7(3):96-102.
33. Mittal V, Chhabra M, Venkatesh S. Ebola Virus - An Indian Perspective. Indian J Pediatr. 2015; 82:207-209.
34. Matua GA, Wal DMVD, Locsin R. Ebolavirus and Haemorrhagic Syndrome. Sultan Qaboos University medical journal. 2015; 15(2):171-176.
35. Structure of Ebola Virus.MicrobiologyInfo.com
36. Kharat AS, Kharat KR. Ebola Fever and Advances in the Antiviral Therapies. Journal of Human Virology & Retro virology. 2015; 2(5):1-9.
37. Rewar S, Mirdha D. Transmission of Ebola Virus Disease: An Overview. Annals of Global Health. 2014; 80(6):444-451.
38. Ebola virus disease-www.who.int
39. Symptoms of ebola.commons.wikimedia.org
40. Laboratory diagnosis of Ebola virus disease – www.who.int
41. Smither SJ, Eastaugh LS, Steward JA, Nelson M, Lenk RP, Lever MS, *et al*. Post-exposure efficacy of oral t-705 (favipiravir) against inhalational ebola virus infection in a mouse model. Antivir Res. 2014; 104:153-155.
42. Warren TK, Wells J, Panchal RG, Stuthman KG, Garza NL, Tongeren SAV, *et al*. Protection against filovirus diseases by a novel broad-spectrum nucleoside analogue BCX4430. Nature. 2014; 508:402-405.
43. Coronavirus (COVID-19, 2019-nCoV) Prevention, Symptoms, Treatment-www.medicinenet.com
44. WHO- SARS (Severe Acute Respiratory Syndrome) www.who.int
45. Tesini BL. Coronavirus and Acute Respiratory syndromes (COVID-19, MERS, and SARS) 2020 www. msd manuals. Com
46. Coronavirus Update (Live) 2,261,397 Cases and 154,726 Deaths from COVID-19 Virus Pandemic – Worldometers.info
47. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol. 2015; 1282:1-23.
48. 2019 Novel Corona virus/SARS-CoV-2 cusabio.com
49. How is Corona virus spread? Corona virus transmission facts. health.com.
50. Corona virus disease 2019 (COVID-19) - Symptoms and causes.www.mayoclinic.org
51. Kathiriya JB, Shah NM, Patel JS, Javia BB, Tajpara MM, Ghodasara SN, Barad DB. Epidemiological surveillance of Dengue fever: An overview. Int J Vet Sci Amin Hasb. 2020;5(6):1-0.