




Review

Emerging Viruses Besides the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

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Abstract: The emergence of deadly viruses is one of the epitomes of major global health threats. Currently the world is going through the COVID-19 pandemic resulting in extreme morbidity and mortality, which is caused by the severe acute respiratory coronavirus 2 (SARS-CoV-2). Besides, SARS-CoV-2, recent global perturbation caused by the chikungunya virus (CHIKV) infection, dengue caused by dengue virus (DENV), zika virus (ZIKV) infection, etc. are worth being noted. Although an array of research on the genome sequences within spatial geographical locations, infectious components, viral transmissibility and dynamics, treatment strategies using *in silico* model, animal/cell culture, and patient trials of these emerging viruses is being conducted, the human population is still at risk of being exposed to the emerging and re-emerging viral infections posing a most dreadful threat to the global public health. Besides the genomic characterization and the proteomic studies for drug repurposing or repositioning as well as the possible candidate vaccine development, the general awareness among the mass public about the preventive care against these emerging viruses is also an important concern. Lots of works have been reported on SARS-CoV-2 since its commencement on December 2019. Besides the elucidation of the respiratory viruses, present review briefly pointed on the viruses from *Flaviviridae* family, *Paramyxoviridae* family, *Filoviridae* family and *Bunyaviridae* family.

Keywords: emerging viruses, severe acute respiratory coronavirus 2 (SARS-CoV-2), respiratory viruses, *Flaviviridae* family, *Paramyxoviridae* family, *Filoviridae* family, *Bunyaviridae* family

1. Introduction

The world population is now suffering from the COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) resulting in 4, 200, 412 deaths so far out of 196, 553, 009 infected cases [1-2]. Indeed, the tribulation created by the respiratory viruses have a long history starting from Russian Influenza in 1889; and still, the emerging variants of SARS-CoV-2 are being noticed [3-4]. However, before the commencement of the running COVID-19 pandemic since December 2019, several viruses especially, the chikungunya virus (CHIKV), dengue

virus (DENV), zika virus (ZIKV), etc. have been noticed to be emergent causing serious morbidity among the mass population around the world [5-7]. Indeed, viruses have been long known to be pervasive and assorted microorganisms generating as a result of interactions within their hosts. Extensive work on their evolution, genomic diversity, selection pressure, host-virus ecology, pathogenesis, control and prevention is being conducted by scientists all around the world in coordination mainly with the World Health Organization (WHO) and the Center for Disease Control and Prevention (CDC) [8-9]. RNA viruses are so far known as the most potentially mutating and diverse viruses. The discovery of several novel insect-specific viruses (ISVs) and arboviruses augmented the access into the mosquito microbiome, to ponder on the prevalence of viruses that are known with poor modes of transmission as well immune-pathogenesis [8-9]. Scientists are working to resolve the mechanisms underlying such viral disease transmission from animals to humans (Zoonoses) which in turn unraveled the emergence of viruses from wildlife species like bats, rodents or non-human primates (NHPs) within distinctive geographic ‘hotspots’ in Africa, Asia and South America [10].

However, the details especially about the viral transmission dynamics and the predictive epidemiology are yet to be resolved. While a lot of incidences have been reported from the perspective of the influenza virus subtypes, CHIKV, ZIKV and dengue virus infection, several other emerging viruses still remain obscure to the health professionals let alone the awareness of the mass population. In this review, based on the previously published literature, the common traits of the deadly viruses from *Flaviviridae* family, *Paramyxoviridae* family, *Filoviridae* family and *Bunyaviridae* family together with the respiratory ones have also been included. This might be helpful to infer the exploration of the other emerging viruses during the ongoing COVID-19 pandemic.

2. Major respiratory viruses

The prevalence of respiratory viruses has been intricate as a constant public health threat for years. Infectious bronchitis viruses (IBVs) from the family *Coronaviridae* have been noticed to be affecting the respiratory tracts as well as the urogenital and/or alimentary tracts of the yellow chickens; and the high mutation rates of the IBV isolates posed economic threats to the poultry industry in southern China over the past decade [8, 10]. Due to the variations in breeding inconsistencies as well as the feeding patterns of chickens in China, the traits of circulating IBVs during different times and in diverse regions have been noticed to be flexible. Moreover, high mutation and recombination rates resulted in the genetic diversity and phenotypic heterogeneity among the IBV strains [10]. Thus, along with such genetic drift, IBV evolution has also been driven by the generation of genetic diversity and selection which is dependent on the microenvironment of the infected hosts, and the host immune responses [10].

Besides IBV, it is to be noted that the H5N1 highly Pathogenic Avian Influenza (HPAI) virus subtypes from the family *Orthomyxoviridae* caused several outbreaks in poultry over 60 countries of Asia, Europe, and Africa with 861 confirmed human cases of the avian influenza A(H5N1) virus infection from 16 countries, which denotes the H5N1 HPAI subtype as a significant health threat both to human and poultry [11]. The detailed biology of the influenza viruses, their transmission, epidemiology, pathology, diagnosis, treatment strategies with trial-based vaccines; and the proper prevention and control measures have been well discussed in the range of literature [12-13]. The pandemic potential of H7N9 subtype has been deduced to be of a great global concern; and interestingly, the early H7N9 viruses were noticed to lack the basic hemagglutinin and neuraminidase (HA) cleavage site with a relatively low pathogenicity whereas the subtype analyzed by Wang and colleagues (in 2017) was found to impart high pathogenicity and the replication potential in chickens together with the contact transmission mode [14]. SARS-CoV-2, a member of the β -coronavirus genus from *Coronaviridae* family, is genetically related to the severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1) causing the epidemic in 2002-2003 and the Middle East respiratory coronavirus (MERS-CoV) causing the epidemic in 2012 [1]. All of the three coronaviruses impart highly conserved genomic organization and have been found to employ nearly the modes life cycles during infectivity, of which SARS-CoV-2 has been noticed to be the most dreadful one with its potential to cause the current pandemic.

3. Emerging viruses other than respiratory ones

3.1 Viruses from flaviviridae family

Of the 26 known virus families, viruses other than the respiratory ones are also clinically important since they have long been known to be associated with the commencement of various diseases as shown in Figure 1 [15]. Among them the *Flaviviridae* family, consisting of four genera, i.e., *Flavivirus*, *Pestivirus*, *Hepacivirus* and *Pegivirus* and other 60 species, comprises the single stranded RNA (SS RNA+) of 9,000-13,000 bases, enveloped viruses that are of prime importance, most infecting mammals and birds; and are arthropod borne [16]. Examples of some emerging viruses include the dengue virus (DENV), Zika virus (ZIKV), Yellow Fever virus (YFV), Japanese Encephalitis Virus (JEV), West Nile Viruses (WNV), and hepatitis C virus (HCV) [15].

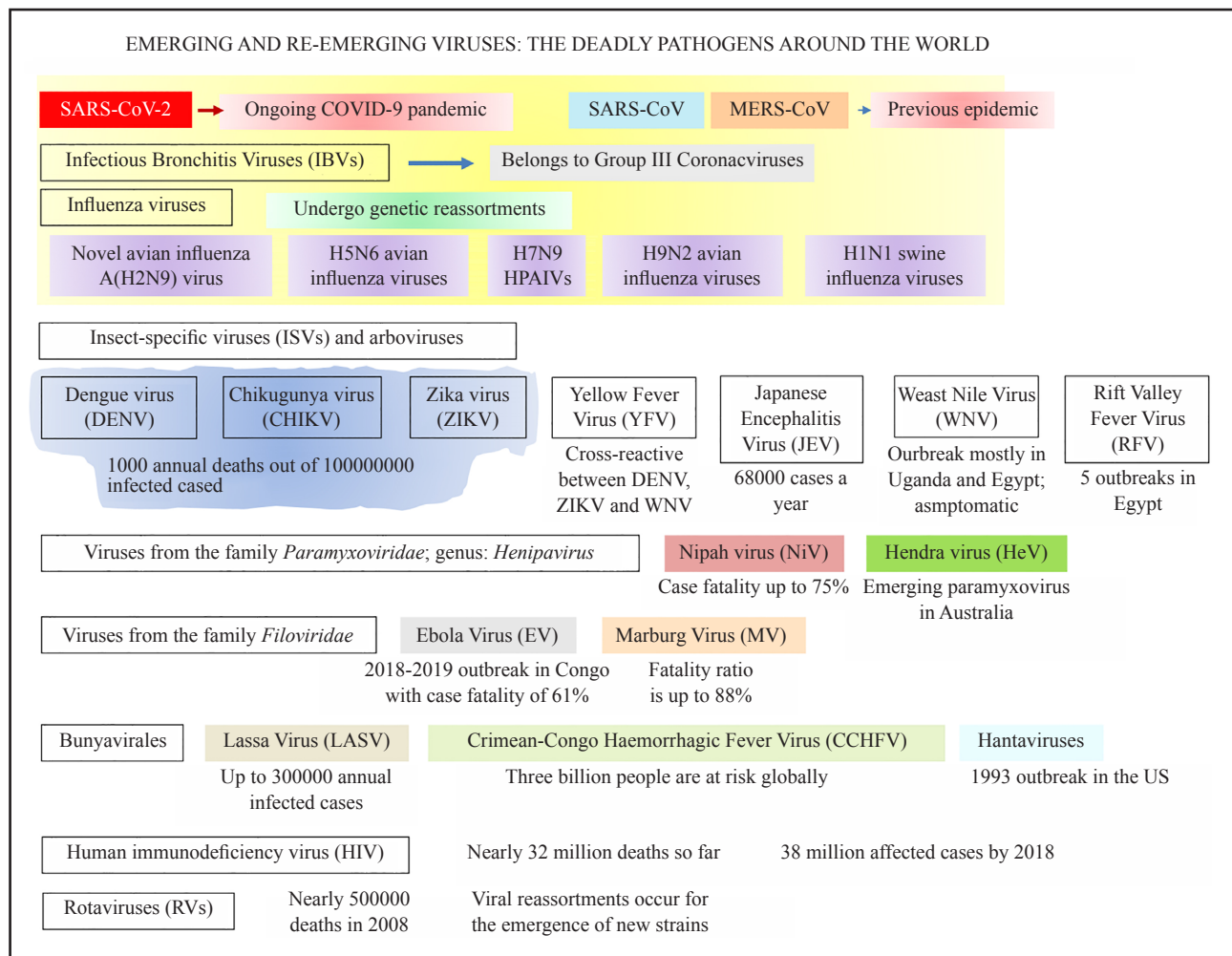


Figure 1. A scheme of dreadful emerging viruses

Unlike SARS-CoV-2 and the other influenza virus subtypes, certain emerging viruses are often unnoticed by the mass people although extensive research is being carried on. Among those, the YFV was first isolated in Ghana in 1927 and later the outbreaks have been observed with endemicity in the West Africa and the southeastern Brazil. And the virus is transmitted by sylvatic species, or by a mix of *Aedes* species, including sylvatic and domestic vectors [17]. Upon bites with an infected mosquito, the symptoms includes fever, headache, myalgia, malaise, nausea and vomiting; and the viruses are detectable in serum or plasma by the viral culture or through the molecular methods during this infection

phase [18]. However, the detection of YFV may be a bit puzzling due to the serological cross-reactions between other flaviviruses such as DENV, WNV and ZIKV [19].

In addition to the YFV, there are other two emerging viruses, namely JEV and WNV, which is indeed little known. According to the WHO report, 24 countries within South-East Asia and the Western Pacific regions encountered the endemic JEV transmission, exposing more than 3 billion people to the risk of the viral infection [20]. Since there are safe and effective vaccines for the prevention against JEV, WHO recommended that JE vaccination should be integrated into national immunization schedules in the areas where the viral spread renders the mass public health to fatality [21]. The emergence of WNV is really interesting due to its ecological generalism; i.e., it can infect an extraordinarily wide array of vertebrate taxa whereas the host/reservoir is restricted to the subset of animal species for most of the flaviviruses [21]. Such a phenomenon of generalism opens up the opportunities to learn more about the viral pathogenesis across various taxa as well as the divergent mechanisms of disease progression [21]. Monkeys, mice, birds and humans all have been noticed to develop long-term persistent infections after acute WNV infection [21].

3.2 Viruses from the *Paramyxoviridae* family

Interestingly, within the family *Paramyxoviridae*, the genus *Henipavirus* principally possesses two emerging viruses: Nipah virus (NiV) and Hendra virus (HeV) that are first identified as the causative agents of severe respiratory and encephalitic disease (neuropathogenesis) in Australia and Southern Asia during the 1990s [22]. The outbreaks of NiV and HeV may be sporadic; however, NiV has been noticed to possess the pandemic potential. Since the first outbreak of NiV in Kampung Sungai Nipah village of Malaysia and Singapore (due to contact with infected pigs) at the end of the last century, there have been more annual outbreaks in India and Bangladesh, possibly due to the direct contact with bats or through the consumption of raw date palm sap contaminated by bats [23]. For treatment purpose, the DNA vaccines, virus-like particles (VLP), the live and recombinant viral vectors have been developed for immunization against NiV and HeV [23].

3.3 Emerging viruses from the *Filoviridae* family

The family *Filoviridae* has been divided into three genera: *Ebolavirus*, *Marburgvirus*, and *Cuevavirus* [15, 24]. The Egyptian rousette bat (*Rousettus aegyptiacus*) has been reported to be the natural reservoir for Marburg viruses (MARV), and these bats may also transmit Ebola Viruses (EVs), consisting of ss (-) RNA which encodes the corresponding virulence proteins triggering severe hemorrhagic fever in humans and non-human primates [24]. Ebola virus disease (EVD) and Marburg virus disease (MVD) have similar traits as observed from their transmission modes as characterized by person-to-person transmission; and the high fatality rates for both viruses [24]. EV is transmitted to humans from wild animals (including the fruit bats of the *Pteropodidae* family) and spreads among the community through human-to-human transmission [25-26]. EV spreads within a human community initially through direct contact with the blood, body fluids and tissues of animals the EV infected. In case of MARV infections, a maculopapular rash may develop accompanying by erythema and desquamation; and in the late stage: shock, convulsions, metabolic disturbances and diffuse coagulopathy may take place [25-26]. No specific treatment for the Marburg hemorrhagic fever (MHF) has been evolved so far. However, the preventive care as well as the supportive hospital therapy will balance the patient's fluids and electrolytes, maintain adequate oxygen supply, keep the patient's blood pressure to an optimum level, and if necessary, the blood transfusion may be applied [25].

3.4 Emerging viruses from the *Bunyaviridae* family

The *Bunyaviridae* family consists of several clinically important viruses, including the California encephalitis virus, Sin Nombre virus, La Crosse virus, Hantaan virus, Crimean-Congo hemorrhagic fever virus, Sandfly fever viruses, Rift Valley fever virus (RVFV) and some others [15]. The complications caused by the mosquito-borne RVFV results in zoonotic viral disease causing severe fatality in both human and ruminant populations (sheep, goat, cattle, camel and buffaloes) especially in the African-and the Middle Eastern countries [26-27]. The outbreaks by RVFV have been noticed in Egypt in 1977, 1993, 1994, 1997, and 2003 [26]. Contact with the infected tissue, drinking unpasteurized milk, direct contact with infected animal's blood, aerosol or the bite of infected mosquitoes have been considered

as principal sources of human infections with this virus [26-27]. The detection of the seroprevalence of anti-RVFPV antibodies in the infected livestock during the inter-epidemic periods may aid the risk assessment both for the animal- and the public health [28]. Rodents of the *Mastomys natalensis* species complex serve as the natural host of Lassa virus (LASV) in West Africa; and 100,000 to 300,000 human LASV infections are reported annually with mild, flu-like symptoms to fulminant hemorrhagic fever [29-30]. Besides, Crimean-Congo haemorrhagic fever (CCHF), a tick-borne disease caused by the Crimean-Congo haemorrhagic fever virus (CCHFV), belonging to the family *Bunyaviridae* was first described in the Crimea in 1944 and thus the name “Crimean haemorrhagic fever” evolved [31]. General supportive care has been reported to be effective for the management of CCHFV-infected patients; and moreover, the anti-viral drug Ribavirin (also used to treat the LASV infection) can be used to treat such viral infections [31].

People can be infected with Hantaan virus, another member of *Bunyaviridae* family, through the inhalation of aerosolized excreta produced by infected rodents [32]. Hantavirus infection has been reported to affect 30,000 individuals annually; and such infection is likely to propagate among people living in relatively lower socioeconomic housing environments [32]. Hemorrhagic fever with renal syndrome (HFRS) has been mainly reported in Asia and Europe; whereas the Hantavirus pulmonary syndrome (HPS) has been profoundly noticed in the United States and Latina America [32-33]. Entry of the Hantaviruses into the host cells is mediated by the attachment of virions to the cellular receptors followed by endocytosis, which in turn triggers the exclusive replication within the host cytosol [32-33]. The symptoms include relatively high body temperature, myalgia, vomiting, nausea, headache, dizziness, diarrhea, lightheadedness and abdominal pain as has been noticed within the Hantavirus infected forestry worker [32]. Besides, acute renal failure with oliguria, increase of serum creatinine and blood urea nitrogen, albuminuria and hematuria can also accompany with the elevated levels of amylase, lipase, and liver enzymes levels concomitant with a low serum albumin level [32].

4. Conclusion

For a number of years people have been suffering from a range of viral infections, which very often instigates secondary bacterial infections when the host immune system is compromised. The evasion of immunity is another dangerous trait exhibited by the emerging viruses as is currently noticed by the SARS-CoV-2 exploring the COVID-19 pandemic. It is also noted that many other viruses described in this mini-review have also been reported to cause outbreaks in different geographical locations. Extensive study and continuous observation of the emerging viruses would be useful not only for the preventive awareness among the mass people but would also aid the effort into the development of effective vaccines and possible design of therapeutic drugs.

Conflict of interest

Authors have declared that they have no conflict of interest.

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