Coronaviruses outbreaks — Then to Now

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ABSTRACT

According to the World Health Organization (WHO), Viral diseases continue to evolve, posing a significant public health concern. Over two decades, several viral epidemics have been recorded wherein several strains of coronaviruses have been associated with epidemics causing severe respiratory complications and even death. Recently, a novel strain of this virus has come into the picture, eventually leading the world towards a pandemic. The situation today is similar to that witnessed earlier named as “SARS-CoV” and “MERS-CoV” which also affected the respiratory system. Current evidence suggests that SARS-CoV-2 is propagating to humans via transmission from illegally sold wild animals in the Huanan Seafood Wholesale Market. Phylogenetically, it has been shown that SARS-CoV-2 is a new member of the Coronaviridae family and yet is distinct from SARS-CoV (79% identical) and MERS-CoV (50% identical). Knowing the origin of such a pathogen is essential to develop the means to prevent further transmission and effective vaccines. This starts a discussion about the very origin of these viruses that have fanned a global emergency in the name of COVID-19. Therefore, the focus of this review is the origin, evolution and emergence of CoV during “SARS-CoV”, “MERS-CoV” and “SARS-CoV-2” along with possibilities of future outbreaks.

INTRODUCTION

“Coronaviruses” (CoV) belong to the order “Nidovirales”, family “Coronavirusidae” and subfamily- “Coronavirinae”. (Payne, 2017) Based on their phylogenetic relationships as well as genomic structures the subfamily consists of the following genera namely Alpha, Beta, Gamma and Delta coronavirus of which only α-and - coronaviruses are known to affect mammals (Figure 1) (Cui et al., 2019). More than 60 coronaviruses have been isolated from bats, most of which are- corona viruses. Bats are recognized as large and highly mobile repositories of CoV and are also linked with the coevolution of these viruses. (Payne, 2017) These viruses are known to cause respiratory as well as gastrointestinal infections. The widespread of Covid-19 is not the first in history. Similar events have occurred over the past decades, with evidence pointing to a crossover of animal -coronaviruses to humans leading to severe diseases, including the ongoing and evolving pandemic.

During the outbreak of “Severe Acute Respiratory Syndrome” (SARS-CoV), a new coronavirus of -genera was identified in the Guangdong region of southern China in 2002-2003. The origin of the spread was traced back to bats and was transmitted to other animals (civet cats and raccoon dogs) which acted as intermediary hosts. An animal-to-human transmission was then reported. According to WHO reports, the epidemic had a mortality rate of 11%, affecting around 26 countries with...
more than 8000 cases reported, globally. In 2012, almost a decade later; the outbreak of another virus, namely “Middle East respiratory syndrome coronavirus” (MERS-CoV), also thought to have originated from mammalian bats emerged in Saudi Arabia. The dromedary camels acted as intermediate hosts. The majority of outbreaks were identified in Saudi Arabia (80%), followed by the UAE and the Republic of Korea. WHO reported 2279 affected cases with a mortality rate of 34%. (Singhal, 2020) Recently, a novel coronavirus, also having bats as their primary host, has been identified and officially termed as “Severe Acute Respiratory Syndrome Coronavirus-2” or “SARS-CoV-2”. The virus has caused havoc in multiple countries all over the world, raising the bar for global health concerns. (Xie and Chen, 2020) The virus emerged at the end of 2019, in Wuhan, Hubei province, China and has fuelled a brewing pandemic. (Shereen et al., 2020) Therefore, these three pieces of evidence indicate and identify coronavirus infections as zoonotic diseases.

In the present review, we highlight and summarise the origin, evolution, geographical data and also discuss recombination and re-appearance of “SARS-CoV”, “MERS-CoV” and “SARS-CoV-2” respectively.

Figure 1: Coronaviruses Affecting Humans

Severe Acute Respiratory Syndrome Coronavirus (Sars-CoV)
Origin and Evolution
In the 1960s, only two strains of coronaviruses were identified that caused disease in humans: namely “HCoV-229E” and “HCoV-OC43”. They were identified to cause only mild symptoms such as cold otherwise and were not reported to affect infants. However, more severe symptoms were observed in old and immunocompromised individuals. As early as 2003, a previously indeterminate virus related to SARS growth, causing severe lung disease was isolated from humans. At the beginning of the SARS epidemic in the Guangdong territory of southern China, all the early indexed patients showed evidence of animal exposure. Detection of the “SARS-CoV” and its antibodies in palm civets as well as in animal handlers led to the identification of the agent responsible for SARS. (Song et al., 2005) Delineation of the transmission route, originating from horseshoe bats regarded the civet cats to be only intermediary hosts of the virus. This finding strengthened the belief that probably ‘bats’ might be the native hosts in SARS-CoV related infections. Over time, other phylogenetically related were recognized in various provinces of China and from some European, South Asian as well as African countries which were said to be variants of “SARS-CoV”.

According to one 5-year long longitudinal research, the cohabitation of broadly varied SARS-CoVs within bat populations found in a cave of Yunnan region in China and this location is considered as a diversity hotspot. (Hu et al., 2017) Moreover, the viral strains from this location comprise of all genetic components required to produce “SARS-CoV”. Also, as no other direct precursor of SARS-CoV was discovered and also as RNA recombination is frequent within these coronaviruses, (Lai and Cavanagh, 1997) it was hypothesized that the direct precursor of SARS-CoV emerged as a result of recombination in the bats and further conveyed to Himalayan civets or other mammals, which might have transferred the virus to civets through the faecal-oral route. These infected Himalayan civets that were shipped to the market in Guangdong underwent further mutations before spreading to humans leading to the spread and epidemic. This particular hypothesis is in agreement with the previous data that shows the emergence of a direct precursor of SARS-CoV before 2002. (Figure 2 shows the possible mechanisms for SARS-CoV emergence)

Figure 2: Possible Mechanisms for SARS-CoV Emergence

Geographical distribution
This distribution is supported by the SARS-CoV epidemic of 2002–2003. The disease first turned up in southern China’s Guangdong province in November 2002. This region is considered a possible SARS-CoV re-emergence zone. Hong Kong Special Administrative Region of China, Toronto in Canada, Singapore, Chinese Taipei, as well as Hanoi situated in Vietnam were other countries/regions where human-to-human transfer chains took place following the initial importation of the cases. (Severe Acute Respiratory Syndrome, 2020)
Middle East Respiratory Syndrome Coronavirus (Mers-CoV)

Origin and Evolution

While the advent of SARS included palm civets, most cases in the “MERS-CoV” were exposed to dromedary camels. (Paden et al., 2018) Furthermore, “MERS-CoV” strains extracted out of camels were similar to those obtained from humans. (Chu et al., 2019) The specific antibodies for “MERS-CoV” were most prevalent in the Middle East, African as well as Asian camels. (Alagaili et al., 2014) The serum samples of a camel that were collected early in 1983 showed evidence of “MERS-CoV” infections suggesting the presence of “MERS-CoV” in camels from 30 years ago. (Hemida et al., 2010) Although first evidence was found in camels and humans, the root of propagation was considered to be bats as they share the identical genomic structure but show differences in their genomic sequences.

Geographical distribution

Since 2012 around 27 countries have registered MERS cases which included Austria, Algeria, Bahrain, China, Egypt, France, Greece, Germany, Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, the Netherlands, Oman, the Philippines, Qatar, Korea, Saudi Arabia, Tunisia, Thailand, Turkey, the UAE, the UK, the US and Yemen. (World Health Organization, 2020)

Saudi Arabia has registered about 80 per cent of human cases. What we have come to understand that people are infected because of unguarded exposure with infected dromedary camels and affected humans. Cases detected exterior to the Middle East were mostly due to travellers who got infected when in the Middle East and travelled outside. Rare outbreaks have taken place in locations exterior to Near East.

Severe Acute Respiratory Syndrome Coronavirus 2 (Sars-CoV-2)

Origin and Evolution

Recently, by the end of December 2019, Wuhan, which is a growing business centre in China, encountered an epidemic of a unique coronavirus killing more than 800 people and infected >70,000 individuals in first fifty days. It was confirmed that this virus belongs to beta coronaviruses. The Chinese researchers called the novel virus Wuhan coronavirus and 2019 novel coronavirus (2019-nCov). Later, The International Committee on Virus Taxonomy (ICTV) finally officially named the responsible virus as “SARS-CoV-2” and the disease as “COVID-19”. Recently, by the end of 2019, the Chinese government reported WHO about numerous cases reporting pneumonia having unknown aetiology. The outbreak started from Hunan seafood marketplace in Wuhan city in China and quickly affected over 50 people. Live animals such as frogs, bats, birds, snakes, rabbits and marmots are frequently sold in this market. Environmental specimens obtained from this market have also been tested positive, implying that the virus began spreading from there. Additional data about the outbreak was published by China’s National Health Commission on 12th January 2020, suggesting viral pneumonia. The virus was described as ‘novel coronavirus’ from series-based analysis of the patient’s isolates. Although the “SARS-CoV-2” originated from bats, there is uncertainty about the intermediate animal which caused the transmission to humans. The current suspects being Pangolins and Snakes.

Geographical Distribution

Countries affected include China, Italy, USA, Russia, South Korea, Iran, Pakistan, Afghanistan, Africa, India, Mexico, Australia, Indonesia, Thailand, Brazil and India. It has been declared as a Pandemic and WHO announced a “public health emergency of international concern” on 30th January 2020.

Ecology of Human Coronaviruses

With the current data and pieces of evidence, seven coronaviruses are well-known to produce infections in humans namely “229E”, “OC43”, “NL63”, “HKU1”, “SARS-CoV”, “MERS-CoV” and “SARS-CoV-2”. Amongst these “229E”, “OC43”, “NL63”, and “HKU1” are now well configured in humans and greatly circulate in humans causing mild infection in immunocompromised individuals with no maintained animal repository. (Su et al., 2016) However, “SARS-CoV” and “MERS-CoV” have not been well preserved in humans and thus disseminate into zoonotic repositories with sporadic spillover within the susceptible human community via an intermediate host.

Possibility of Future Outbreaks and Coronavirus Recombination

Although the primary human outbreak (SARS-CoV and MERS-CoV) were managed efficiently and possible host cities were eliminated as a preventive practice, also there exists growing data that various bat species act as repositories not merely for SARS-like coronaviruses besides that for several variants of CoV, many of which are reasonably close associates of circulating human strains. Bats have been subject to higher scrutiny as harbingers of the RNA-mediated infections and were identified as the primary repository of pre-existing HCoV strains. (Graham and Baric, 2010)
With multiple circulating species of CoVs in various animal species that share constant interaction, the next recombinant CoV might likely emerge, causing another explosion within the human population. Presently no efficient drug or vaccine is available for management of emerging “SARS-CoV-2” pathogen. It propagates rapidly leading to the death of affected patients with a present fatality rate of 2.3%, which can alter with coming time (Wu and Mcgoogan, 2020). The high rate of infection in the elderly group may be attributed to the existence of underlying diseases such as hypertension, diabetes mellitus, obesity, etc., which are more prevalent in old age. Besides, the body’s immune system is weakened in older individuals. (Ganguly et al., 1995) Developments in the field of prevention need to be in harmony with developments in case management. (Jain and Sharma, 2017)

CONCLUSIONS

The outbreak of these viruses has threatened the economic, medical, and public health systems of the countries involved. Due to the incidence and high genetic variation of bat “SARS-CoV”, “MERS-CoV” and “SARS-CoV-2” and the frequent recombination of coronaviruses, new variants are expected to emerge coming future. It has been widely accepted that many viruses existed for quite a long time in their natural reservoirs. The consistent spillover of these viruses into humans as well as other animals from natural hosts is contributed significantly to various human actions like advanced agricultural methods plus urbanization. Hence, the supreme way of preventing viral zoonotic diseases is by establishing constraints and following crucial measures, including 1) knowledge about the prevalence of pre-existing and circulating HCoV. 2) Coronavirus recombination and widespread in animals. 3) knowing potential animals that could serve in mixing and recombination of these viruses. 4) A monitoring system to track and predict potential virulence of recombinant animal CoV. 5) preventing possible zoonosis (animal-to-human) and reverse zoonosis (human-to-animal).

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Conflict of Interest

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