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Ebola Virus and SARS-CoV-2: Similarities and Differences

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Abstract

Ebola virus and the novel coronavirus of 2019, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) share many similarities in origin although transmission, morbidity and mortality are vastly different. In both cases the viruses are zoonotic pathogens and are thought to have originated in bats. The intermediate animals for Ebola virus include primates, antelopes and various rodents, and contact with these animals resulted in infection of humans. As of this writing, the intermediate host for SARS-CoV-2 remains a mystery although pangolins have been implicated. Ebola virus disease is spread by direct contact with body fluids and is not considered to be an airborne disease. SARS-CoV-2 is a respiratory tract infection, is highly infectious (more contagious than previous SARS-CoV and MERS-CoV, two betacoronaviruses causing the Severe Acute Respiratory Syndrome or SARS, and the Middle East Respiratory Syndrome, respectively) and is spread via airborne means. The other main difference is in regard to pathology and mortality. The Zaire Ebolavirus strain was 90% fatal and was eventually contained to small areas whereas fatality of SARS-CoV-2, as of this writing varies apparently across countries (from 2.1 % in Turkey to 12.8 % in Italy and Belgium) although the precise case fatality ratio is still unknown. The fact that most SARS-CoV-2 cases have resulted in asymptomatic or in a mild disease (COVID-19) mimicking a common cold or flu, has made it difficult to contain the infection. Infected individuals may think they have a seasonal cold, contact others and travel to new areas where the disease can spread. This has resulted in COVID-19 becoming a pandemic, which is currently going throughout the world. Therefore, a final picture for a more precise comparison between these two infections may be concluded in the next months.

KEY WORDS: ECOVID-19; SARS-CoV-2; coronavirus; Ebola virus

Riassunto

stuIl virus Ebola ed il nuovo Coronavirus 2019, chiamato SARS-CoV-2 (Sindrome respiratoria acuta severa da coronavirus 2) condividono molte somiglianze nella loro origine, nonostante la trasmissione, la morbilità e la mortalità siano largamente differenti. In entrambi i casi, i virus sono patogeni che causano zoonosi e si pensa che abbiano origine nei pipistrelli. Gli ospiti intermedi dell'Ebola includono i primati, le antilopi e vari roditori, ed il contatto con questi animali determina l'infezione negli uomini. In questo momento, l'ospite intermedio del virus resta un mistero sebbene i pangolini sono stati implicati. La malattia causata dal virus Ebola si diffonde attraverso il contatto diretto con i fluidi corporei e non è considerate una malattia trasmessa per via aerea. Il SARS-CoV-2 da un' infezione del tratto respiratorio, è altamente contagioso (più contagioso del precedente SARS-CoV e del MERS-CoV, due betacoronavirus che causano rispettivamemte la Sindrome Respiratoria Acuta Grave e Sindrome Respiratoria del Medio Oriente) ed è diffuso pe via aerea. L'altra principale differenza riguarda la patologia e la mortalità. Il ceppo Zaire dell'Ebolavirus ha una mortalità del 90% ed era in realtà confinato a piccole aree dove la mortalità del SARS-CoV-2, in questo momento, varia apparentemente tra i Paesi (dal 2.1 % in Turchia al 12.8 % in Italia e Belgio) sebbene il tasso di mortalità preciso è ancora sconosciuto. Il fatto che la maggior parte dei casi di SARS-CoV-2 determinano una forma asintomatica o leggera di malattia da COVID-19 che simula un commune raffreddore o un influenza, ha reso difficile il contenimento dell'infezione. Individui infetti possono credere di avere un influenza stagionale, entrare in contatto con gli altri e viaggiare in nuove aree dove la malattia può diffondersi. Questo ha fatto si che il Covid 19 sia diventato una pandemia, che si sta attualmente diffondendo in tutto il mondo. Pertanto, il quadro finale per un confronto più preciso tra queste due infezioni può essere concluso nei prossimi mesi.

TAKE-HOME MESSAGE

Ebola virus and SARS-CoV-2 are thought have originated in bats and spread to humans through intermediate hosts. Ebola virus disease has high fatalities whereas the majority of COVID-19 cases are mild with many not knowing they are infected. This has resulted in COVID-19 becoming a pandemic due to difficulty in containing its spread.

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INTRODUCTION

In 2020, a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Figure 1) literally held the world captive as a remarkable pandemic emerged. The entire world had to shut down normal everyday operations, particularly in regards to how people gather together for meals and other events. In December, 2019, the coronavirus outbreak began in the city of Wuhan, in China's Hubei province, and has since spread across the world, infecting over a million of people and killing hundreds of thousands, as of April, 17 2020 [1, 2]. Borders to Canada and Mexico were closed and entire states mandated that people stay indoors. In the United States, numerous activities and gatherings were cancelled or postponed as the nation scrambled to halt the spread of the highly contagious disease. In most cases, these actions were unprecedented [3]. The pandemic has had a major economic impact across the globe and these stringent measures were necessary in order to hopefully contain the virus.

It is interesting to note that this virus had a similar origin to the Ebola virus, which was highly fatal [4]. Both of these diseases were zoonotic in origin, probably originating in bats, and there was no preexisting immunity in the human population to either one. So far, the disease from SARS-CoV-2 (COVID-19) has been relatively mild in most infected patients although it is considered to be more deadly than the flu [5]. However, this becomes a double-edged sword in that those who are infected with SARS-CoV-2 may not know that they are infected or think that they have a common cold, flu or allergy and consequently spread the disease to others. Thus, this has made COVID-19 difficult to contain and could result in continued spread worldwide resulting in more deaths [2, 6]. It is further hoped that adequate treatment and eventually a vaccine can be developed. Thus, it is the aim of this article to compare the similarities in the origin of Ebola virus and SARS-CoV-2, how they have vastly different consequences and why it was so difficult to contain COVID-19.

DISCUSSION

Origin and transmission of Ebola virus and SARS-CoV-2

Ebola viruses belong to the *Filoviridae* family of viruses and are negative-sense RNA viruses with helical symmetry. There are several subtypes of Ebola viruses and are named after the region in Africa where they were identified. These viruses cause an acute and devastating disease that is often deadly (as high as 90% fatalities) and is now referred to as Ebola virus disease (previously known as Ebola hemorrhagic fever). Surprisingly, although these viruses were first identified in 1976, they are not considered to be new viruses and are suspected of splitting from other viruses thousands of years ago [4, 7]. Ebola virus is transmitted by direct contact, via body fluids (such as blood, feces or vomit) or fomites which have been contaminated by body fluids [4]. Thus, this virus is not transmitted via typical airborne means (coughing, sneezing, etc.) meaning that it does not spread as easily as many other viral diseases [8]. Humans are neither the natural host nor reservoir for Ebola virus. It is believed that fruit bats serve as the natural hosts and the infected bats then transmit the virus to primates, antelope, rodents and other animals via excrement. Humans then contact the virus when they hunt and kill these animals [7]. Thus, it is a zoonotic disease that is spread between animals and humans.

The novel coronavirus (SARS CoV-2) is a member of the *Coronaviridae* family of viruses. This family includes the SARS (severe acute respiratory syndrome) virus (SARS CoV) and the MERS (Middle East respiratory syndrome) virus (MERS-CoV) [9, 10]. This is a positive-sense RNA virus with helical symmetry. It has several projections from the surface of the virion that give it a crown-like appearance or that of a solar corona, hence the name coronavirus [10].

Like Ebola, SARS CoV-2 is thought to use bats as the main host. This is because a comparison of the genetic sequences of SARS

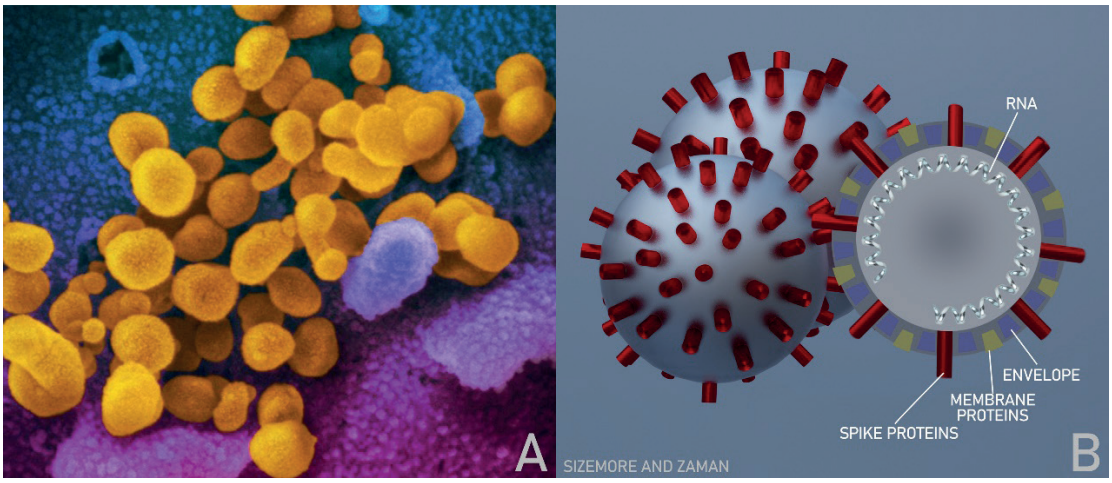

Figure 1(A) An electron micrograph released by the U.S. National Institutes of Health showing the Novel Coronavirus SARS-CoV-2 (in yellow), on cell surfaces (in blue and pink), and (**B**) An illustration of the virus with spike proteins and other viral components.

CoV-2 and two coronaviruses that originated in bats showed 88% similarity [11]. Bats are large animals, live in colonies and are able to travel over wide areas. Somehow, they manage to harbor viruses without becoming sick. Thus, it is not surprising that bats serve as reservoirs for many diseases [12]. However, in the case of COVID-19, it is not clear at present which animal served as the intermediary link between the bat and humans. Apparently, bat droppings infected another animal which was then used for food or other purposes and when butchered, infected humans. The original outbreak in China of COVID-19 is thought to have occurred at the Huanan seafood market (a wet market) in Wuhan, China where several exotic animals were sold. Bats were not thought to be at the market, so another animal probably was the intermediate host. Although snakes were suggested as hosts, it is not clear if they could be infected with SARS Cov-2 [5]. Many believe that pangolins (often called a scaly anteater) were involved. These animals, which were present at the market in Wuhan, are prized in China as a delicacy and the scales are used for various remedies. Wildlife markets as such were supposed to be banned in China and it may take an outbreak such as this to finally close them and protect animals that could become endangered [13]. Thus, both Ebola virus and SARS CoV-2 probably originated in bats and then spread to humans via an intermediate animal. However, while Ebola is extremely deadly, most cases of the novel coronavirus have been mild. Infection with SARS-CoV-2 can be transmitted also by asymptomatic people [14], and cause mild to severe respiratory illnesses including cough, shortness of breath and fever. The very first cases of COVID-19 were identified in China in December 2019, and then quickly spread to many countries of the world [1, 2, 15, 16].

Morbidity and mortality of Ebola virus and SARS-CoV-2

Ebola viruses are some of the deadliest viruses known to man. It was first identified in 1976 in separate outbreaks in Africa. The virus is transferred via bodily fluids and enters through contact with mucosal tissue or breaks in the skin. The incubation period is usually 8-10 days. The virus replicates in monocytes, macrophages or dendritic cells which facilitate dissemination of the virus throughout the body via the lymphatic system [17]. Other cells can then be secondarily infected. This is followed by a strong cytokine and inflammatory mediator release resulting in a 'cytokine storm' [17]. This brings on inflammation and an increase in permeability. This leads to endothelial damage, increased vascular permeability, a reduction in blood pressure, shock, and various blood vessels leaking blood and plasma. There can be diffuse intravascular coagulation which leads to hemorrhage and bleeding from

the mouth, rectum, eyes, ears and/or nose [18]. The average Ebola virus disease fatality rate is approximately 50% although the Zaire strain showed 90% fatality [4].

The novel coronavirus, SARS-CoV-2, is an airborne disease and is spread by respiratory secretions in much the same manner that flu viruses are spread [19]. The virus shares 86% of the same genetic sequences with the original SARS virus (SARS-CoV1, now referred to as SARS-classic) [20]. However, SARS-CoV-2 is more contagious than both SARS-classic and the related Middle East Respiratory syndrome-related coronavirus, MERS-CoV [9]. This is thought to be due to the spike protein of SARS-CoV-2 having a site that is activated by furin, an enzyme found in several human tissues. This allows the virus to bind about 10 times more tightly to its receptor (angiotensin-converting enzyme 2 - ACE2) than SARS-classic, and to attack several organs at once. It has been suggested that blocking ACE2 receptors could prevent the virus from entering cells [20].

The resulting disease from SARS-CoV-2, named COVID-19, has various sequelae although the upper respiratory tract and the lower respiratory tract are the main points of attack. Symptoms can mimic a common cold, flu or allergic response. However, in some cases it can lead to severe pneumonia and patients may require ventilation [19]. According to a large Chinese study, more than 80% of cases were not severe [9]. The cases were classified as mild if they did not show pneumonia or only had mild pneumonia. Severe cases showed lung involvement including shortness of breath and other lung problems. Critical cases involved respiratory failure and multiple severe organ problems. In an Italian study, in 20–30% of COVID-19 patients admitted to the intensive care unit (ICU), severe hypoxemia was associated with compliance values $< 40\,ml/cmH_2O$, indicating severe ARDS [21]. In a Chinese study, about 14% of cases were severe and under 5 per cent were critical and fatalities were 2.3% [6, 9].

A federal study reported by CNN on March 19, 2020, has given the breakdown of the hospitalized COVID-19 patients by percentage [22]. The CDC analyzed 2,500 cases, of which 508 patients were hospitalized. Among the hospitalized, 20 percent were aged between 20-44, 18 percent between 45-54, and 26 percent between 65-84. The report indicated that of the 121 patients who were admitted to ICU, none of them were 19 or younger, 12 percent were between the ages of 20-44 and 36 percent between 45-64. The report also indicated that fatality accounted for 10-27 percent among the patients over 85 years, 3-11% among 65-84 years old and less than 1 percent among 20-54 years old. No fatalities were reported in patients who were 19 or younger. Several pre-existing conditions including asthma, diabetes, hypertension, heart disease and obesity have been associated with severe cases [23]. Thus, in most individuals, the disease is mild. However, in those who are older or with co-morbidity, it can lead to a very serious illness with the potential for fatality.

Prevention, treatment and vaccination for Ebola virus and SARS- CoV-2

A recent article suggested that many lessons learned from Ebola could have helped prevent the spread of COVID-19 [8]. The author noted that both Ebola and COVID-19 could be considered as 'family diseases' since they are often spread in homes. Thus, in response to Ebola, West Africans have had to implement not only restricted travel but various safeguards in the home to prevent transmission. Currently, measures are in place around the world where the entire human population has been asked to quarantine themselves, practice 'social distancing', wear facemasks when they venture out and wash their hands often. These measures should curtail not only the transmission of SARS-CoV-2 and Ebola but numerous other diseases including influenza [24].

With regard to treatment of SARS CoV-2, Chloroquine, an antimalarial drug had shown the potential to treat various viruses in mice. Earlier studies indicated that this drug was effective against the original SARS virus, a

close relative of SARS CoV-2 [25]. The drug is toxic in high doses and French researchers have tested hydroxychloroquine, a less toxic version of chloroquine on a few dozen SARS CoV-2-infected patients. The trial indicated that the drug might help shorten the infection time; however, WHO has indicated that there is no evidence that the drug could be effective treating COVID-19 patients [26]. Nevertheless, WHO then announced a 'megatrial' of potential coronavirus treatments including hydroxychloroquine [27].

In mid-March of 2017, China's National Center for Biotechnology Development announced that a Japanese anti-influenza drug called Avigan Favipiravir (T-705) was found to be effective against SARS-CoV-2. This drug is a broad-spectrum inhibitor of viral RNA polymerase. This drug was used in 2 clinical trials in Wuhan and Shenzhen involving 240 and 80 patients respectively. Chinese authorities also said that this medicine is effective treating COVID-19 related pneumonia without any apparent side effects and infected patients showed positive results after 4 days of treatment. One of these clinical trials reported improvements in lung conditions in 91 patients which was confirmed by X-ray. This report also indicated that a Chinese pharmaceutical company has been approved for mass production of this drug. Although Avigan was originally developed in Japan, it was not distributed in the Japanese market. According to this report, Avigan could be a promising drug against other untreatable RNA viral infections such as arenaviruses, bunyaviruses, and filoviruses. All of these infections cause fatal hemorrhagic fever [28]. Currently, there is no effective vaccine to prevent infections with SARS-CoV-2. Therefore, developing a safe and effective vaccine against SARS-CoV-2 is an urgent health priority. The NIH (National Institute of Health) reported the first human trial of an investigational COVID-19 vaccine on March 16, 2020. This trial will involve 45 healthy adult volunteers ages 18 to 55 years and they will receive the vaccine over a period of 6 weeks. The vaccine, called mRNA-1273 was developed by NIAID (National Institute of Allergy and Infectious Disease) scientists and their collaborators. The vaccine was made using a short segment of genetic code that scientists were able to copy from the COVID-19 virus. In order to determine the safety and ability of this mRNA vaccine to trigger an immune response, the study will evaluate various doses of the vaccine in three different cohorts with 15 people in each dose regiment. Each cohort will receive two treatments of this vaccine, 28 days apart with doses of 25 microgram (mcg), 100 mcg or 250 mcg [29]. According to British Broadcast Center (BBC), if everything goes well, it might take up to 18 months before a vaccine is available for the public [30]. Regeneron Pharmaceutical in New York is developing a passive vaccine called REGN 3048-3051. This will be an antibody cocktail made of antibodies developed in genetically engineered mice and antibodies isolated form patients who recovered from COVID-19. This cocktail should be able to fight both the virus and its mutants by blocking spike proteins on the surface of the virus and prevent them bonding with the host cells. According to Regeneron, this drug can be used to treat both the SARS CoV-2-infected patients and healthy people as a preventive measure. The drug could be available for human testing by the summer of 2020. Using the same technology, this company has developed a treatment for the Ebola virus, which is under FDA (Federal Food and Drug Administration) review [31]. INO-4800 is a DNA plasmid developed by Inovio Pharmaceutical in Pennsylvania, USA. These small circular pieces of DNA are designed to enter cells where the virus may be replicating and trigger natural immune responses. INO-4800 was developed following the publication of the sequence of COVID-19 online. This vaccine has produced desirable immune responses in animal models and the company hopes to begin human trials in April 2020 with 30 health human subjects. Inovio has already developed a vaccine for MERS using the same method [31]. Gonoshasthaya Kendra (GK), a public healthcare organization in Bangladesh, in collaboration

with its sister concern, RNA Biotech Limited has developed a rapid method called 'Gonoshasthaya Rapid Dot Blot' to test for COVID-19. According to Dr. Zafrullah Chowdhury, the founder of GK, the US Centers for Disease Control and Prevention (CDC) has confirmed that they would adopt the system. The new method would take only 5-10 minutes to test for coronavirus and would cost about 2.5-3.0 USD per test [32].

Comparison of Ebola Virus and SARS-CoV-2: Why one was more challenging to contain

Ebola virus, SARS-classic and MERS CoV all had their origins in bats. It is currently thought that SARS-CoV-2 also originated in bats and like the others, spread to humans via an intermediate animal. The intermediate animal for COVID-19 is not known at this time. However, Ebola virus and SARS-CoV-2 have vastly different means of spread and result in totally different types of illnesses. Ebola Virus Disease (EVD) has an average fatality rate of 50% but has been as high as 90% in certain strains. One key point is that it killed quickly. In over 80% of COVID-19, the disease is likely to be relatively mild with fatalities mainly in older individuals or those with underlying medical problems. Depending on the country, fatalities have ranged from 2.1% in Turkey to 17.8% in Italy and Belgium [2]. However, the precise case fatality ratio is not known. Unlike COVID-19, EBV did not become a pandemic and was able to be contained to small areas. However, with SARS-CoV-2 many individuals either did not know that they were infected or had symptoms similar to a common cold, a seasonal allergy or the flu. Thus, because of globalization so many in the early stages of an infectious disease could be halfway around the world in 12–15 hours therefore functioning as a vector for that disease, the SARSCoV2 virus spread world-wide resulting in a major pandemic [33].

The consequences of this pandemic has thus resulted in major social and economic disruptions. Borders to neighboring countries have been shut down and people have been forced to be on lock-down. Many every day routines came to a halt. Schools were shut down and people were told not to gather in groups of more than ten. Numerous sporting and entertainment events were cancelled or postponed, including the 2020 Olympics in Japan. Several individuals, particularly those in the food and entertainment industries, have either lost their jobs or are working with very few clienteles. We will not know the full economic impact until much later but the world-wide economy has suffered a great deal.

Thus, COVID-19 has been a double-edged sword in that, while the disease is usually mild, this caused it to not be contained and the virus was able to be spread world-wide. Of course, no one is suggesting that it would have been better to have a more fatal disease spread since it could have been contained easier. But it does show that any disease that is more deadly, potentially could be spread throughout the world if it did not kill its victims quickly. In short, any disease is only an airplane ride away from becoming a pandemic.

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