Journal of Education for Pure Science- University of Thi-Qar
Vol.13, No.3 (Sept.2023)
Website: jceps.utq.edu.iq *Email jceps@eps.utq.edu.iq*

DOI: http://doi.org/10.32792/utq.jceps.10.01.01

COVID19 – Brief review of SARS-CoV-2

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Received 18/5/2023, Accepted 1/9/2023, Published 21/9/2023

Abstract:

In December 2019, a respiratory disease called COVID19 appeared in the city of Wuhan, China, and spread globally. This disease is caused by the SARS-CoV-2 coronavirus, and constitutes the greatest threat to public health in recent decades. Currently, it is vital to study this disease at a multidisciplinary level to find effective treatments, as well as to understand its development and impact within human history. This review article focuses on recapitulating the information known to date about this virus, its origin, characteristics, and the strategies that various governments have adopted in recent months.

Keywords: COVID19, coronavirus, SARS-CoV, SARS-CoV2.

1-Introduction

In December 2019, an unusual case of respiratory illness was reported in Wuhan, China. Quickly, this disease spread throughout the world, creating global alarm and concern. The pathogen causing this disease was identified as a new RNA-type virus belonging to the genus Betacoronavirus, which is within the Coronaviridae family. Due to the phylogenetic similarity of said virus with the previously identified SARS-CoV (Coronavirus causing severe acute respiratory syndrome), it was renamed SARS-CoV-2 (Guan *et al.*, 2020).

The disease was then named COVID19 by the World Health Organization. Currently, more than 6.7 million people have been affected by this disease, causing the death of almost 400,000 people worldwide (figure 1) (Guan *et al.*, 2020; Castagnoli *et al.*, 2020; WHO, 2020).

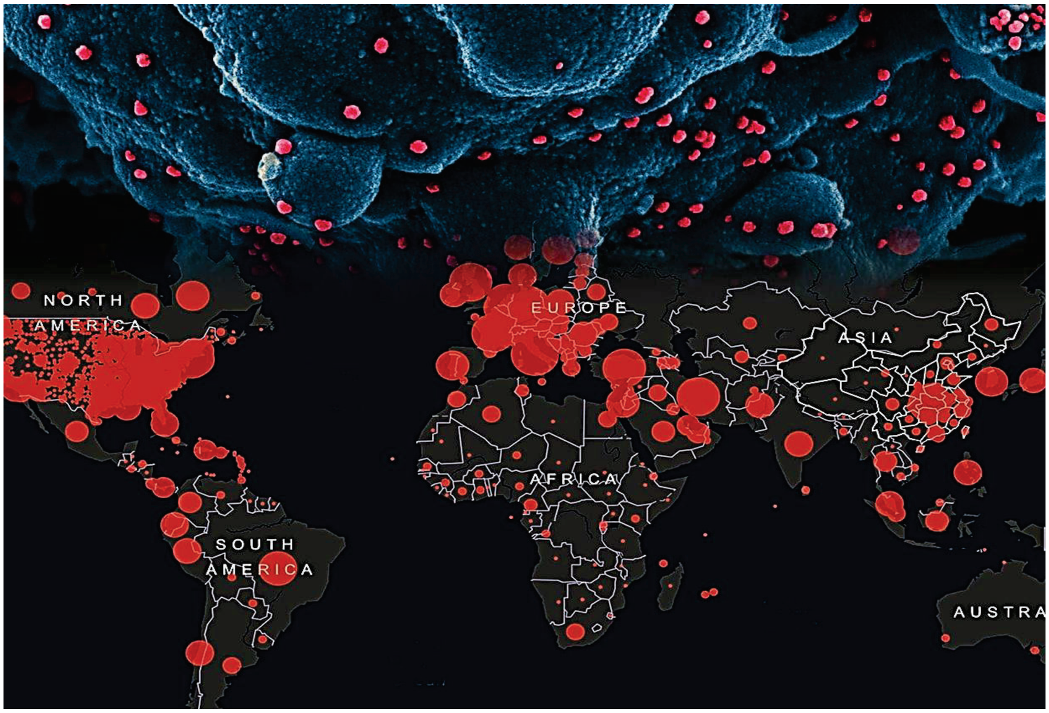

Fig.1: A global view of SARS-CoV-2 cases from the Center for Systems Science and Engineering at Johns Hopkins University (JHU)

The possible origin of this virus has been widely discussed. However, there are no definitive studies that can answer this question. Since this disease appeared in Wuhan, it was directly related to the commercialization and consumption of wild animals in local markets. Based on this, in recent months different studies have been compiled that aim to elucidate the origin of SARS-CoV-2, as well as its impact at the epidemiological level and possible treatments (Guan *et al*., 2020). This article discusses the different theories concerning to (1) the origin of said virus, (2) the characteristics of the virus, (3) the symptoms of the disease, and (4) the medical and social strategies adopted in recent weeks.

2- Origin of SARS-CoV-2: Was it a bat or a pangolin

The origin of SARS-CoV-2 is a mystery, however, various genomic studies carried out on this virus determined that its sequence is 96% identical to a type of coronavirus found in bats. This virus, named RaTG13, was previously isolated and reported in Yunnan province, China. Despite the similarity in its genomic sequence, RaTG13 has important differences with respect to the virus in humans (Forster *et al*., 2020; Zhang *et al*., 2020).

The “spike” proteins present in all coronaviruses have a cavity called the receptor-binding domain, which is vital for the virus to recognize certain molecules (receptors) on the surface of cells and enter them (ACE2 receptors, in the case of humans). This domain is different between both coronaviruses, which means that RaTG13 is not capable of infecting humans. Since various publications in recent years have shown a high incidence of these coronaviruses in bats, these animals are considered to be a natural reservoir of this family of viruses (Cyranoski, 2020).

Other studies have made it possible to identify similar coronaviruses in other animals, such as the pangolin. In fact, the Pangolin-CoV virus is 91% identical to SARS-CoV-2, and is the second closest phylogenetically to this virus, after RaTG13 (Zhang *et al*., 2020) (Figure 2). However, this virus does have a receptor binding domain, almost identical to that of humans (Cyranoski, 2020). Previous studies identified diverse populations of pangolins infected with this virus. In 2019, a study reported in December 21 pangolins that were recovered in poor conditions within a nature reserve, of which 16 died. All animals that died had pulmonary fibrosis, and some also had hepatomegaly and splenomegaly. These symptoms are common in people who develop SARS-CoV-2 and suggest similarities in the pathologies caused by both viruses (Liu *et al*., 2019).

The only sure thing is that SARS-CoV-2, or a very similar ancestor, was hidden in one of these animals for decades. In fact, it is believed that the lineage that gave rise to the current coronavirus may have diverged from Pangolin-CoV about 140 years ago. Then, 40-70 years ago, that ancestor split from the coronavirus in bats (which lost its human receptor-binding domain). This hypothesis suggests a long evolutionary history within bats and pangolins, and that the virus is still present within these "natural reservoirs" (Cyranoski, 2020).

3- Characteristics of SARS-CoV-2

After the appearance of SARS-CoV in 2003, the current outbreak of SARS-CoV-2 has made it possible to study how the virus has evolved and has developed various adaptations that have given it greater lethality. Unlike other nearby viruses, SARS-CoV-2 easily attacks human cells at different levels: first in the lungs and throat, and once inside, the virus makes use of an arsenal of molecules that attack various organs (Cyranoski, 2020).

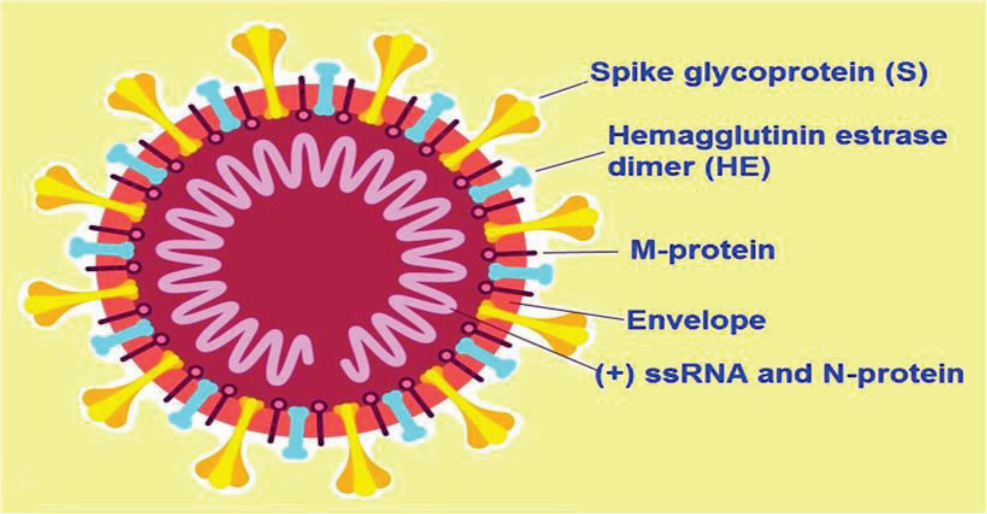

Fig. 2: Typical structure of SARS-CoV-2

SARS-CoV-2 is approximately 125nm in diameter, and is large compared to other RNA-type viruses. In fact, its genome consists of 30,000 bases and encodes 29 proteins, which makes it the RNA virus with the longest genome (3 times larger than the HIV and Hepatitis C viruses; and 2 times larger than the influenza virus) (Kim *et al*., 2020; Cyranoski, 2020).

SARS-CoV-2 are also among the few RNA viruses that have a genomic proofreading mechanism, which prevents them from accumulating unfavorable mutations. For this reason, some drugs such as ribavirin (which induces mutations) are ineffective against this virus. In fact, mutations can both benefit and favor viruses. In the case of influenza, it mutates 3 times faster than coronaviruses, and this allows it to evolve faster (Cyranoski, 2020).

However, SARS-CoV-2 capable of frequent recombination by exchanging part of their RNA with other coronaviruses. In other words, when two distant coronaviruses manage to find each other within the same cell, they can recombine and create new versions capable of infecting new cell types, and even jumping to other species. This is often the case in bats, which carry 61 viruses capable of infecting humans. In fact, the three coronaviruses that have caused respiratory diseases worldwide (SARS-CoV, SARS-CoV-2 and MERS-CoV) are known to come from bats (Cyranoski, 2020).

To infect cells, SARS-CoV-2 uses a spike-shaped protein that protrudes from its surface and attaches to the cell membrane. Genomic analyzes of this new coronavirus have revealed that these proteins, known as “spikes”, have an activation site that is recognized by an enzyme called furin. This is significant because furin is found in many human tissues, including the lungs, liver, and small intestine; which means that the virus has the potential to attack multiple organs (Mallapaty, 2020).

4- Symptoms of SARS-CoV-2

The main symptoms that occur in this disease are airway complications and the development of pulmonary fibrosis in patients at risk (Ledford, 2020). Patients may initially experience symptoms in the nose or throat, producing cough and a disruption between taste and smell, and the symptoms may end there; or it can travel down to the lungs and damage them. How it gets there, either by moving from cell to cell, or through fluids, is unknown. However, if it reaches the lung, pneumonia occurs. The ability of SARS-CoV-2 to rapidly infect and reproduce in the upper respiratory tract was surprising to the researchers, as SARS-CoV does not have such an ability (Cyranoski, 2020).

In fact, in the case of SARS-CoV-2, the viral particles are capable of passing from the throat to the saliva (infecting other people) even before the symptoms begin. In addition, SARS-CoV-2 is known to possess an ACE2 receptor-binding domain that is 10-20 times more efficient than that present in SARS-CoV. These characteristics make the new SARS-CoV-2 much more effective at infecting people than SARS-CoV (Cyranoski, 2020).

However, despite the large number of fatalities associated with SARS-CoV-2, the risk of death appears to be lower than that of SARS-CoV or MERS-CoV, which they are also transmitted through the air and affect the respiratory tract (Guan *et al*., 2020; Lu *et al*., 2020).

At the pulmonary level, all these coronaviruses infect and destroy the cellular barrier that separates the pulmonary alveoli from the capillaries, causing the liquid inside the alveoli to leak and block the passage of oxygen into the blood. In addition to this, other cells, such as macrophages, also block the airways at the same time. A good immune system can clean this up, but an over activated system can create tissue damage if the inflammation is too severe. If this is the case, the lungs never recover and the person dies.

Despite all the information collected, it is not known exactly if the lethality comes from the virus itself, or from the response of the immune system, which overloads the patient's organs and this makes it difficult for specialists to determine the best way to treat the virus. infected people (Cyranoski, 2020).

In fact, various clinical data suggest that the immune system plays a large part in the decline and death of people diagnosed with SARS-CoV-2. That is, after the virus affects the lungs, high levels of cytokines are produced in the blood that increase the immune response. This response depends on a small but powerful signaling protein called interleukin-6 (IL-6). This protein attracts some components of the immune system, such as macrophages, which increase inflammation and are capable of damaging normal lung cells. For such reasons, certain treatments against this disease are aimed at suppressing the immune response (such as the use of steroids), however, this may decrease the body's ability to monitor the infection (Ledford, 2020).

The ideal strategy would then be to use a drug that blocks the activity of IL-6 and reduces the flow of macrophages into the lungs. Such drugs (IL-6 inhibitors) already exist, and are frequently used in the treatment of rheumatoid arthritis and other disorders (Ledford, 2020).

All these characteristics make SARS-CoV-2 a highly contagious disease, but also one that is difficult to treat as it widely affects the immune system, since patients not only present direct damage to the respiratory tract, but also other damage (such as that caused by excess cytokines) generate failures in various tissues and organs such as the intestine, heart, blood, sperm, eyes and possibly the brain (Cyranoski, 2020).

5- Strategies adopted against SARS-CoV-2

Classically, it is believed that viral diseases that affect the respiratory tract require very small infectious agents (<5um) since the larger particles settle and do not remain in the air. However, many of these respiratory diseases can also be transmitted by skin contact, or ventilation in certain circumstances (by artificial ventilation or intubation in hospitals). Regarding the SARS-CoV-2 outbreak, it was long discussed whether the virus could be transmitted through the air and what precautionary measures should be taken to prevent its spread (Seto, 2015).

The first measure suggested by the WHO, and adopted by various countries, was social distancing, which consists of avoiding crowds of people and keeping a distance of 2 meters between them. This suggestion is based on the premise that SARS-CoV-2, being a large and heavy virus, cannot remain in the air and settles less than 2 meters after being expelled through the respiratory tract. Rapid reaction, quarantine, and social distancing measures (such as school and business closures) have helped reduce transmission of the virus in many countries (Seto, 2015).

The effectiveness of the measures adopted by different governments to predict transmission and infection rates in their regions is currently being studied. This information will be vital so that these governments can design strategies that allow the population to return to normal activities and avoid secondary waves of infection. The platform put into service by the WHO collects information from various countries and research centers in order to standardize this information and allow it to be understood globally (Gibney, 2020; WHO, 2020).

In the case of the American continent, the bad decisions made by some governments have triggered the number of cases during the last two months. Countries such as the United States and Brazil currently have the highest number of infections in their respective regions, and this number is increasing day by day. Unlike America, a flatter curve has been reached in Europe, in which the number of infections is stable and has begun to decrease. This context has allowed various countries to resume work activities, still protecting their public health (WHO, 2020).

6. Conclusions

The scientific and medical community has struggled to understand the nature of SARS-CoV-2 in recent months, and has struggled to contain the spread of this disease in almost every nation in the world. Despite efforts, it is still not possible to control the progress of this pandemic, nor has it been possible to obtain an effective treatment against it.

The origin of SARS-CoV-2 is also a mystery, however, there is evidence suggesting a zoonotic origin, involving both bats and pangolins, in China. The eating habits in this region probably facilitated the jump of this virus to humans. This, added to the little political and social organization worldwide, has influenced the spread of the virus in all countries. Within the historical context, this pandemic marks a before and after in global public health, which we hope can be taken responsibly and as an example in the face of future health crises.

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