

**ARTÍCULO DE REVISIÓN**  
**Sección "Shakespeare"**

## COVID-19: deadly disease for patients with chronic non-communicable diseases

### COVID-19: enfermedad mortal para pacientes con enfermedades crónicas no transmisibles

Miguel Alejandro Montalvo Sosa<sup>1</sup>  , Rafael Alejandro Ávalo Valdés<sup>1</sup> , Francisco Javier Rodríguez Molina<sup>1</sup> 

<sup>1</sup>University of Medical Sciences of Cienfuegos, Cuba

 Correspondence to: [alejandro24@nauta.cu](mailto:alejandro24@nauta.cu)

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## ABSTRACT

COVID-19 is the most recently discovered infectious disease caused by the coronavirus. Both this virus, and the disease it causes were unknown before the outbreak in Wuhan, China, in December 2019. COVID-19 is currently a pandemic that affects many countries around the world. Chronic non-communicable diseases are among the leading causes of death and disability in the world, so their controls are important since it is a tendency for people suffering from any of these diseases to develop a serious form of COVID-19. The objective of this bibliographic review was to explain why people with chronic non-communicable diseases develop more serious forms of COVID-19. For this, a total of 25 bibliographic sources were consulted. It was concluded that the presence of chronic non-communicable disease causes a decrease in the immunity of people making them with it more vulnerable to serious forms of the disease.

**Key words:** COVID-19; coronavirus; pandemic; chronic diseases

## RESUMEN

La COVID-19 es la enfermedad infecciosa descubierta más recientemente causada por el coronavirus. Tanto este virus como la enfermedad que causa eran desconocidos antes del brote ocurrido en Wuhan, China, en diciembre de 2019. La COVID-19 es actualmente una pandemia que afecta a muchos países del mundo. Las enfermedades crónicas no transmisibles se encuentran entre las principales causas de muerte y discapacidad en el mundo, por lo que su control es importantes ya que es una tendencia para las personas que padecen alguna de estas enfermedades a desarrollar una forma grave de COVID-19. El objetivo de esta revisión bibliográfica fue explicar por qué las personas con enfermedades crónicas no transmisibles desarrollan formas más graves de COVID-19. Para ello, se consultaron un total de 25 fuentes bibliográficas. Se concluyó que la presencia de enfermedades crónicas no transmisibles causa una disminución en la inmunidad de las personas que las hacen más vulnerables a las formas graves de la enfermedad.

**Palabras clave:** COVID-19; coronavirus; pandemia; enfermedades crónicas

## INTRODUCTION

The coronavirus, which is scientifically known as Orthocoronavirinae, is not new. Its ancestors date back to the 9<sup>th</sup> century B.C. and there have been several outbreaks that have emerged throughout history. It was in the 1990s that the first common relatives of the coronavirus were identified. In the year 3 300 B.C. Betacoronavirus existed; in 3 000 B.C. Deltacoronavirus; in 2 800 BC, researchers discovered that the Gammacoronavirus spread; and in 2 400 B.C. Alphacoronavirus emerged. However, it is not necessary to go so far in time to find direct relatives of this virus. In the 18th century, the bovine coronavirus was linked to the human one, and researchers agree that it was between 1890 and 1899 when the birth that affected people occurred, but they do not know if it was due to a separation from the bovine or by a mutation.<sup>1</sup>

The closest common relative dates back to the 1950s. It is OC43 and is closely related to several species of bats, according to the latest studies. It was first detected in humans in the 1960s, specifically in the nasal cavities, and since then six new members of this family have been identified, the last being the 2019-nCoV or coronavirus.<sup>1,2</sup>

Severe Acute Respiratory Syndrome (SARS) is a viral respiratory illness caused by a coronavirus, called SARS-associated coronavirus (SARS-CoV). SARS was first reported in Asia in February 2003. Within a few months, the disease spread to more than two dozen countries in North America, South America, Europe, and Asia before the global outbreak could be contained. According to the World Health Organization (WHO), a total of 8 098 people worldwide fell ill with SARS during the 2003 outbreak. Of this number, 774 people died. In the United States, only eight people were infected with SARS-CoV as confirmed by laboratories. All of these people had traveled to other parts of the world where SARS was present.<sup>2,3</sup>

COVID-19 has been defined as an acute respiratory infection that can potentially produce a severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2), with a clinical spectrum ranging from a disease very similar to the common cold to a severe pneumonia and severe acute respiratory failure.<sup>4</sup>

The COVID-19 crisis erupted in China on December 31<sup>st</sup>, and since then it has experienced an upward and continuous spread, with Europe and America being the con-

tinents most affected by COVID-19 to date. Since then, more than 10 000 000 infections have been known worldwide. This disease has prevailed in carriers of chronic diseases worldwide, and Cuba is an example of this since of the total of its deceased, the highest percentage had an associated chronic base disease.<sup>5</sup>

The WHO specified that the neglect of chronic diseases is a very worrying situation since they cause the annual death of more than 40 million people, in addition to the fact that those who suffer from them are at greater risk of dying if they are infected with the coronavirus. According to a search in 115 countries during the last three weeks of May, although the impact is general, this scenario is more marked and difficult in low-income nations, although it is known that the world's leading power is the United States, epicenter of the pandemic that together with Brazil due to the mismanagement of health policies, people have suffered who do not have easy access to health entities such as the undocumented, African-American and poor.<sup>6,7</sup>

The Pan American Health Organization (PAHO) states that between 20% and 35% of the adult population in Latin America and the Caribbean is hypertensive, diabetic, or has Chronic Obstructive Pulmonary Disease (COPD), a value that has increased in recent years. In Cuba, with a high life expectancy, there are a large number of people with this type of chronic illness, which generally tend to be more frequent over the years. The authorities of the PAHO Health Secretariat have already indicated that people with these diseases are those who are most at risk from the SARS-Cov2, this means that there is a large percent of the population that suffers from COVID-19 could be more at risk of complications.<sup>8</sup>

The presence of chronic diseases has negatively influenced people who have contracted COVID-19 leading the vast majority to death. Therefore, the main objective of this bibliographic review was to explain why people with chronic non-communicable diseases develop more severe forms of COVID-19, highlighting the influence of these diseases on the clinical evolution of patients with COVID-19.

## DEVELOPMENT

### SARS-CoV-2 classification and structure

Coronaviruses are members of the Orthocoronavirinae subfamily within the Coronaviridae family (order Nido-

virales). This subfamily comprises four genera: alphacoronavirus, betacoronavirus, gammacoronavirus and deltacoronavirus according to their genetic structure. Alphacoronaviruses and betacoronaviruses infect only mammals and are normally responsible for respiratory infections in humans and gastroenteritis in animals.<sup>6</sup>

Structurally, coronaviruses are spherical viruses 100-160 nm in diameter, with a lipid bilayer envelope and containing positively polarized single-stranded RNA (ssRNA) between 26 and 32 kilobases in length. The SARS-CoV-2 virus genome encodes 4 structural proteins: protein S (spike protein), protein E (envelope), protein M (membrane) and protein N (nucleocapsid). Protein N is inside the virion associated with viral RNA, and the other three proteins are associated with the viral envelope. Protein S contains the receptor binding domain of the cells it infects and, therefore, is the protein that determines the tropism of the virus.<sup>6</sup>

### How is COVID-19 spread?

A person can get COVID-19 from contact with someone who is infected with the virus. The disease is spread mainly from person to person through droplets that fly out of an infected person's nose or mouth by coughing, sneezing, or talking. These droplets can fall on objects and surfaces around the person, such as tables, knobs, and railings, so other people can become infected if they touch those objects or surfaces and then touch their eyes, nose, or mouth. People without symptoms can transmit the virus.<sup>5</sup>

### SARS-CoV2 Mechanism of Action

The mechanism of action of the virus within our cells, although it is not 100% molecularly identified, follows the usual pattern of all viruses:<sup>6</sup>

- 1. Adsorption.** The virus binds to the host cell and introduces its genetic material. In the case of SARS-CoV-2, it binds to the Angiotensin Converting Enzyme 2 (ACE 2) protein, which is present in various tissues of the human body, particularly in the oral mucosa, considered the main route of entry into our body.
- 2. Penetration.** The membrane of these viruses is of the same nature as the cell membrane, so a fusion of membranes can occur, and only the capsid enters. Or, it can enter by endocytosis, and the virus envelope fuses with

the lysosome.

- 3. Decapsulation.** The genetic material is released into the cytoplasm through different enzymes that degrade viral proteins.

- 4. Synthesis and replication.** In SARS-CoV-2, being an RNA virus, this phase occurs in the cytoplasm. The virus uses the cellular machinery for its replication (creation of copies) of the RNA and for the synthesis of the 4 proteins that we have already discussed.

- 5. Assembly.** At this time, the cell is filled with copies of the virus's RNA and proteins floating in the cytoplasm. By different mechanisms, these proteins unite, leaving inside a copy of the viral RNA.

- 6. Release.** It occurs through mechanisms of exocytosis, which makes it easier for them to surround themselves with a membrane.

The virus is constantly reproducing and the problem comes because the ACE 2 protein, to which the Coronavirus SARS-CoV-2 binds, has a blood pressure regulating activity which ceases to take place, leading to a lack of control in blood pressure, which prevents adequate blood flow to different tissues. COVID-19 begins in the lungs as the coronaviruses of the common cold, but then causes chaos in the immune system that can cause long-term damage to the lungs or death.<sup>9</sup>

SARS-CoV-2 grows in lung cells called type II pneumocytes, these secrete a soapy substance that helps air penetrate deep into the lungs and into the cells that line the throat. Most of the damage caused by COVID-19 is caused by the immune system. Millions of cells of the immune system invade infected lung tissue and cause massive damage in an attempt to kill the virus and any infected cells. Another problem caused by SARS-CoV-2 is that they inhibit the production of interferon, one of the body's defense response mechanisms. They do this by blocking the synthesis of this molecule through a combination of camouflage, separation of cellular protein markers that make stress beacons, and finally fragmentation of any antiviral instructions manufactured by the cell before it can be used.<sup>10,11,12</sup>

## What are the symptoms and signs of COVID-19?

The most common of COVID-19 are fever, dry cough and tiredness. Other less frequent that affect some patients are pain and discomfort, tachycardia, headache, sore throat, diarrhea, loss of taste or smell and skin rashes or color changes in the fingers or feet. These symptoms are usually mild and begin gradually. Some of the infected people only show very slight symptoms.<sup>13</sup>

## Why can people with chronic diseases have more severe forms of COVID-19?

As COVID-19 is a recent disease, doctors and scientists have little experience of its impact, but several studies indicate that a significant percentage of those infected, who suffered from one or more chronic diseases such as cardiovascular, respiratory, diabetes, among others, they have presented a more serious picture of the disease and a higher mortality rate than patients without comorbidities.

In a common flu, symptoms with fever above 38 °C may occur, in which the heart rate increases. This situation is normally tolerated by a very healthy organism, while some people with heart problems or other chronic diseases can generate decompensation since these patients tend to have less immunity due to the systemic damage that chronic diseases cause. This is generally the case with the flu, which could be equivalent to COVID-19, which can also cause more respiratory and oxygenation complications, which increases the risk of patients with cardiovascular problems. As previously mentioned, patients with comorbidities such as coronary heart disease, those who have had a previous heart attack, heart and respiratory failure, COPD and diabetes mellitus are at greater risk of complications, also autoimmune diseases such as systemic erythematosus lupus.<sup>14,15,16</sup>

## What happens to patients with hypertension?

As explained previously, the virus to enter the human body needs to bind to a receptor that in this case is the Angiotensin Converting Enzyme 2 (ACE 2) which is directly related to the regulation of blood pressure. There is a hypothesis that people with hypertension may have changes in this enzyme, either in its structure or in the number of units per cell that favor that the virus can give a more serious infection since, when more viruses enter, the greater

the viral load favoring more serious forms of the disease.<sup>17,18</sup>

## How does the virus work in people with diabetes mellitus?

Over time, high blood sugar levels, a hallmark of diabetes, are said to damage the body's blood vessels, thereby compromising lung function, potentially making you more susceptible complications to someone with a respiratory infection, such as COVID-19. High blood sugar levels damage many different body systems, including the immune system. Viruses and bacteria present on their surface two types of sugar, mannose and fucose, which are used as targets by specialized receptors of the immune system to detect the presence of these microorganisms and act against them. However, this detection mechanism is blocked when glucose levels are too high, therefore preventing the normal functioning of the body's defenses, making it more vulnerable. That is why keeping diabetes under control also leads to better immune function.<sup>19,20,21</sup>

Diabetes and cardiovascular disease are not the only disorders that can complicate coronavirus infection. People with a compromised immune system are also more likely to become seriously ill if they contract the infection. The same goes for those with kidney disease.

## COVID-19 complications

Complications of COVID-19 are associated with severe symptoms of fever and pneumonia that can lead to acute respiratory distress syndrome (ARDS). Manifestations similar to cytokine release syndrome (or "cytokine storm") similar to those in patients infected with other coronaviruses (SARS-CoV and MERS-CoV), as well as in leukemia patients receiving T-cell therapy, have been observed. Complications can be characterized by ARDS and secondarily by hemophagocytic lymphohistiocytosis (LHH) syndrome. Furthermore, in severe patients due to COVID-19, multiple organ failure can also be observed. It is unknown whether this multiorgan failure is a direct consequence of direct coronavirus-induced tissue damage, the "cytokine storm," or the synergistic effects of both.<sup>22,23</sup>

## TREATMENT

Although some western or traditional medicine solutions or home remedies can be comforting and alleviate mild symptoms of COVID-19, so far no medicine has been

shown to prevent or cure this disease. It is recommended not to self-medicate with any drug, including antibiotics, to prevent or cure COVID-19. However, there are several clinical trials underway, both for western and traditional medications. WHO is coordinating vaccine and drug development work to prevent and treat COVID-19.<sup>5,6</sup>

All people suffering from a chronic disease are recommended to strictly follow the treatment scheme provided by their doctor in order to better cope with COVID-19 in case of infection.

The most effective ways to protect yourself and others from COVID-19 are:<sup>5,24</sup>

- Wash your hands thoroughly and frequently.
- Avoid touching your eyes, mouth and nose.
- Cover your mouth with your elbow flexed or with a handkerchief. If a handkerchief is used, it must be discarded immediately after use and hands must be washed.
- Maintain a distance of at least one meter with other people.
- The use of medical masks is mainly recommended in healthcare settings, but can be considered in other circumstances such as crowded places.
- Anyone who is sick and has mild symptoms, such as muscle aches, mild cough, sore throat, or tiredness, should isolate herself at home and wear a medical mask.

Isolation is an important measure that people with symptoms of COVID-19 take to avoid infecting others in the community, including their families. In our country, the government has declared it mandatory for 14 days to all people who arrive in national territory from other countries in this period of pandemic, constituting one of the measures by which said disease has been kept under control in Cuba. It is important to strictly adhere to each measure designated by the health authorities for the well-being of all.

### Situation in Cuba

In Cuba, Ministry of Public Health has published non-communicable diseases are the main cause of morbidity, mortality and disability and that for several years, 9 of the top 10 causes of death have responded to non-communicable diseases, representing around 80 percent of deaths, and of these cardiovascular diseases represent 39%.<sup>8</sup>

Cuba exceeds 100 days of constant struggle against COVID-19. Reports of asymptomatic patients confirmed to the disease continue, as well as people who do not know how they were infected. Until the last week of June 2020, 2 340 cases have been diagnosed. For this reason, it became necessary to implement a protocol of action, with a national scope, that contributes to the prevention, control and better management of positive cases of COVID-19. In Cienfuegos to date, 25 cases have been counted and 1 death, a small number compared to other provinces of the country such as Havana, thanks to the strict control that has been maintained at borders and the hard work of research and active surveillance that are currently in force.<sup>9,10</sup>

### What role does primary assistance play in the fight against COVID-19?<sup>25</sup>

Actions against COVID-19 begin and end in the community. For this reason, primary care plays a fundamental role in the identification of vulnerable people, in the detection of patients and in surveillance and support actions for the recovery of those affected.

Among the main responsibilities of this area of medical care, the protocol establishes:

- Enable differentiated consultation for patients with manifestations of acute respiratory infection in polyclinics.
- Conduct an interrogation and physical examination of the patient, allowing an evaluation of the patient and her case classification.
- Execute the active investigation of the entire population to identify cases with acute respiratory infections, as well as contacts and suspects.

It is also important to highlight the importance of keeping every person in the community dispensed. Another aspect of vital importance is the updating of each patient's treatments, as well as the periodic check-up of the most vulnerable patients.

## CONCLUSIONS

COVID-19 is a recent disease caused by the SARS-Cov-2 virus that has unleashed a pandemic in this century. In order to enter the human body, the virus needs to bind to a receptor, which in this case is Angiotensin Converting Enzyme 2 (ACE 2), which is directly related to the regu-



lation of blood pressure. People who suffer from chronic diseases and contract this disease develop severe forms of COVID-19 since it acts negatively on the people's immune system or in the case of high blood pressure where the Angiotensin Converting Enzyme is restructured; penetration is favored of higher viral load, making people more vulnerable to fulminant forms of the disease. The most effective ways to protect yourself are to wash your hands, maintain social distance, wear face masks, and sneeze or cough by covering your mouth and nose with your forearm. Currently there is no drug capable of curing the disease, but it is working hard around the world looking for the earliest possible solution.

### CONFLICT OF INTERESTS

The authors declare that does not exist conflict of interest.

### AUTHORS CONTRUBUTION

All the authors participated in the writing, revision and approval of the article and its final version.

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