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Infection, treatment and virological features of SARS-CoV-2. A brief overview

Infección, tratamiento y características virológicas del SARS-CoV-2. Un breve resumen

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Abstract

A new coronavirus, the SARS-CoV-2, and its resulting disease, the COVID-19, originated in Wuhan, China, in December 2019, affecting human health by causing respiratory, digestive and systemic problems. In symptomatic patients, the clinical manifestations of the disease usually begin within a week after being infected with the virus, and consist of fever, dry cough, nasal congestion, fatigue and airway problems, which can lead to pneumonia. The virus is also present in patients who do not have symptoms, and therefore it is quite difficult to identify and quantify them. In this work, an overview of the virological features of SARS-CoV-2, its transmission and infection, as well as of the clinical signs and treatment of COVID-19 is carried out.

Keywords: COVID-19; Infection; Diagnosis; Virology (MeSH).

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Resumen

Un nuevo coronavirus, el SARS-CoV-2, y su enfermedad resultante, la COVID-19, se originó en Wuhan (China) en diciembre de 2019, afectando la salud humana al causar problemas respiratorios, digestivos y sistémicos. En los pacientes sintomáticos, las manifestaciones clínicas de la enfermedad suelen comenzar dentro de la semana siguiente a la infección por el virus y consisten en fiebre, tos seca, congestión nasal, fatiga y problemas de las vías respiratorias, que pueden provocar neumonía. El virus también está presente en pacientes asintomáticos, por lo que es bastante difícil identificarlos y cuantificarlos. En este trabajo se realiza una breve revisión de las características virológicas del SARS-CoV-2, su transmisión e infección, así como los signos clínicos y tratamiento de la COVID-19.

Palabras clave: COVID-19; Infección; Diagnóstico; Virología (DeCS).

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Introduction

Coronaviruses (CoV) are a group of enveloped, single-stranded RNA viruses. Like other RNA viruses, they exhibit a wide capacity for genetic mutation and recombination that enables them to adapt to different ecological niches and to evade host immune responses. They are classified within the *Nidovirales* order, *Coronaviridae* family, and *Orthocoronavirinae* subfamily.[1] In addition, there are four different genera of coronaviruses: *alpha*, *beta*, *gamma* and *deltacoronavirus* (of these, the first two can infect humans).

Lu *et al.*,[2] in a study conducted in nine patients at the end of December 2019 and the beginning of January 2020, found 99.8-99.9% nucleotide identity; also, in the same study, sequencing studies revealed the presence of a new beta-CoV strain.[2] The genetic sequence of coronavirus disease 2019 (COVID-19) showed a similarity of more than 80% and 50% with SARS-CoV (Severe acute respiratory syndrome coronavirus) and MERS-CoV (Middle East respiratory syndrome coronavirus), respectively.[1] In addition, both, SARS-CoV and MERS-CoV, originate from bats. Therefore, evidence from phylogenetic analysis shows that SARS-CoV-2 belongs to the *betacoronavirus* genus, which includes SARS-CoV, which can infect humans, bats, and wild animals.[3]

So far, data suggest that bats are the initial cause of the current COVID-19 pandemic, a disease caused by the infection with the new SARS-CoV-2, which originated in a seafood market of Wuhan, China.[4] This new coronavirus has caused millions of infections and thousands of deaths worldwide. As of November 7, 2020, worldwide there were almost 49 million confirmed cases of COVID-19 and more than 1 200 000 deaths. John Hopkins University updates this data daily.[5] Although the virus originated in China, it has spread rapidly, affecting virtually every country in the world.

There are several subtypes of coronaviruses that can infect humans. *Betacoronaviruses* can cause quite serious diseases and even death, while *alphacoronaviruses* usually result into asymptomatic or very mild symptomatic infections. SARSCoV-2 belongs to the B lineage of *beta*-coronaviruses, it can infect type II pneumocytes and epithelial cells, and is closely related to the SARS-CoV virus.[6,7]

Similar to SARS-CoV, SARS-CoV-2 uses the cell receptor of angiotensin-converting enzyme 2, which is expressed in the epithelium of the airway, lung parenchyma, vascular endothelium, kidney, heart, brain, testicular tissue, and intestine. It is believed that both SARS-CoV and MERS-CoV can remain on contaminated surfaces (such as metal, glass, or plastic structures) for up to 9 days, but can be efficiently inactivated with the application of disinfectants such as ethanol (62-71%), hydrogen peroxide (0.5%), or sodium hypochlorite (0.15%).[8]

There are four endemic human coronaviruses (HCoVs) that usually cause cold-like upper respiratory infections in immunocompetent individuals: HCoV-229E, HCoVNL63 (both *alphacoronavirus*), and HCoV-OC43 and HCoV-HKU1 (both *betacoronavirus* of the *embevovirus* subgenus).[9]

The high transmissibility of COVID-19 has been associated with a mutation in the ORF1ab region (Open Reading Frame 1ab) affecting nonstructural protein 2 (nsp2).[10] However, the exact route of initial transmission to humans remains unknown, although live contaminated animals have been suggested as the most likely option.[11]

On January 30, 2020, the new coronavirus outbreak was declared a global health emergency.[12] Then, on March 11, and due to its rapid spread and the number of deaths caused by it, COVID-19 was declared a pandemic.[13] Taking this into account, the objective of this paper is to carry out an overview of the virological features of SARS-CoV-2, its transmission and infection, as well as of the clinical signs and treatment of COVID-19 in order to provide a brief and easy to understand summary of the main characteristics of this disease in pandemic times.

Virological features of SARS-CoV-2, and COVID-19 infection and treatment

The main sign of patients hospitalized with COVID-19 is pneumonia. The most common symptoms caused by the infection with SARS-CoV-2 include fever, cough, and shortness of breath. In some cases, there may also be a loss or decrease in smell and taste, chills, sore throat, headache, asthenia, diarrhea, or vomiting. Various injuries to the skin, chest, or fingers and toes have also been observed, usually in children and adolescents without other symptoms.[14] Most of asymptomatic cases are children and adolescents. On the other hand, it has been reported that the incubation period of the virus ranges between 1 and 14 days.[14] In addition, most infected persons may show symptoms within 12 days of infection.[15] It is transmitted by respiratory droplets that are released when someone with the virus coughs, sneezes, or speaks. Also, if a person touches a surface where the virus is present and then touches their mouth, nose, or eyes, it is also quite possible that they will become infected.[16]

The infection can become serious and lead to severe illness with shortness of breath and severe chest pain symptoms, resulting in pneumonia.[17] Some of the most prominent signs of this pneumonia include decreased oxygen levels, breathing difficulty, fast and painful breathing, altered blood gases levels, and lung changes visible through chest x-rays.[18]

Regarding sociodemographic characteristics of COVID-19 patients, a study conducted in COVID-19 inpatients, mainly from Wuhan, China, describes that their average age is 50 years and that there is a slight predominance of males.[19] Also, approximately 25% of these patients experience severe complications and require intensive care, of which, almost 10% need mechanical ventilation.[19]

Older adults (≥60 years), as well as people with underlying medical conditions including diabetes, heart disease, obesity, cancer and kidney disease, regardless of their age, are at increased risk of developing severe illness from COVID-19.[20]

In addition, the possibility of inter-human transmission during the asymptomatic period must be taken into account.[21] In this regard, the possibility that children, who normally present a subclinical picture or milder symptoms, may spread the infection to the rest of the community has been proposed.[22] Somehow, recent studies report that while children can be infected, they are not expected to spread it as much as adults do.[23,24]

Many questions remain uncertain about the ease of spread of the new SARS-CoV-2, but like other respiratory viruses, it seems its main way of transmission is

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the airborne route from secretions (droplets) of infected individuals. Other possible routes under study are environmental contamination and the fecal-oral route.[25] The R0 value, which in the case of the novel coronavirus ranges between 1.4 and 6.47,[26] estimates the number of secondary cases occurring in a susceptible population from an infected individual, and a R0>1 is considered to allow epidemic spread.

The World Health Organization has indicated different management scenarios of COVID-19 according to its severity, and classifies the disease as: a) mild pneumonia; b) severe, if pneumonia is accompanied by fever, tachypnea, respiratory distress and/or oxygen saturation <90%; c) acute respiratory distress, if respiratory symptoms worsen and bilateral opacities or nodules or pulmonary edema are observed in chest x-rays; d) sepsis, when signs of organic dysfunction are also present; and, e) septic shock, the most severe scenario.[27]

Furthermore, three phases of COVID-19 in symptomatic patients have been described: first, symptoms and clinical signs such as malaise, fever, and dry cough are experienced; then pulmonary involvement, with or without hypoxia, occurs at different degrees of severity; finally, extra-pulmonary systemic inflammation takes place. During the course of COVID-19, changes in hemostasis tests are observed, such as prothrombin lengthening and activation of partial thromboplastin times, as well as increased D-dimer levels. When the patient's condition worsens due to COVID-19, D-dimer levels rise and microthrombi are formed in peripheral blood vessels.[28]

As far as the therapeutic management of the disease is concerned, at present no treatment has definitively proven its efficacy. Some of the treatments that have been proposed include the administration of lopinavir/ritonavir and remdesivir, nucleoside analogues, neuraminidase inhibitors, tenofovir, lamivudine, and chloroquine.[29]

In this regard, Zhang *et al.*[30] suggest the possibility of designing a drug that acts by blocking the angiotensin-converting enzyme 2 receptor.[30] Currently, antiviral drugs for adult patients with COVID-19 mainly include the combination lopinavir/ritonavir (to which interferon can be added) and remdesivir, although there are many other combinations, since they vary depending on the country where they are used.

Regarding the possibility of immunoprevention, the spicule protein receptor has been identified as a possible antigenic candidate for the design of a vaccine.[31] In the meantime, the use of usual support measures such as oxygen therapy and fluid therapy, and the admission to intensive care unit of patients who develop severe illness from COVID-19, is recommended. Furthermore, in the systemic hyperinflation phase, steroids and cytokine inhibitors such as tocilizumab or anakinra may be considered.[28] Also, it should be noted that all health personnel, whether in direct or indirect contact with these patients, must adopt infection prevention measures such as constant handwashing and the use of personal protective equipment.

Conclusions

In this paper, an attempt to show a brief and updated review, as of September 2020, of the main characteristics of the new SARS-CoV-2 has been made. Most of deaths caused by COVID-19 have occurred in older adults (≥60 years) and in people with underlying medical conditions, for their weakened immune systems allow a faster progression of the virus. Decontamination reagents should be provided in public places for routine hand cleaning. Also, in health facilities, healthcare workers should work at all times using personal protective equipment and other biosecurity measures in order to reduce the risk of contagion and, thus, slow down the spread of the virus. However, in some countries there is currently a shortage of personal protective equipment, which increases the risk of contagion of health workers, thus putting their lives and the lives of those around them at risk.

Regarding the clinical manifestations of the disease, they usually begin within a week after being infected with the virus, and mainly consist of fever, dry cough, nasal congestion, fatigue and airway problems, which can lead to pneumonia.

Since this is a new virus, the conditions of the current pandemic are constantly evolving, and many changes are likely to be adopted by health authorities as time passes. It is very important that the general population and health care workers continue to adhere rigorously to infection prevention and control measures such as the use of masks, social distancing, and hand washing. Over time, more details about the virus and its pathology will be known, which may allow more effective therapeutic measures to be implemented until an effective vaccine is created.

Conflicts of interest

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