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COVID-19: origin, pathogenesis, transmission, clinical aspects and current therapeutic strategies

COVID-19: origem, patogênese, transmissão, aspectos clínicos e atuais estratégias terapêuticas

COVID-19: origen, patogénesis, transmisión, aspectos clínicos y estrategias terapéuticas actuales

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ABSTRACT

Introduction: In December 2019, the novel 2019 coronavirus disease (COVID-19) in China caused a global outbreak and is a major public health problem; and the World Health Organization declared that COVID-19 constituted an International Public Health Emergency. The objective is to inform about COVID-19, highlighting its history, genomic organization of the novel coronavirus, pathogenesis, diagnosis, clinical manifestations, transmission, control, prevention and current therapeutic strategies. **Outline**: This is a narrative review, in which searches were carried out for articles in the PubMed and Science Direct databases. **Implications**: COVID-19 is highly pathogenic, and no specific treatment or vaccine is currently available. Given these facts, countless countries have adopted extensive control measures to reduce the transmission of the disease from person to person. **Conclusion**: Various studies are underway to identify potential treatments for COVID-19. Currently, controlling the infection is the best way to prevent the spread of the novel coronavirus.

DESCRIPTORS

Coronavirus; Coronavirus Infections; Pandemics.

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INTRODUCTION

Respiratory diseases are a major cause of morbidity and mortality for humans, and most of these are associated with infectious conditions caused by viruses. A significant number of new respiratory viruses have been discovered since the beginning of the 21st century and it is estimated that they cause 95% of respiratory diseases in children and babies and about 30-40% in the elderly.[1-2] Among the various respiratory viruses, coronaviruses (CoVs) stand out, as they are of great pathogenic importance to humans and other animals. Generally, coronaviruses that infect humans reach the upper respiratory tract, where they are mainly associated with symptoms of common colds. However, because they are opportunistic pathogens, they can also affect the lower respiratory tract in more vulnerable populations, such as newborns, infants, the elderly and immunocompromised individuals, causing pneumonia, asthma exacerbations, acute respiratory distress syndrome (ARDS), even severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).[3]

In the last decade, the emergence and reemergence of avian influenza (Influenza A H5N1) in 2003, SARS in 2002, Influenza A H1N1 in 2009 and Zika in 2015 have raised many doubts about the role of epidemiological surveillance. Pandemics have emerged frequently and, since 2018, the World Health Organization (WHO) has recognized the need to prepare in advance for the emergence of new pathogens, including diseases still unknown with potential for international emergence in the list of priorities for research and development in the context of emergency.[4]

At the end of 2019, COVID-19 (or disease from the novel 2019 coronavirus) spread rapidly across China and then to the rest of world. A novel beta coronavirus of severe acute respiratory syndrome 2 (SARS-CoV-2) has been identified as a pathogen of COVID-19, triggering severe pneumonia and acute lung failure, including death. In the existing cases, some individuals with pneumonia developed ARDS and, in some of them, the situation worsened in a short period of time and died due to multiple organ failure.[5]

The worldwide effort to provide information about the novel coronavirus is extraordinary. By the end of March, the new virus had been cited in more than three thousand publications in PubMed and Science Direct on analysis of genomic sequences, therapeutic strategies, pathogenesis, clinical aspects, among other approaches. This action is the result of sensitive international surveillance, as well as an organization in data sharing. While certain groups are quickly organizing to monitor cases in real time, others are dedicated to applying statistical models to monitor the novel coronavirus and define mechanisms of action. On the other hand, the growing use of social media, as a means of information, also brought the challenge of monitoring and responding quickly to the fake content that is disseminated in these channels and that confront science, offering unnecessary health risks.[6] Pandemic must be combated with knowledge and strategies.

This narrative literature review provides information on COVID-19, highlighting the history of the disease, genomic organization of the novel coronavirus, pathogenesis, transmission, clinical manifestations, diagnosis, as well as control, prevention and current therapeutic strategies.

METHOD

This is a literature narrative review, in which searches were carried out in the PubMed and Science Direct databases aimed at the publication of scientific articles at national and international levels.

RESULTS AND DISCUSSION

Coronavirus

Coronaviruses (Order Nidovirales, Family Coronaviridae, Subfamily Coronavirinae) are enveloped viruses, with a single-stranded “positive” RNA genome of approximately 26 to 32 Kb in size, which is the largest known genome for an RNA virus.

The term "coronavirus" refers to the appearance of CoV virions, when observed under electron microscopy, where the projections of the virus membrane resemble a "crown" or corona, in Latin.[7] CoVs may exhibit a typical biennial seasonality different from that occurs with other respiratory viruses.[8] They mainly cause respiratory and enteric pathologies, with neurotropic and neuroinvasive properties in several hosts, including cats, pigs, cows, birds, dogs and humans.[9] Coronavirinae are subdivided into alpha (α), beta (β), gamma (γ) and delta (δ) coronavirus. Gamma and delta generally infect birds, although some of them can reach mammals; alpha and beta coronaviruses are known to infect humans and other animals. Viruses were initially classified into these groups based on serology, but are currently divided into phylogenetic grouping.[10]

The first human coronavirus (HCoV), called B814, was isolated in 1965 from the nasal secretion of patients with a common cold.[11] There are seven known HCoVs, among them SARS-CoV (which causes SARS), MERS-CoV (which causes MERS) and SARS-CoV-2 (virus responsible for COVID-19). SARS, MERS and COVID-19 can cause respiratory, intestinal, liver and neuronal diseases and can lead to ARDS, multiple organ failure and death.[12]

SARS-CoV-2

SARS-CoV was identified as the causative agent of the SARS outbreak in late 2002 in Hong Kong and southeastern China. During this outbreak, there were more than 8,000 cases with 774 deaths, resulting in a 10% mortality rate. SARS-CoV causes more serious diseases in neonates, the elderly and individuals with pre-existing diseases, with a higher incidence of lower respiratory tract infection in these patients. Although the number of deaths is not comparable to influenza, AIDS or hepatitis C, the SARS outbreak has caused worldwide public concern and seriously affected the global economy. Before SARS, coronaviruses were considered to cause mild and self-limiting respiratory infections in humans.[13]

The initial transmission of SARS-CoV from animals to humans was investigated in public markets that sell live animals and the hypothesis was raised that the virus would have reached the human population using the Asian palm civet (*Paradoxurus hermaphroditus*) as an intermediate host. However, the fact that a bat CoV can also infect human airways suggests that an intermediate host between humans and bats may not be necessary for SARS transmission.[14]

In fact, bat CoV also uses the same receptor as the human virus, the angiotensin-converting enzyme 2 (ACE2), providing additional evidence that human SARS-CoV may have originated in bats. Although some humans in public markets had serological evidence of SARS-CoV infection before the outbreak, they had no apparent symptoms. Therefore, it is likely that a closely related virus has been circulating in the markets for several years before several factors facilitate its spread in a larger population group.[15]

SARS-CoV has spread around the world, with outbreaks in China, Singapore, Vietnam, Taiwan and Canada. After the 2002 outbreak, it became apparent that coronaviruses could cross barriers and cause potentially fatal infections in humans. Therefore, it is necessary to pay more attention to new coronaviruses. The continued emergence of these reemerging viral threats emphasizes the unpredictability of these pathogens and poses challenges to the development of control strategies.[16-17]

In late 2019, an outbreak of pneumonia caused by beta coronavirus (β-CoV) strain 2B,[18-19] occurred in Wuhan, Hubei province, China and spread rapidly around the world. This coronavirus was initially named as the novel coronavirus of 2019 (2019-nCoV) on January 12, 2020 by WHO. This organization officially named the disease as Coronavirus Disease 2019 (COVID-19) and the International Committee's Coronavirus Study Group has proposed naming the novel coronavirus as SARS-CoV-2, both issued on February 11, 2020.[20]

The WHO announced on January 30, 2020 that the outbreak of the disease caused by the novel coronavirus constituted a Public Health Emergency of International Importance (the highest level of alert in the Organization) as provided for in the International Health Regulations. According to the report published on the WHO official website, until April 25, 2020, 2,719,897 cases and 187,705 deaths worldwide were confirmed by COVID-19.[21] In Brazil, the Ministry of Health confirmed, in the same period, 58,509 cases (highest concentration in the Southeast Region) with 4,016 deaths, which represents 6.9% of lethality.[22]

The SARS-CoV-2 genome is packed inside a helical capsid formed by the nucleocapsid protein and enclosed by an envelope. Significantly, SARS-CoV-2 shares 79.5% of its genetic sequence with SARS-CoV. After the identification and sequencing of this new virus, extensive research was carried out in the GenBank genetic sequence database, where, after a comparative analysis, it was discovered that the SARS-CoV-2 genome has 96% similarity with that of the RaTG13 coronavirus obtained from the bat *Rhinolophus affinis*. Bats are the natural reservoir for a wide variety of coronaviruses, including SARS-CoV and MERS-CoV.[15,23]

The incubation period and the duration of the disease course by SARS-CoV-2 follow the general trend of the other six HCoVs. On the one hand, SARS-CoV-2 infection has more common characteristics during infection with community-acquired HCoVs, including the presentation of non-specific, mild or even non-existent symptoms. On the other hand, a subset of serious cases of COVID-19 can also be seen as in the case of SARS-CoV infection. Human-to-human transmission was confirmed by the presence of cases between family members and health professionals.[24]

Genomic organization, replication and pathogenesis

The CoV genome encodes four main structural proteins: the spike (S), the envelope (E), the membrane (M) and the nucleocapsid (N), all necessary to produce a structurally complete viral particle; some CoVs additionally have a hemagglutinin esterase (HE) protein. It has become clear that some CoVs do not require all structural proteins to form a complete infectious virus, suggesting that some of these proteins may be expendable or that these CoVs may encode additional proteins with compensatory functions. Individually, each structural protein plays a specific role in the structure of the viral particle, but is also involved in other aspects of the replication cycle.[25]

Protein S is a large glycosylated type 1 transmembrane protein, responsible for recognizing the cell receptor, used by the virus, to infect a target cell. During infection of susceptible hosts, protein S represents an important virulence factor, because it is associated with most cytotoxic effects that lead to the degeneration of infected cells. Adaptation to the human host required mutations in the spike receptor binding domain, which mediates the binding of SARS-CoV to the cell membrane, allowing the entry of viral particles into the host cells. Protein E is anchored to the viral envelope and plays a role in morphogenesis, traffic in infected cells, and virion sprouting, and appears to be responsible for the curvature of the viral envelope. This protein, during infection of host cells, can induce the response to cell stress and apoptosis,[26-27] and may be associated with rupture of the pulmonary epithelium and participate in immunopathology in the respiratory tract. Protein M interacts with all other viral structural proteins and therefore helps to shape and maintain the structure of the microorganism. During cell infection, this protein can participate in the inhibition of interferon type 1 response by infected cells and, therefore, influence the infection outcome and the cell fate after infection. Protein N, associated with the viral genome, plays an essential role in encapsulating it in a helical nucleocapsid within the viral particle. It has been shown that the SARS-CoV N protein is partially located in the nucleolus and disrupts the host cell cycle.[28-29] Protein N from different coronaviruses also participates in the inhibition of interferon type 1 response by the infected cell and apoptosis induction. Hemagglutinin esterase (HE) is present only in β-CoVs. Like protein S, HE is a Type 1 transmembrane protein and can be important during infection or in the release of viral particles by infected cells at the end of β-CoV replication.[30]

In order to understand the rate of coronavirus spread among humans, it is crucial to determine whether SARS-CoV-2 is mutating to improve its binding to human receptors. Like an RNA virus, SARS-CoV-2 has intrinsic genetic variability, which results in a high mutation rate. It has been suggested that any adaptation to the SARS-CoV-2 sequence may make it more efficient in transmitting from person to person, as well as increasing its virulence.[31]

Although the respiratory tract epithelium represents the first line of defense against pathogens, it can become the target of infection by different respiratory viruses. Several epithelial infections, including those involving coronavirus, are self-limiting and the infection remains local, as the virus will be eliminated by the respiratory tract immune system, with minimal clinical consequences. However, opportunistic viral pathogens, such as HCoVs, can overcome the immune response and cause more severe respiratory diseases or even spread to other tissues, including the central nervous system (CNS), where they could induce other types of pathologies.[32] HCoVs are molecularly related to the structure and mode of replication with neuroinvasive coronaviruses from other animals, such as the porcine hemagglutinating encephalomyelitis virus (PHEV) and the murine hepatitis virus (MHV).[33]

Primary replication of SARS-CoVs is usually confined to the epithelial cells of the respiratory or gastrointestinal tracts. Epithelial cells are functionally polarized. Since CoVs usually spread via the oral or respiratory pathways, polarized epithelial cells constitute their first natural barrier. Therefore, their interaction with these cells largely determines the infection outcome.[29]

SARS-CoV mainly infects lung cells. It is able to enter macrophages, but leads to an abortion infection. Despite this, the infection can induce the release of pro-inflammatory cytokines that will contribute to the progression of the disease. In fact, many cytokines and chemokines are produced and rise in the serum of patients infected with SARS-CoV.[20] There are reports that, in Wuhan, rodents sold in open markets and infected with SARS-CoV, presented clinical characteristics similar to those of human disease, including increased levels of pro-inflammatory cytokines and reduced T-cell responses, suggesting a possible immunopathological mechanism of disease.[34-35]

Studies have investigated the potential use of receptors for the novel coronavirus based on knowledge about SARS-CoV sequencing. They found that the sequence of SARS-CoV-2, which comes in direct contact with the ECA2 receptor, is similar to that of SARS-CoV. They further stated that a single mutation significantly increases the ability of SARS-CoV-2 to bind to human ECA2. After exposure of the host to this virus, it binds to cells that express the virus receptors, of which ECA2 is one of the main ones and CD209L is an alternative receptor, but with a much lower affinity. Coronavirus S protein can bind to the ECA2 receptor on the surface of human cells. Studies show that the affinity between ECA2 and the SARS-CoV-2 receptor-binding domain (RBD) is 10 to 20 times greater than that of the SARS-CoV RBD. ECA2 has also been reported to be widely expressed in the cardiovascular system, kidneys, brain and lungs, providing a variety of cells susceptible to SARS-CoV-2, in addition to providing an explanation as to why some patients with COVID-19 die from multiple organ failure.

In the respiratory tract, ACE2 is widely expressed in the epithelial cells of alveoli, trachea, bronchi, bronchial serous glands, monocytes and alveolar macrophages. The virus enters and replicates in these cells. The mature virions are then released from the primary cells and infect new target cells. Respiratory secretions, urine, feces and sweat from patients with SARS-CoV-2 contain infectious viral particles, which can be excreted and contaminate the environment.[36]

Diagnosis

Molecular RT-PCR (Reverse Transcriptase Enzyme Polymerase Chain Reaction) test in real time is considered the standard for the diagnosis of coronavirus infection and detects viral RNA in samples collected by swab from the nasal cavity and oropharynx by secretion aspirate nasopharynx or even lower airways. Currently, it is the national reference method for confirming COVID-19, but it has the disadvantages of the time needed to collect the sample and disclose the result, in addition to the indispensability of a laboratory infrastructure and qualified professionals for its realization. RT-PCR remains the test of choice for symptomatic patients in the acute phase.[37] The Ministry of Health recommends that the test be collected between the 3rd and 7th day of symptoms, when the viral load is higher, and can be collected until the 10th day. After the seventh day, RT-PCR positivity starts to drop, reaching 45% between days 15 and 39. It has high sensitivity and specificity, especially in the first days of symptoms. However, some aspects may reveal a negative result in an infected individual, here are some: 1) insufficient amount of sample, 2) sample collected at a very early or late stage of the disease, 3) the sample has not been handled properly, 4) reasons inherent to the test, such as virus mutation or PCR inhibition. There are cases (high clinical suspicion with a negative result) which the test must be repeated with materials from samples of the lower respiratory tract. In cases of SARS, it is advisable to use the same sample with extracted RNA to investigate other respiratory viruses.[38]

Immunological tests (rapid test, ELISA - Enzyme-Linked Immunosorbent Assay - and immunofluorescence) reveal antibodies IgG (immunoglobulin G) and IgM (immunoglobulin M) to the novel coronavirus in patients with current or past infection. In studies with other coronaviruses, IgM became detectable from three to six days after infection, IgG from eight days and both remained positive even after the infection resolved. Studies have shown that the presence of antibodies increases rapidly after the seventh day of COVID-19, being present between the 8th and 14th day in 89% of patients for total antibodies, 73.3% for IgM and 54.1% for IgG. After the 15th day of illness, the presence of total antibodies reaches 100%. Only these serological tests, mainly IgG, allow us to say what percentage of the population has been infected, but without getting sick.[39]

Rapid tests expose results in minutes and do not require laboratory infrastructure for their application. They use capillary or venous blood samples. It is considered a qualitative test for screening and diagnostic assistance.[40] It is important to note that these tests have limitations and the main one is that they need to be performed, in general, from the 8th day of symptom onset.

The use of immunological tests can determine the prevalence of SARS-CoV-2 infections during the epidemic, and, for this, neighborhood tests could be carried out by sampling. In addition, they can be used to identify patients with high clinical suspicion for COVID-19, but with negative RT-PCR. It is important to highlight that negative results do not exclude infection by the novel coronavirus and positive results cannot be used as absolute evidence of the disease.

The result must be interpreted with the aid of clinical data and other confirmatory laboratory tests.[39]

At the moment, Brazil has resources for real-time RT-PCR testing for SARS-CoV-2 for hospitalized SARS cases, with sample collection indicated to 100% of cases.[38] The Ministry of Health intends to gradually make serological tests available to detect antibodies against SARS-CoV-2 to health services, guiding their performance in symptomatic people who fall into one of the following categories: 1) health service workers in action, 2) public safety service workers in action, 3) people diagnosed with SARS who live in the same household as a health professional in action. The collection of the blood sample should occur from the 8th day of symptoms and 72 hours after the disappearance of the symptoms, in order to avoid the circulation of symptomatic people and the transmissibility of the virus. This is due to evidence of a significant reduction in viral load 72 hours after the end of symptoms.[38]

The WHO issued safety recommendations in laboratories when testing samples from patients suspected of being infected with the novel coronavirus. The guidelines recommend that the handling of potentially infectious samples be carried out in biosafety cabinets, if there is the potential for spatter or the generation of droplets or aerosols. Viral culture should be performed in a safety laboratory level 3 (NB3).[21]

Clinical manifestations

The clinical manifestations of COVID-19 are diverse, ranging from asymptomatic status to acute respiratory distress syndrome and multiple organ dysfunction. Symptoms usually appear 2-14 days after viral exposure; they are: fever (88.7%), cough (67.8%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%) and headache (13.6%). Other relevant features in some cases are infection of the gastrointestinal tract, liver, kidney and brain. Diffuse alveolar damage, proliferation of epithelial cells and increased macrophages are seen in pulmonary SARS-CoV infection.[12,42] Diarrhea and conjunctivitis have also been reported in some patients.[41] According to the WHO, the majority of patients with COVID-19 (about 80%) may be asymptomatic and about 20% of cases may require hospital care because they have difficulty breathing.[21]

Pneumonia is one of the most serious symptoms and can progress quickly to acute respiratory distress syndrome. Elderly people and those with comorbidities (hypertension, chronic obstructive pulmonary disease, diabetes, cardiovascular disease) tend to develop ARDS, septic shock, metabolic acidosis and coagulation dysfunction more quickly, leading to death. About 20 to 30% of these types of patients require intensive care and mechanical ventilation. In the results of laboratory tests, critically ill patients have significantly higher levels of neutrophils, uremia and creatinine, in addition to worsening lymphocytopenia. In addition, the inflammatory factors IL-6, IL-10, tumor necrosis factor-α (TNF-α) increase, indicating the immunological status of patients.[12,42]

The average time between the onset of symptoms and dyspnea has been five days, hospitalization, seven days, and ARDS, eight days. The complications observed include acute lung injury, shock and acute kidney injury. Recovery begins in the 2nd or 3rd week after the onset of symptoms. The average length of hospital stay for those who have recovered has been ten days. Serious complications and death are more common in the elderly and in individuals with underlying comorbidities (50% to 75% of fatal cases). The prevalence for diabetics was 20% and for hypertensive patients, 30%, in the first cases analyzed for risk factors for severe disease.[12]

In addition, in relation to laboratory studies, patients may also have elevated levels of transaminases and troponin I, reported in patients who have heart failure as a complication of COVID-19. Acute phase reagents, such as C-reactive protein and erythrocyte sedimentation rate were high, but with negative procalcitonin in most cases, except for those who develop secondary bacterial infections.[20]

During pregnancy, accurate information about the clinical picture and perinatal results after infection with COVID-19 are still limited. It is known that the SARS-CoV family may result in intrauterine growth restriction, premature birth, abortion and the mother's death. Therefore, a bimonthly assessment by specialized health professionals is essential to check for complications during pregnancy.[43] Currently, pediatric patients have shown a more benign course, however at least two cases of death have been reported in China - a 10-month-old baby and a 14-year-old boy.[44] in this age group, patients may be asymptomatic or have fever, dry cough, fatigue, upper respiratory tract symptoms (such as nasal congestion and rhinorrhea), as well as gastrointestinal symptoms (nausea, vomiting, diarrhea and abdominal pain), which are seen more frequently compared to adults. Progression to pneumonia occurs in some cases; however, pediatric cases are scarce to make new claims regarding the risk of complications and death[20]

TRANSMISSION, PREVENTION AND CONTROL

The SARS-CoV-2 infection has not been fully clarified to date. The epidemiological and clinical characteristics indicate that the outbreak of COVID-19 is different from the SARS in 2002. It is assumed that this virus is transmitted from person to person through coughing or sneezing or during aerosolization. However, the virus is present in the feces of infected individuals, and oral-fecal transmission, due to contamination of water and / or food by the feces, as well as its carrying through the hands, has been reported.[45] Asymptomatic people are believed to be potential sources of infection with the novel coronavirus, which is one of the reasons why the control strategy based on isolating patients was not very successful.[46]

Studies have shown higher viral loads in the nasal cavity when compared to the throat and with no difference in viral load between symptomatic and asymptomatic people. Patients can be infectious for the duration of symptoms and even during clinical recovery. The virus can remain viable on surfaces for days in favorable atmospheric conditions, but is quickly destroyed by common disinfectants such as sodium hypochlorite and hydrogen peroxide.[47]

Currently, the only accepted method to prevent transmission is to circumvent exposure to the coronavirus according to the following guidelines: 1) regularly, clean your hands with soap and water or with 70% alcohol and save touching your unwashed hands on your nose, mouth and eyes; 2) stay at least one meter away from other people; 3) exercise the cough etiquette (if disposable tissue is not available, cough or sneeze on the forearm instead of the hands, which are important vehicles of contamination); 4) seek medical help in case of fever, cough and difficulty breathing.[45]

The indiscriminate use of a mask can cause a false sense of security, leading the population to neglect simple preventive measures, such as hand hygiene. Before using the face mask, it is important to follow good practices for use, removal and disposal, as well as washing your hands thoroughly with water and soap or 70% gel alcohol. The Ministry of Health has disclosed that the use of cloth masks can be an important restriction method when combined with the other hygiene care previously mentioned.[45]

COVID-19's greatest risk is transmission to healthcare professionals. In the SARS outbreak in 2002, 21% of those affected were health professionals. It is important to protect these workers to ensure continuity of care and to prevent the transmission of the disease to other patients. These must be placed in separate rooms. Rooms, surfaces and equipment must undergo regular decontamination, preferably with sodium hypochlorite. Airborne precautions should be taken during aerosol generation procedures, such as intubation, suction and tracheostomy. Patients can be discharged from the isolation since they have not been feverish for at least 3 days and have two consecutive negative molecular tests within the sampling interval of one day. At the community level, people should avoid crowded areas and postpone nonessential travel to places with continuous transmission[36]

Several properties of the novel coronavirus hinder prevention, that is, nonspecific characteristics of the disease, infectivity even before the onset of symptoms in the incubation period, transmission by asymptomatic people, long incubation period, prolonged disease duration and transmission even after recovery clinic. Home isolation is recommended for confirmed cases with mild or suspected disease. Ventilation at home must be adequate with sunlight to allow the virus to be destroyed.[48]

The global effort for vaccine research and development in response to the COVID-19 pandemic is unprecedented in terms of scale and speed. Based on the urgency in the current scenario, safe and effective vaccination strategies are under development to control the ongoing risk and future of epidemics or pandemics[49]

It is conceivable that some vaccine platforms may be more suitable for specific population subtypes (such as the elderly, children, pregnant women or immunocompromised patients). There is an indication that the vaccine could be available, under emergency use or similar protocols, by the beginning of 2021. This would represent a fundamental change in the traditional path of vaccine development, which takes an average of 10 years, even compared with the accelerated five-year timeline for the development of the first Ebola vaccine and will require new vaccine development paradigms that involve, for example, large-scale manufacturing capacity.[50] Even if there is still no specific vaccine for SARS-CoV-2, it is advisable that the population keeps the vaccination schedule up to date so that infections that can be confused with COVID-19 or that can weaken the organism and accentuate a possible infection are avoided. infection by this agent.[51]

A striking feature of the vaccine development scenario for COVID-19 is the variety of technology platforms being evaluated, including nucleic acids (DNA and RNA), virus-like particles, peptide, viral vector (replicating and non-replicating), recombinant protein, live attenuated virus and inactivated virus approaches. To assess the effectiveness of the vaccine, animal models specific to COVID-19 are being developed, including transgenic mice, hamsters, ferrets and non-human primates. Containment measures at biosafety level 3 are required for studies in animals involving challenges with live viruses, and the demand for these resources is likely to require international coordination to ensure the availability of sufficient laboratory capacity.[50]

The Ministry of Health has adopted measures to curb the spread of contagion by SARS-CoV-2, organizing health services for the care of patients with suspicious symptoms or who have a positive diagnosis for COVID-19, as well as in the training of this service. Among these measures are the National Contingency Plan for Human Infection with the novel coronavirus, the Coronavirus Clinical Management Protocol (COVID-19) in Primary Health Care and Informative Note nº 6/2020 - DAF / SCTIE / MS.[38,45]

Treatment

Patients with suspected or confirmed symptoms with COVID-19 should be treated in hospitals that have adequate conditions of isolation and protection. It is interesting to organize severity groups, with bases that allow to correctly guide the patient, improving the use of beds and avoiding overcrowding in hospitals and increasing the spread of infection. The admission and discharge deliberation in the Intensive Care Unit must be discussed daily in collaboration with infectologists.[48,52]

Treatment for COVID-19 includes options for controlling fever, pain, dry cough and nausea. Thus, it is advisable to use analgesics, expectorants, and antiemetics whenever there is a clinical indication, respecting the patient's clinical condition and contraindications. To contain fever, dipyrone or paracetamol is recommended. Following the statement of French health authorities, WHO initially recommended to avoid the use of ibuprofen in patients with COVID-19, based on the replication mechanism of SARS-CoV-2, and later, WHO reversed that recommendation.[53] Patients who use ibuprofen constantly should not stop treatment without medical advice. For patients with dyspnea, cough and breathing difficulties, the use of anticholinergics (ipratropium bromide, for example) is suggested due to the increased secretion of the airways. In patients with coagulation disorder, an anticoagulant may be used to reduce the risk of thromboembolism. Auxiliary pharmacological therapies must follow the directions for use and respect any contraindications. In addition, it is important to ensure adequate energy supplementation, encouraging the intake of a diet adapted to the needs of the patient. A liquid diet, with the aid of a probe, can be adopted when the patient cannot eat food in the oral routine.[48]

Considering the adverse results of the current COVID-19 pandemic, it is necessary to develop effective therapeutic strategies to deal with the lack of effective drugs and the high mortality rate. At present, there is no evidence to indicate a specific pharmacological therapy for COVID-19. Since December 2019, several researches have been carried out in order to develop therapeutic strategies for the treatment of this disease. Among the strategies used, the following stand out: antiviral therapy (nucleoside analogs with antiviral activity, broad-spectrum antivirals and protease inhibitors) and immunotherapy.[54] Antiviral drugs and corticosteroid treatment, commonly used in clinical practice, including neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, etc.), ganciclovir and ribavirin, as well as methylprednisolone for influenza viruses, are being investigated for the treatment of COVID-19. Chloroquine is a drug with potential to treat COVID-19. For many years, it has been used to treat malaria, with a mechanism that is not well known against some viral infections. Several possible mechanisms are investigated: chloroquine can inhibit the pH-dependent steps of the replication of various viruses, with a potent effect on SARS infection and spread. In addition, chloroquine has immunomodulatory effects, suppressing the production / release of TNF-α and IL-6. It also works as a new class of autophagy inhibitor, interfering with viral infection and replication. Several studies have found that chloroquine interferes with the glycosylation of SARS-CoV cell receptors and works in the entry and post-entry stages of infection by the novel coronavirus in Vero E6 cells. A combination of remdesivir and chloroquine has been shown to effectively inhibit SARS-CoV-2 recently emerged in vitro.[42]

Treatment with remdesivir alone or in combination with chloroquine or interferon beta was found to be effective against COVID-19 infection. This strategy has not yet caused obvious side effects. However, further research is needed to confirm the impacts of remdesivir. As coronaviruses share the main genomic elements, common therapeutic targets may be of greater importance. Therapeutic agents targeting nucleotides, viral nucleic acids and enzymes / proteins involved in coronavirus replication and transcription can be promising strategies for the treatment of coronavirus diseases. Protein S is an important target for antiviral agents, due to its vital role in the interaction between the virus and its cell receptor.[42]

There are antiviral candidates that exhibit only a narrow spectrum of activity, as they are effective only at extraordinarily high therapeutic doses causing severe side effects or immune suppression. In vitro, interferon beta is partially effective against the novel coronavirus. Interferons, in combination with ribavirin, may have increased activity in vitro when compared to interferons isolated against some coronaviruses; however, the effectiveness of this in vivo combination requires additional evaluation.[55]

An interesting feature of plasma from recovered patients is the presence of active antibodies, and thus transferring plasma from people recovered from COVID-19 to infected individuals can increase immunity against SARS-CoV-2. Monoclonal antibodies that can inhibit cell-virus receptor binding and interrupt cell-virus fusion have been developed.[56] The combination of two or more monoclonal antibodies may be suitable for faster recovery of patients. Finally, antiviral peptides targeting different regions of protein S, should also be considered against COVID-19.[57] Immunotherapy is considered an effective method for the clinical treatment of infectious diseases. The use of monoclonal antibodies is a new era in the prevention of infectious diseases that overcomes many drawbacks associated with serum therapy and intravenous immunoglobulin preparations in terms of specificity, purity, low risk of contamination and safety of blood-borne pathogens. Monoclonal antibodies are a versatile class of pharmaceutical products that have been used successfully by the pharmaceutical industry, which can provide an efficient therapeutic intervention with a highly specific treatment against a specific disease.[12]

CONCLUSION

The current COVID-19 pandemic is clearly an international public health problem. There have been rapid advances in what we know about the pathogen, but further studies are needed to provide an in-depth understanding of replication, pathogenesis and biological properties using reverse genetics and related molecular techniques. These investigations will assist in the control and prevention of SARS-CoV-2-mediated pneumonia and future emerging diseases.

There are several studies underway with the aim of discovering potential treatments for this disease. Currently, effective intervention in infection control measures is the best way to prevent the spread of SARS-CoV-2.

RESUMO

Introdução: Em dezembro de 2019, a doença do novo coronavírus 2019 (COVID-19), na China, causou um surto global e é um grande problema de saúde pública; e a Organização Mundial de Saúde declarou que COVID-19 constituiu uma Emergência de Saúde Pública Internacional. O objetivo é informar sobre COVID-19, destacando o seu histórico, organização genômica do novo coronavírus, patogênese, diagnóstico, manifestações clínicas, transmissão, controle, prevenção e atuais estratégias terapêuticas. **Delineamento**: Trata-se de uma revisão narrativa, na qual foram realizadas buscas de artigos nas bases *PubMed* e *Science Direct*. **Implicações**: COVID-19 é altamente patogênica e nenhum tratamento específico ou vacina estão atualmente disponíveis. Diante desses fatos, inúmeros países adotaram medidas extensivas de controle para reduzir a transmissão da doença de pessoa para pessoa. **Conclusão**: Várias pesquisas estão em andamento no intuito de identificar potenciais tratamentos para COVID-19. Atualmente, controlar a infecção é a melhor maneira de impedir a disseminação do novo coronavírus.

DESCRITORES

Coronavirus; Infecções por Coronavirus; Pandemias.

RESUMEN

Introducción: En diciembre de 2019, la nueva enfermedad de coronavirus 2019 (COVID-19), em China, causó un brote global y es un gran problema de salud pública; y la Organización Mundial de la Salud declaró que COVID-19 constituía una emergencia internacional de salud pública. El objetivo es informar sobre COVID-19, destacando su historia, organización genómica del nuevo coronavirus, patogénesis, diagnóstico, manifestaciones clínicas, transmisión, control, prevención y estrategias terapéuticas actuales. **Delineación**: Es una revisión narrativa, en la que se realizaron búsquedas de artículos en las bases de datos *PubMed* y *Science Direct*. **Implicaciones**: COVID-19 es altamente patógeno y actualmente no hay un tratamiento específico o vacuna disponible. Dados estos hechos, numerosos países han adoptado amplias medidas de control para reducir la transmisión de la enfermedad de persona a persona. **Conclusión**: Se están realizando varias investigaciones para identificar posibles tratamientos para COVID-19. Actualmente, controlar la infección es la mejor manera de prevenir la propagación del nuevo coronavirus.

DESCRIPTORES

Coronavirus; Infecciones por Coronavirus; Pandemias.

REFERENCES

1. Li YH, Hu CY, Wu NP, Yao HP, Li LJ. Molecular characteristics, functions, and related pathogenicity of MERS-CoV proteins. Engineering [Internet]. 2019 Oct [cited 2020 Apr 12]; 5(5):940–947. Available from: https://doi.org/10.1016/j.eng.2018.11.035

2. Rodriguez-Morales AJ, Balbin-Ramon GJ, Rabaan AA, Sah R, Dhama K, Paniz-Mondolfi A, et al. Genomic epidemiology and its importance in the study of the COVID-19 pandemic. Infez Med [Internet]. 2020 Jun [cited 2020 Apr 13]; 28(2):139–142. Available from: https://doi.org/10.1186/s13054-019-2491-9

3. Chow EJ, Doyle JD, Uyeki TM. Influenza virus-related critical illness: prevention, diagnosis, treatment. Crit Care [Internet]. 2019 Jun [cited 2020 Apr 13]; 23(1):214. Available from: https://doi.org/10.1186/s13054-019-2491-9

4. Cousins S. WHO hedges its bets: the next global pandemic could be disease X. BMJ [Internet]. 2018 May [cited 2020 Apr 13]; 361:1–12. Available from: https://doi.org/10.1136/bmj.k2015

5. Grange ES, Neil EJ, Stoffel M, Singh AP, Tseng E, Resco-Summers K, et al. Responding to COVID-19: The UW medicine information technology services experience. Appl Clin Inform [Internet]. 2020 Mar [cited 2020 Apr 10]; 11(2):265–275. Available from: https://doi.org/10.1055/s-0040-1709715

6. Lana RM, Coelho FC, Gomes MFC, Cruz OG, Bastos, LS, Villela, DAM, et al. Emergência do novo coronavírus (SARS-CoV-2) e o papel de uma vigilância nacional em saúde oportuna e efetiva. Cad. Saúde Pública [Internet]. 2020 Jan [cited 2020 Apr 10]; 36(3):1–12. Available from: https://doi.org/10.1590/0102-311x00019620

7. Masters PS. The molecular biology of coronaviruses. Adv Virus Res [Internet]. 2006 Mar [cited 2020 Apr 10]; 66:193–292. Available from: https://doi.org/10.1016/S0065-3527(06)66005-3

8. Vabret A, Mourez T, Gouarin S, Petitjean J, Freymuth F. An outbreak of coronavirus OC43 respiratory infection in Normandy, France. Clin Infect Dis [Internet]. 2003 Apr [cited 2020 Apr 10]; 36:985–989. Available from: https://doi.org/10.1086/374222

9. Talbot PJ, Desforges M, Brison E, Jacomy H. Coronaviruses as encephalitis-inducing infectious agents. In: Tkachev, S. (Ed.), Non-flavirus Encephalitis. In-Tech; 2011. p. 185–202. Available from: https://doi.org/10.5772/24967

10. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. Respirology [Internet]. 2018 Oct [cited 2020 Apr 13]; 23:130–137. Available from: https://doi.org/10.1111/resp.13196

11. Hamre D, Procknow JJ. A new virus isolated from the human respiratory tract. Proc Soc Exp Biol Med [Internet]. 1966 Jan [cited 2020 Apr 13]; 121:190–193. Available from: https://doi.org/10.3181/00379727-121-30734

12. Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication, and pathogenesis. J Med Virol [Internet]. 2020 Apr [cited 2020 Apr 13]; 92(4):418–423. Available from: https://doi.org/10.1002/jmv.25681

13. Keogh-Brown MR, Smith RD. The economic impact of SARS: how does the reality match the predictions? Health Policy [Internet]. 2008 Oct [cited 2020 Apr 13]; 88:110–120. Available from: https://doi.org/10.1016/j.healthpol.2008.03.003

14. Banerjee A, Kulcsar K, Misra V, Frieman M, Mossman K. Bats and Coronaviruses. Viruses [Internet]. 2019 Jan [cited 2020 Apr 15]; 11:41–51. Available from: https://doi.org/10.3390/v11010041

15. 15. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet [Internet]. 2020 Feb [cited 2020 Apr 15]; 395:565–574. Available from: https://doi.org/10.1016/S0140-6736(20)30251-8

16. Demurtas OC, Massa S, Illiano E, Martinis DD, Chan PKS, Bonito PD, et al. Antigen production in plant to tackle infectious diseases flare up: the case of SARS. Plant Sci [Internet]. 2016 Feb [cited 2020 Apr 15]; 7(54):1–12. Available from: https://doi.org/10.3389/fpls.2016.00054

17. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol [Internet]. 2019 Mar [cited 2020 Apr 15]; 17:181–192. Available from: https://doi.org/10.1038/s41579-018-0118-9

18. Conforti C, Giuffrida R, Dianzani C, Di Meo N, Zalaudek I. COVID-19 and psoriasis: is it time to limit treatment with immunosuppressants? A call for action. Dermatol Ther [Internet]. 2020 Mar [cited 2020 Apr 18]; 11:1–10. Available from: https://doi.org/10.1111/dth.13298

19. Yan Y, Chen H, Chen L, Cheng B, Diao P, et al. Consensus of Chinese experts on protection of skin and mucous membrane barrier for healthcare workers fighting against coronavirus disease 2019. Dermatol Ther [Internet]. 2020 Mar [cited 2020 Apr 18]; 13:1–12. Available from: https://doi.org/10.1111/dth.13310

20. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet [Internet]. 2020 Jan [cited 2020 Apr 18]; 395:497–506. Available from: https://doi.org/10.1016/S0140-6736(20)30183-5

21. World Health Organization (WHO). Advice on the use of masks in the community, during home care and in healthcare settings in the context of the novel coronavirus (2019-nCoV) outbreak. Genebra: WHO; 2020.

22. Brasil. Ministério da Saúde. Coronavírus Brasil. Painel Geral. Brasília: MS; 2020. Available from: https://covid.saude.gov.br/

23. Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, et al. Commentary Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China. Cell Host Microbe [Internet]. 2020 Mar [cited 2020 Apr 18]; 27(3):325–328. Available from: https://doi.org/10.1016/j.chom.2020.02.001

24. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S. et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically-Proven Protease Inhibitor. Cell [Internet]. 2020 Apr [cited 2020 Apr 23]; 181(2):271–280. Available from: https://doi.org/10.1016/j.cell.2020.02.05

25. Brison E, Jacomy H, Desforges M, Talbot PJ. Novel treatment with neuroprotective and antiviral properties against a neuroinvasive human respiratory virus. J Virol [Internet]. 2014 Feb [cited 2020 Apr 18]; 88(3):1548–1563. Available from: https://doi.org/10.1128/JVI.02972-13

26. Ruch TR, Machamer CE. The coronavirus E protein: assembly and beyond. Viruses [Internet]. 2012 Mar [cited 2020 Apr 18]; 4(3):363–382. Available from: https://doi.org/10.3390/v4030363

27. Nieto-Torres JL, DeDiego ML, Verdia-Baguena C, Jimenez-Guardeno JM, Regla-Nava JA, Fernandez-Delgado R, et al. Severe acute respiratory syndrome coronavirus envelope protein ion channel activity promotes virus fitness and pathogenesis. PLoS Pathog [Internet]. 2014 May [cited 2020 Apr 18]; 10 (5). Available from: https://doi.org/10.1371/journal.ppat.1004077

28. Jimenez-Guardeno JM, Nieto-Torres JL, DeDiego ML, Regla-Nava JA, Fernandez-Delgado R, Castano-Rodriguez C, et al. The PDZ-binding motif of severe acute respiratory syndrome coronavirus envelope protein is a determinant of viral pathogenesis. PLoS Pathog [Internet]. 2014 Aug [cited 2020 Apr 20]; 10(8):1–12. Available from: https://doi.org/10.1371/journal.ppat.1004320

29. Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses [Internet]. 2019 Jan [cited 2020 Apr 20]; 11(1):5969. Available from: https://doi.org/10.3390/v11010059

30. Ng OW, Keng CT, Leung CSW, Peiris JSM, Poon LLM, Tan YJ. Substitution at aspartic acid 1128 in the SARS coronavirus spike glycoprotein mediates escape from a S2 domain-targeting neutralizing monoclonal antibody. PLoS One [Internet]. 2014 Jul [cited 2020 Apr 22]; 9(7):1–10. Available from: https://doi.org/10.1371/journal.pone.0102415

31. Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. Int J Antimicrob Agents [Internet]. 2020 Mar [cited 2020 Apr 22]; 55(3):105924. Available from: https://doi.org/10.1016/j.ijantimicag.2020.105924

32. Enjuanes L, Zuniga S, Castano-Rodriguez C, Gutierrez-Alvarez J, Canton J, Sola I. Molecular basis of coronavirus virulence and vaccine development. Adv Virus Res [Internet]. 2016 Aug [cited 2020 Apr 22]; 96:245–86. Available from: https://doi.org/10.1016/bs.aivir.2016.08.003

33. Brian DA, Baric RS. Coronavirus genome structure and replication. Curr Top Microbiol Immunol [Internet]. 2005 [cited 2020 Apr 22]; 287:1–30. Available from: https://doi.org/10.1002/jmv.25681

34. Peiris JS, Chu CM, Cheng VC, Chan KS, Hung IF, Poon LL, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet [Internet]. 2003 May [cited 2020 Apr 22]; 361(9371):1767–1772. Available from: https://doi.org/10.1016/s0140-6736(03)13412-5

35. Spiegel M, Schneider K, Weber F, Weidmann M, Hufert FT. Interaction of severe acute respiratory syndrome-associated coronavirus with dendritic cells. J Gen Virol [Internet]. 2006 Jul [cited 2020 Apr 22]; 87(7):1953–1960. Available from: https://doi.org/10.1099/vir.0.81624-0

36. Phadke M, Saunik S. Use of angio-tensin receptor blockers such as Telmisartan, losartan in n-CoV Wuhan corona virus. Rapid response. The BMJ [Internet]. 2020 Jan [cited 2020 Apr 20]; 368, m406. Available from: https://doi.org/10.1136/bmj.m406

37. Loeffelholz MJ, Tang Y-W. Laboratory diagnosis of emerging human coronavirus infections: the state of the art. Emerg Microbes Infect [Internet]. 2020 Mar [cited 2020 Apr 20]; 30; 9:1–11. Available from: https://doi.org/10.1080/22221751.2020.1745095

38. Brasil. Ministério da Saúde. Secretaria de Atenção Primária à Saúde. Coronavírus COVID-19: protocolo de manejo clínico do Novo Coronavírus (COVID-19) na Atenção Primária à Saúde: versão 6. Brasília, DF: Ministério da Saúde; 2020. Available from: https://www.unasus.gov.br/especial/covid19/pdf/37

39. Li Z, Yi Y, Luo X, Xiong N, Liu Y, Li S, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. J Med Virol [Internet]. 2020 Feb [cited 2020 Apr 20]. Available from: https://doi.org/10.1002/jmv.25727

40. McIntosh K. Coronavirus disease 2019 (COVID-19): epidemiology, virology, clinical features, diagnosis, and prevention [Internet]. Waltham (MA): UpToDate; [updated 10 Apr 2020, cited 14 Apr 2020]. Available from: https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19

41. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ [Internet]. 2020 Feb [cited 2020 Apr 20]; 368:m606. Available from: https://doi.org/10.1136/bmj.m606

42. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA [Internet]. 2020 Feb [cited 2020 Apr 20]; 323(11):1061–1069. Available from: https://doi.org/10.1001/jama.2020.1585

43. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet [Internet]. 2020 Mar [cited 2020 Apr 22]; 395(10226):809–815. Available from: https://doi.org/10.1016/S0140-6736(20)30360-3

44. Carlotti APCP, Carvalho WB, Johnston C, Rodriguez IS, Delgado AF. COVID-19 Diagnostic and Management Protocol for Pediatric Patients. CLINICS [Internet]. 2020 Apr [cited 2020 Apr 22]; 75:e1894. Available from: https://doi.org/10.6061/clinics/2020/e1894

45. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Centro de Operações de Emergências em Saúde Pública. Centro de Operações de Emergência em Saúde Pública para Infecção Humana pelo Novo Coronavírus (COE-nCoV). 2020. Especial: doença pelo Coronavírus 2019. Boletim Epidemiológico. Brasília: MS; 2020. Available from: https://www.saude.gov.br/images/pdf/2020/April/06/2020-04-06-BE7-Boletim-Especial-do-COE-Atualizacao-da-Avaliacao-de-Risco.pdf

46. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med [Internet]. 2020 Mar [cited 2020 Apr 20]; 382:970–971. Available from: https://doi.org/10.1056/NEJMc2001468

47. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med [Internet]. 2020 Feb [cited 2020 Apr 18]; 382:1177–1179. Available from: https://doi.org/10.1056/NEJMc2001737

48. Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res [Internet]. 2020 Feb [cited 2020 Apr 18]; 7(1):4–14. Available from: https://doi.org/10.1186/s40779-020-0233-6

49. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci [Internet]. 2020 Mar [cited 2020 Apr 19]; 63(3):364–74. Available from: https://doi.org/10.1007/s11427-020-1643-8

50. Le TT, Andreadakis Z, Kumar A, Román RG, Tollefsen S, Saville M, et al. The COVID-19 vaccine development landscape. Nature [Internet]. 2020 May [cited 2020 Apr 20]; 19(5):305–306. Available from: https://doi.org/10.1038/d41573-020-00073-5

51. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. Mil Med Res [Internet]. 2020 Mar 13 [cited 2020 Apr 20]; 7(1):11. Available from: https://doi.org/10.1186/s40779-020-00240-0

52. Bouadma L, Lescure FX, Lucet JC, Yazdanpanah Y, Timsit JF. Severe SARS-CoV-2 infections: practical considerations and management strategy for intensivists. Intensive Care Med [Internet]. 2020 Feb [cited 2020 Apr 20]; 46:579–582. Available from: https://doi.org/10.1093/cid/ciz544

53. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? The Lancet [Internet]. 2020 Mar 11 [cited 2020 Apr 20]; 8:1–10. Available from: https://doi.org/10.1016/S2213-2600(20)30116-8

54. Kang S, Peng W, Zhu Y, Lu S, Zhou M, Lin W, et al. Recent progress in understanding 2019 novel coronavirus (SARS-CoV-2) associated with human respiratory disease: detection, mechanisms and treatment. Int J Antimicrob Agents [Internet]. 2020 May [cited 2020 Jun 01]; 55: 105950. Available from: https://doi.org/10.1016/j.ijantimicag.2020.105950

55. Arabi Y, Balkhy H, Hajeer AH, Bouchama A, Hayden FG, Al-Omari A, et al. Feasibility, safety, clinical, and laboratory effects of convalescent plasma therapy for patients with Middle East respiratory syndrome coronavirus infection: a study protocol. Springerplus [Internet]. 2015 Nov [cited 2020 Apr 17]; 4(709). Available from: https://doi.org/10.1186/s40064-015-1490-9

56. Both L, Banyard AC, Dolleweerd CV, Wright E, Ma JK-C, Fooks AR. Monoclonal antibodies for prophylactic and therapeutic use against viral infections. Vaccine [Internet]. 2013 Mar [cited 2020 Apr 17]; 31(12):1553–1559. Available from: https://doi.org/10.1016/j.vaccine.2013.01.025

57. Zumla A, Chan JFW, Azhar EI, Hui DSC, Yuen KY. Coronaviruses-drug Discovery and therapeutic options. Nat Rev Drug Discov [Internet]. 2016 May [cited 2020 Apr 14]; 15:327–347. Available from: https://doi.org/10.1038/nrd.2015.37

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CONFLICTS OF INTEREST

There are no conflicts of interest to declare.