REVIEW
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COVID-19 pandemic: the biggest challenge for the 21st century

Pandemia da COVID-19: o maior desafio do século XXI

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ABSTRACT

Introduction: The pandemic caused by the new coronavirus 2019, COVID-19 has severely impacted the global scenario, worsening the rates of morbidity and mortality. Given that scenario, there is an urgent need to train and qualify healthcare professionals in coping with this disease. **Objective:** This study carried out a narrative review on COVID-19, analyzing aspects related to epidemiology, etiology, clinical manifestations, diagnosis and treatment. **Method:** It is a narrative review of the literature, developed from scientific research indexed in the PubMed/MEDLINE database, from January to April 2020. The following search terms were used for the search, "COVID-19", "SARS-CoV-2" and "2019nCoV". **Results:** The articles showed that the origin of SARS-CoV-2, the causative agent of COVID-19, is uncertain. The rapid spread of the virus may be related to the form of transmission and its ability to survive in the external environment. Most hospitalized patients are over 60 years old, have immunosuppression and comorbidities such as hypertension and diabetes. The diagnosis is basically clinical and/or associated with molecular examination. There is no specific drug for the treatment of COVID-19. However, some drugs look promising and are in clinical trials phases. **Conclusions:** The results presented can guide strategy and practice of healthcare professionals in direct contact with the care of people with COVID-19. However, further studies are needed to better conduct pandemic coping strategies.

KEYWORDS: COVID-19; SARS-CoV-2; Pandemic; Betacoronavirus

RESUMO

Introdução: A pandemia da doença causada pelo novo coronavírus 2019, COVID-19, tem impactado sobremaneira o cenário mundial, agravando as taxas de morbidade e mortalidade. Diante desse cenário, é urgente a necessidade de capacitar e qualificar profissionais da área de saúde no enfrentamento dessa doença. **Objetivo:** Este estudo se propôs a realizar uma revisão narrativa sobre a COVID-19, abordando os aspectos relacionados à origem, à etiologia, às manifestações clínicas, ao diagnóstico e ao tratamento. **Método:** Trata-se de uma revisão narrativa da literatura, realizada a partir de periódicos científicos indexados na base de dados PubMed/MEDLINE, durante o período de janeiro a abril de 2020. Os seguintes descritores foram utilizados na pesquisa: "COVID-19", "SARS-CoV-2" e "2019nCoV". **Resultados:** Os artigos evidenciaram que a origem do SARS-CoV-2, agente causador da COVID-19, é incerta. A rápida propagação do vírus pode estar relacionada à forma de transmissão e capacidade de sobrevivência no ambiente externo. Os pacientes hospitalizados apresentam, em sua maioria, idade acima de 60 anos, presença de imunossupressão e comorbidades como hipertensão e diabetes. O diagnóstico é, basicamente, clínico e/ou associado ao exame molecular. Não há medicamento específico para o tratamento da COVID-19. No entanto, alguns parecem promissores e encontram-se em fase de ensaios clínicos. **Conclusões:** Os resultados apresentados podem orientar a prática de profissionais de saúde no contato direto com o cuidado às pessoas com a COVID-19. No entanto, mais estudos são necessários para melhor condução das estratégias de enfrentamento da pandemia.

PALAVRAS-CHAVE: COVID-19; SARS-CoV-2; Pandemia; Betacoronavírus

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INTRODUCTION

The disease pandemic caused by the new coronavirus 2019 (COVID-19) has become one of the greatest challenges of the 21st century. It currently affects over 100 countries and territories on five continents[1]. Its impacts are still invaluable but they directly and/or indirectly affect the health and economy of the global population.

COVID-19 is an infectious disease caused by the Severe Acute Respiratory Syndrome 2 coronavirus (SARS-CoV-2). According to the World Health Organization (WHO), on December 31, 2019, in Wuhan, China, the first cases of pneumonia caused by a foreign agent were described and reported to the health authorities[1]. On January 7, 2020, Zhu et al.[2] announced the sequencing of the viral genome, and on January 12, China shared the genetic sequence with WHO and other countries through the Global Initiative on Sharing All Influenza Data (GISAID) international database. Since then, cases started to spread rapidly across the world, initially across Asia, with cases reported in Thailand, Japan, and South Korea on January 13, 15, and 20, respectively. Then, the virus was imported into other countries and continents. On January 23, the first cases of the disease in the United States of America (USA) were registered[3,4,5,6].

The coronavirus (CoV), initially isolated in 1937, became known in 2002 and 2003 for causing a severe acute respiratory syndrome in humans called SARS. At the time, the epidemic was responsible for several cases of severe infections in the lower respiratory system, accompanied by fever and, frequently, respiratory failure[7]. However, it was quickly controlled and only a few countries such as China, Canada, and the USA were affected by the virus[8]. The exhaustive work of researchers, health professionals, among others, led to the containment of the "giant".

Eighteen years after the first cases of SARS-CoV, this new CoV, called SARS-CoV-2, is responsible for the rapid spread and dissemination of the disease at national and international levels. This new strain is less lethal than other members of the family, such as SARS-CoV and the virus that causes Middle East Respiratory Syndrome (MERS-CoV), which appeared in 2012 in Saudi Arabia. However, although the strains originated from a common ancestor, SARS-CoV-2 has a greater potential for spreading[9,10]. China was the first country to report the disease and, by April 21, 2020, 213 countries, territories, or areas reported cases of COVID-19, corresponding to a total of 2,397,216 confirmed cases[11]. In Brazil, the first case was registered on February 26, 2020, in the state of São Paulo[12]. The epidemiology of COVID-19 is still poorly understood, because, for many countries, it is ongoing, which makes it difficult to compare results. The current scenario is not satisfactory and urges the adoption of public health measures by managers at federal, state, and municipal levels, to mitigate morbidity rates and eradicate the disease[13].

Although the first isolation of CoV was carried out in 1937, little is known about this new strain and its consequences for humans. Considering the current global classification of COVID-19 as a pandemic and the need to train and qualify health professionals in coping with this disease, this study was based on a narrative review of the literature, that aimed to gather and synthesize available evidence about COVID-19, as well as aspects related to etiology, epidemiology, transmission, clinical manifestations, diagnosis, and treatment.

METHOD

A narrative review of the literature was carried out by surveying scientific journals indexed in the PubMed/MEDLINE database on COVID-19 and aspects related to this disease. The manual search strategy was also used in reference lists of articles selected by the database, in order to identify eligible articles that might not have been retrieved by the search strategy. The following descriptors, in English, were considered: "COVID-19", "SARS-CoV-2", and "2019nCoV". Articles included in the study were published between January and April 2020, selected according to their degree of relevance for the purpose of this review. As exclusion criteria, we opted for articles that were not fully available online, studies with an animal model, in addition to journals that did not address the theme of the review. Then, the data were systematized in six categories: i) Origin, ii) Etiology and viral characteristics, iii) Transmission and clinical manifestation, iv) Diagnosis, v) Treatment, and vi) Public health policies and perspectives.

RESULTS AND DISCUSSION

i) Origin

Initially, it was speculated that the new CoV originated at a seafood market in Wuhan, Hubei province, and that it spread rapidly from there, making it the epicenter of the epidemic. It is known that bats represent the main natural reservoir for a diverse range of CoV, such as SARS-CoV, SARS-CoV-2, and MERS-CoV[14]. A study published by Paraskevis et al.[15] suggested that SARS-CoV-2 is phylogenetically related to BatCoV RaTG13 detected in bats in Yunnan province, China. Genomic sequencing showed a similarity of approximately 96.0%. However, BatCoV RaTG13 does not have the exact variant that caused the current outbreak in humans but it strengthens the hypothesis that SARS-CoV-2 originated in bats. As bats are not sold on the Wuhan market, the possibility that the virus may have appeared in this location has been ruled out[16].

Some studies speculate that SARS-CoV-2 was transmitted from bats to pangolins and, from these intermediate hosts, to humans. Although there is no data that support this hypothesis, the results are based on phylogenetic analyzes and viral protein sequencing that shows similarities between SARS-CoV-2 and other CoV, capable of infecting cells of other species, such as pangolins and turtles[16,17]. According to Liu et al.[17], the S protein of SARS-CoV-2 and that of the pangolin CoV SRR10168377 have a homology of 88.0%, which intensifies the possibility that the

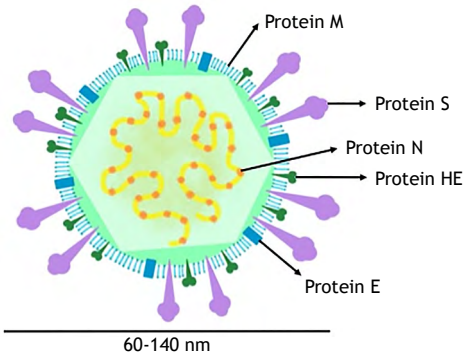
pangolin is a possible intermediate host, suggesting the interspecies transmission until reaching humans (bat - pangolin - humans). Although many studies have attempted to identify the exact location and timing of the virus' emergence, we do not know when CoV gained the ability to cross the species barrier, infecting humans, and becoming SARS-CoV-2.

ii) Etiology and viral characteristics

CoV are positive-sense single-stranded RNA viruses, not segmented, and with a protein envelope, consisting mainly of protein E[18]. Its particles have rounded or oval conformation, usually polymorphic, with a diameter that varies between 60 and 140 nm[19]. It is evident, through electron microscopy, the presence of large projections on its surface, similar to a crown, hence the origin of its name, *corona* (crown). Such structures represent the large glycoproteins of the surface spikes, called S protein. In addition to these proteins, others that are quite characteristic of CoV are the nucleocapsid protein (N Protein), hemagglutinin-esterases (HE) protein that mediates the viral binding process, and the M protein that ensures the maintenance of the envelope shape (Figure)[18,20].

CoV are representative of the order Nidovirales and classified in four distinct genera called Alphacoronavirus (Alpha-CoV), Betacoronavirus (Beta-CoV), Gammacoronavirus (Gamma-CoV), and Deltacoronavirus (Delta-CoV). Alpha-CoV and Beta-CoV have the ability to infect mammals, while Gamma-CoV and Delta-CoV infect only birds. Among the Alpha-CoV and Beta-CoV genera, there are different CoV capable of infecting humans. HCoV-229E and HCoV-NL63 are the most representative of the Alpha-CoV genera. HCoV-OC43, HCoV-HKU1, MERS-CoV, SARS-COV, and SARS-CoV-2 are the most representative of the Beta-CoV genera[7].

All these viruses have a zoonotic origin, bats are usually the hosts of CoV 229E, NL63, SARS-CoV, MERS-CoV, and SARS-CoV-2, while OC43 and HKU1 are found in rats. In addition to these animals, CoV has also been identified in domestic and wild mammals.



Source: Own elaboration, 2020.
Protein M: Membrane protein; Protein S: Peak (spike) protein; Protein N: Nucleocapsid protein; Protein HE: Hemagglutinin esterase protein; Protein E: Envelope protein

Figure. Graphic representation of SARS-CoV-2 highlighting its main viral structures.

Usually, these animals adapt evolutionarily over the years and do not present complications resulting from the virus infection, representing only potential reservoirs. The transmission of a CoV to a new host, such as humans, can provide point mutations that culminate in the development of pathogenic strains and therefore pose a risk to the population[7].

Existing CoV before the emergence of SARS-CoV, such as HCoV-229E and HCoV-NL63, do not represent a major public health problem, as they were responsible only for mild respiratory diseases, restricted to the upper respiratory tract, such as the common cold. Medically important are restricted to SARS-CoV, MERS-CoV, and SARS-CoV-2[7]. All three have phylogenetic similarities and share the ability to encode non-structural proteins such as 3-chymotrypsin-like protease (3CLpro), papain-like protease (PLpro), helicase, and RNA-dependent RNA polymerase (RdRp). All of these non-structural proteins are essential enzymes for viral replication and highly conserved among the medically important CoV. In addition to these, structural protein S also plays a major role, as it is through it that SARS-CoV-2 interacts with the specific receptor on the host's cell membrane, allowing the virus to enter the cell's cytosol. Given these findings, it is reasonable to consider that the existing inhibitors against MERS and SARS-CoV can be used as a therapeutic strategy for COVID-19[20,21,22].

iii) Transmission and clinical manifestation

As it is an acute respiratory infection, SARS-CoV-2 spreads mainly through droplets, respiratory secretions, and direct contact with the infected patient. Given this perspective, it is highlighted the virus's ability to be transmitted from human to human (direct transmission), mainly among family members, among whom there is greater close contact and for a prolonged time[23]. A study carried out by Van Doremalen et al.[24] demonstrated that SARS-CoV-2 can remain viable and infectious in aerosols for up to 3 hours after being eliminated in the environment. However, this survival time can vary depending on the location, the quantity, the thickness of the secretion released by the patient, and the surface on which it will be deposited.

Although direct transmission is recognized as one of the main dissemination mechanisms, indirect transmission through contaminated surfaces also contributes to the perpetuation of the virus. Plastic and stainless-steel surfaces, when compared with copper and cardboard, give the virus the ability to remain viable and infectious for up to 72h[24]. Other forms of transmission were also recorded. A study carried out by Zhang et al.[25] demonstrated that, in some patients, it was possible to detect the presence of viral particles in blood samples and rectal swabs, which indicates the possibility of different transmission routes. Together, the results suggest that it is a dangerous virus due to the spread speed and that it is highly resistant to the external environment.

The entering process of the virus on the host cell involves the interaction between protein S and the cell surface receptor, known as angiotensin-converting enzyme 2 (ACE2), which

is present mainly in the cells of the lower respiratory tract of humans[26]. Once inside the host cell, the viral replication process begins, culminating in the formation of new particles, release by budding, and consequent destruction of the host cell. The incubation period averages 7 days, with reports in some studies of up to 21 days. After this period, individuals may remain asymptomatic or present a mostly mild clinical picture, except for those belonging to risk groups. However, in the most severe cases, the delay in the outcome of the disease implies a prolonged hospitalization for an average of 14 to 21 days, reflecting an overload on the health system[7,19].

A study by Guan et al.[27] with 1,099 infected and laboratory-confirmed patients showed that the most common symptoms were: fever (43.8% on admission and 88.7% during hospitalization), cough (67.8%), and fatigue (38.1%). When analyzing the temperature, it was observed that approximately 56.0% were afebrile at the moment of diagnosis, that is, the absence of fever does not rule out the disease. Interestingly, diarrhea was present in 3.8% of individuals. The presence of ACE2 protein at other sites in the human body, such as small intestine enterocytes, may explain the gastrointestinal symptoms reported by patients[14]. Usually, hospitalized patients present themselves as the "tip of the iceberg", that is, report more severe signs and symptoms and, therefore, represent an unreliable epidemiological picture. It is believed that 86.0% of infected individuals were not assessed as a result of the absence or presence of nonspecific symptoms[28].

According to Li et al.[28] and Wang et al.[29], these "undocumented cases" represent, approximately, 80.0% of the sources of infection. The number of tests available is insufficient for mass testing of the population and this directly impacts the planning and performance of public health actions and control of epidemiological surveillance. Given these findings, all individuals should be considered as potential disseminators of the infection and, therefore, social distancing, use of masks, and hygiene habits should be considered for all individuals[28]. Thus, the actual number of asymptomatic, pre-symptomatic, and oligosymptomatic individuals represent a major bottleneck for the competent organs, especially because it compromises the current statistics in dealing with the disease[28,29,30,31].

The demographic profile of COVID-19 cases is still debatable and needs further studies, due to the lack of characterization of asymptomatic cases not known to the health system. Thus, the vast majority of articles are based on hospitalized patients, who have more complex care demands and, therefore, may not represent a reliable assessment of the demographic profile of the disease. However, these data are essential to identify priority groups and, in this context, develop specific preventing and caring strategies against COVID-19. Among the population segments that present fragility, making them more vulnerable to hospitalization for SARS-CoV-2, the following stand out: men, over the age of 60, with immunosuppression and the presence of comorbidities such as hypertension and diabetes[27].

When in serious condition, patients infected with SARS-CoV-2 may have symptoms related to respiratory failure, such as: shortness of breath, low breathing sounds, dullness to percussion, elevation, and decrease in tactile speech tremor[19]. This moment represents the most critical stage of COVID-19 and is believed to be caused by a "storm of pro-inflammatory cytokines". That is, an exacerbated inflammatory response that, in an attempt to eliminate the viral agent, causes several lesions affecting the type I and II pneumocytes, cells found in the pulmonary alveoli. Thus, inadequate alveolar ventilation with little oxygen uptake and decreased carbon dioxide removal are factors that lead to multiple organ failure and, ultimately, the death of the patient[32]. When performing pulmonary auscultation, it is possible to identify the presence of wet rales, in addition to, in a few cases, bronchophonies (egophonia, pectoriloquy)[19].

iv) Diagnosis

The confirmatory diagnosis of COVID-19 is made by molecular testing of respiratory secretions. The non-specific symptoms of the pathology and the absence of pathognomonic tomographic findings make it imperative to use other complementary tests to assist in the differential diagnosis. In times of pandemic, the first hypothesis is almost always automatic, however, other viruses such as influenza, respiratory syncytial, and metapneumovirus should not be excluded. Therefore, the etiological diagnosis must always be prioritized.

The current molecular biology test applied in Brazil is the polymerase chain reaction with reverse transcription and real-time amplification (RT-qPCR). This COVID-19 diagnosis kit is produced by the Bio-Manguinhos Institute of Oswaldo Cruz Foundation (Fiocruz)[33]. For this test, material collected from the nasopharynx, oropharynx, or a small blood sample is used[19,33]. The test, approved by the Brazilian Health Regulatory Agency (Anvisa), allows the amplification and detection of viral genetic material in a few hours. This technology is also applied for the identification of other common respiratory pathogens, such as: mycoplasma, adenovirus, parainfluenza, respiratory syncytial virus, influenza A and influenza B virus[19]. So far, this is the most reliable test, with a sensitivity that can vary from 63.0% to 93.0% and specificity of 100.0%[34]. In addition, tests that amplify a second genomic region guarantee greater sensitivity[35]. On the other hand, one of the limitations of the molecular biology test consists in the generation of false-negative results, especially when performed in the first three days after the onset of symptoms. In this period, the viral load and viral excretion are much lower, which compromises test results[36]. Likewise, those who have been exposed should be tested only after this period. Although the test is very efficient in detecting the viral genome, it is certainly important to evaluate the mass performance of rapid tests (immunochromatography) in the general population and thus detect mainly oligosymptomatic or asymptomatic cases more quickly.

China and South Korea have implemented a comprehensive free and rapid testing program[37]. The test is based on the detection of

IgM and IgG class antibodies against the MK201027 antigen present in the SARS-CoV-2 protein S, allowing the test result to be read within 15 min after sample application[38]. As in any disease, the IgM antibody can appear from the fifth day after infection, being the most suitable time for testing[39].

In Brazil, within the scope of the public health emergency, 21 rapid tests were approved by Anvisa until April 17, 2020[40]. These tests are not routinely used for the diagnosis of infection, as they need to be assessed for sensitivity, specificity, positive predictive value, and negative predictive value[41]. In addition, the window period, the time between infection and the production of antibodies, is not yet known. If the test is performed during the window period, there is a possibility of giving false-negative results. However, given the current scenario, the mass use of the respective tests may be useful in epidemiological surveillance, including the investigation of asymptomatic and/or oligosymptomatic individuals[36,42].

Bacterial origin lung infection is the main differential diagnosis of COVID-19. Guan et al.[27] showed that, in COVID-19, the leukogram is normal, except in severe cases where lymphopenia is evident. Another important piece of information is the platelets: they are close to the lower limit of the reference used. Among the inflammatory biomarkers, procalcitonin seems to be the most promising marker since its values change little during this infection. Thus, when comparing these laboratory findings to those of a bacterial infection (left shift leukocytosis, platelets within the reference values, and elevated procalcitonin), there are elements that corroborate the diagnostic hypothesis of viral infection, as well as indicate a worse prognosis in the most severe cases. Another evident fact was that 43.0% of the patients with COVID-19 evolved, during hospitalization, with liver disorders. This finding has numerous implications for the management of these patients, from avoiding hepatotoxic drugs to the need for daily monitoring of transaminases.

Regarding imaging tests, several studies have used chest computed tomography (CT) as the examination of choice. Guan et al.[27] showed that, of the 975 CT performed in the study, 86.0% showed altered results. The most common pattern was ground-glass opacity (56.0%). At the beginning of the infection, the finding of ground glass may be isolated in the subpleural space and, with the evolution of the condition, it is distributed to the pulmonary lobes. These findings point to interstitial or alveolar lesions, usually found in the acute or chronic phase of inflammatory, tumoral, and infectious diseases, such as influenza and SARS. Other signs that may also be identified in the CT but which have a lower prevalence were: air bronchograms, rare pleural effusion, and enlargement of the mediastinal lymph nodes[43,44,45]. Although these findings are rarer, it is important to note that they also occur and that, in the absence of other diseases that can lead to this change, COVID-19 should be considered. Given the results, the major concern of medical teams is: will there be pulmonary sequelae in patients with the severe form of the disease? New works using CT are expected to answer this shortly[19,46].

v) Treatment

Due to the lack of a specific and efficient therapy against COVID-19, its current treatment relies on symptomatic control and the provision of ventilatory support[14,43]. The search for effective antiviral therapy moves the scientific community in search of curative care. Almost daily, numerous articles, some with dubious methodologies, present potential uses of drugs already known.

A study by Elfiky showed the effectiveness of ribavirin, remdesivir, sofosbuvir, galidesivir, and tenofovir in vitro as potential therapeutic agents against SARS-CoV-2. Such drugs have the ability to bind to RNA-RdRp-dependent RNA polymerase (NSP12) and to inhibit its function[47], however, now it is necessary to develop studies to evaluate the effectiveness of this drug in the treatment of COVID-19 patients. Remdesivir was used intravenously, in combination with other drugs, for treating a USA-resident patient, and he showed a significant improvement and no adverse reactions. However, the importance of promoting more studies to prove the real therapeutical effectiveness of remdesivir and the presence of potential adverse effects in humans should be noted[48].

More recently, the role of chloroquine for treating COVID-19 is being discussed. This drug, known since the 1940s, is used in the treatment of malaria for many years and has a mechanism not fully understood in viral infections. Its in vitro action against the rabies virus, poliovirus, HIV, HAV, HBV, HCV, influenza A and B, Chikungunya, Zika, Dengue, and some arenaviruses is known. Its role against MERS-CoV has yielded conflicting results. Clinical trials published recently lack methodological refinement: there is a lack of data concerning the doses used, the absence of control groups, and a small sample population, almost always less than 100 volunteers. So far, there is insufficient data regarding the effectiveness and safety of the drug. The adverse effects of chloroquine should not be overlooked: macular retinopathy, hemolytic anemia, especially in patients with more advanced age, and prolongation of the QT interval. Several possible lines of action by the drug are studied, including the inhibition of pH-dependent steps for viral replication, such as the interaction between viral proteins and those of the host, as well as the process of viral penetration, which could be the main mechanism for controlling SARS-CoV-2 infection. Chloroquine also has immunomodulatory activity, suppressing the production and release of cytokines as a tumor necrosis factor (TNF) and interleukin-6 (IL-6)[14]. On the other hand, new studies have already shown that the drug interferes in the glycosylation process of SARS-CoV cell receptors and is effective against the invasion and maintenance stages of SARS-CoV-2 infection in some cells. Together, the results have demonstrated that the association between remdesivir and chloroquine can present an effective inhibition of SARS-CoV-2 in vitro[49].

Protease inhibitors such as lopinavir and ritonavir, already used in the treatment of other diseases such as Acquired Human Immunodeficiency Syndrome (AIDS), have shown

promising results in patients with MERS-CoV and SARS-CoV[14]. When used in COVID-19 patients, a significant reduction in the viral load of SARS-CoV-2 was shown[50]. Given the current circumstances, there is an unprecedented great scientific race to find effective treatments. However, it is necessary to be cautious when considering the use of these drugs in therapy, as specific medical interventions may further compromise the patient's health.

Clinical trials ongoing in several countries, such as China, France, Italy, USA, and Brazil, may soon answer the real role of these drugs in the treatment of COVID-19[51,52]. In parallel to these studies, an initiative launched by WHO in partnership with more than 100 countries aims to evaluate the effectiveness of four treatment options (remdesivir, lopinavir/ritonavir, interferon beta-1a, and chloroquine and hydroxychloroquine), in order to identify the best drug that increases patient survival and/or delays disease progression[53].

vi) Public health policies and perspectives

The COVID-19 pandemic represents the greatest global challenge of this 21st century so far. It is the first time that a virus reaches alarming proportions, affecting all continents. The repercussions of the disease, especially considering the number of Intensive Care Unit (ICU) beds and artificial respirators available, expose structural and health care problems in the world and, especially, in Brazil. How did some countries manage to keep the spread of SARS-CoV-2 under control? Many years ago, at a time when microorganisms and the microscope were not yet known, sanitary and hygiene measures were essential to control epidemics. Sanitary barriers are important and, today, through studies, it is possible to prove that, since we cannot prevent the emergence of epidemics, it is possible to control them.

According to Wilder-Smith and Freedman[54], the COVID-19 pandemic brings us a warning of how much we need to rely on classic public health measures to face it, in a scenario where we do not yet have specific vaccines or therapies. At the moment, the most effective measures aim to avoid the spread of the disease from person to person. For this, the most common measures are: isolation, quarantine, and social distancing. A study published by Pan et al.[55] showed that behavior interventions, including travel restrictions, contributed significantly to mitigating the epidemic and, consequently, to the control of the disease in China. Another study, published by Kupferschmidt and Cohen[37], demonstrated that social distancing imposed by public bodies and health services were also essential to decreasing the number of confirmed cases.

An interesting strategy used by South Korea is the drive-through (DT) triage system. A short and quick flow with the following stages: entry, registration, examination, sample collection, instructions, and exit was carried out aiming to identify the largest possible number of asymptomatic individuals, who can represent the mains source of transmission and who may be contributing to the spread of the virus in the country. The strategy worked and the number of cases dropped sharply in the country[56]. Against these guidelines, a study by Lazzerini and Putoto[57] showed that, in Italy, the late imposition of sanitary barriers allowed the violent spread of the disease, causing, until March 31, 2020, approximately 12,428 deaths, 274.2% more than in China[58].

Unprecedented health actions, such as the total isolation of Wuhan associated with the massive investment in scientific research, with the early publication of the viral genome and the development of diagnostic methods[55,59], showed how the example of China can help other countries. However, the Chinese government has also suffered from other problems, also faced on Brazilian soil, such as the shortage of hospital supplies, mainly personal protective equipment, such as masks and protective clothing for health professionals, who are in the frontline in caring for infected people[60]. For the authors, this problem brings a warning regarding the weaknesses of our health system and the need for international cooperation in coping with the disease.

In China, solving this problem involved cooperating and sending materials from other parts of the country[55], showing that, in times of pandemic, the more articulate the countries, their governments, and populations are, more chances of success. For Griffith[61], a crucial point in this fight against the virus is people's cooperation, as it is from there that we can limit the spread of COVID-19. Following this line, Gates[10] evidenced in his study that the donation of financial resources from countries classified as "high income" to those of "low and middle income" is a measure that needs to be considered, since these have weaknesses in the political, economic, and social system. Together, the findings suggest that the world's great difficulty in coping with this scenario lies under the social and economic differences between countries and, especially, those with fragile health systems. In this sense, the public health measures advocated, mainly education for hand hygiene and social distancing, will help to delay the spread of infections and reduce the pressure of hospital care[62].

The result of these measures directly affects the lethality rate. Until April 2nd, 2020, Germany had a relatively low lethality rate (1.2%) when compared to countries such as Italy (11.9%) and Spain (9.0%). These figures are believed to reflect the rapid adoption of measures to prevent the spread of SARS-CoV-2 compared to other countries. Among the measures adopted to control and prevent COVID-19, the state decrees that establish the closing of businesses and non-essential services, the good practices related to hygienic-sanitary conditions, and the distance of 1.5 to 2 meters between individuals who attend essential establishments stand out. Added to this, the high number of tests performed, which allows an increase in the detection of oligosymptomatic or symptomatic individuals. In addition, there is an expansion of actions related to population testing, allowing rapid tests to be carried out throughout the national territory with quality standards appropriate to the needs in the context of public health emergencies. On the other hand, it is observed that the data are partial and there are signs that

demand concern, such as the lethality rates disclosed in daily reports, which, despite remaining low when compared to SARS and MERS, show rising values[63].

This unprecedented struggle has also been reinforced by the spread of false information, which has undermined many public health measures implemented and has been considered by WHO as a pandemic parallel to COVID-19[64,65]. To face this problem, WHO has partnered up with Facebook, Twitter, YouTube (Google), and Pinterest to combat the spread of false information about the new CoV[64]. There are no doubts that the broader impact extends way beyond the number of cases and deaths it causes. The resources necessary to fight the disease and/or generated by the adoption of prevention and control measures, such as social distancing, can economically collapse the country.

Countries need to invest in scientific research, in strengthening health systems, in health education measures to the population, in continuing education for health professionals, in the development of social policies and/or programs targeted to people in vulnerable situations and to those who, directly or indirectly, have been affected by this great challenge of the 21st century that is the COVID-19 pandemic.

CONCLUSIONS

The advances of the current pandemic require quick and conscious measures to preserve the population. Such measures, based on a solid scientific basis, promote and guarantee the strengthening of strategic actions to face COVID-19. The scientific evidence reported in this review do not answer all the questions but opens paths and perspectives for a better understanding of SARS-CoV-2 and COVID-19, in the sense of qualifying health surveillance actions and services, for caring suspected or confirmed COVID-19 cases. Nevertheless, epidemiological data, as well as research for new drugs and vaccines, can ultimately help humanity in controlling and mitigating the impacts of the epidemic on society.

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Authors' Contributions

Brito SBP, Braga IO, and Takenami T - Conception, planning (study design), acquisition, analysis, data interpretation, and writing of the work. Cunha CC and Palácio MAV - Analysis, data interpretation, and writing of the work. All authors approved the final version of the work.

Conflict of Interest

Authors have no potential conflict of interest to declare, related to this study's political or financial peers and institutions.