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Epidemiology, diagnosis, treatment, and future perspectives concerning sars-cov-2: a review article.

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Em um momento em que há uma emergência mundial de saúde pública, é fundamental que o conhecimento científico gerado durante a pandemia chegue rapidamente à classe médica classe médica.

Dentro desta dinâmica a Revista da Associação Médica Brasileira (Ramb) está adotando uma série de medidas a fim de acelerar o processo editorial para publicação de artigos sobre a Covid-19. A partir de hoje (14/04/2020), a AMB publicará o Boletim Ramb Covid-19, que antecipará os artigos científicos selecionados pelos editores da Ramb sobre o tema.

“Os artigos foram escritos por especialistas e selecionados dentro dos critérios da Ramb para esclarecer temas fisiopatológicos, assim como oferecer orientações de prevenção e tratamento da doença. Dessa forma, esperamos colaborar com os médicos para o melhor atendimento aos seus pacientes, com a disponibilidade mais ágil desses artigos, antes de sua publicação na Ramb”, comenta Carlos Serrano Jr., editor-chefe da Ramb.

Para o diretor científico da AMB, Antonio Carlos Palandri Chagas, “neste momento ímpar vivido no mundo por conta da pandemia de Covid-19, a AMB cumpre seu papel de estar levando à comunidade científica brasileira os recentes artigos sobre os mecanismos fisiopatológicos e aspectos clínicos relevantes dessa situação que assola a saúde pública”.



Carlos Serrano Jr.



Antonio Carlos Palandri Chagas

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Epidemiology, diagnosis, treatment, and future perspectives concerning sars-cov-2: a review article.

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SUMMARY

The present study aimed to review the epidemiology, clinical manifestation, laboratory diagnosis, treatment, and future perspectives related to COVID-19 infections. The following electronic databases were used searched: MEDLINE, SCIELO, and LILACS. It became clear that COVID-19 infections occur through exposure to the virus, and both the immunosuppressed and healthy population appear susceptible. The clinical course of COVID-19 is still not clear, although the SARS-CoV-2 infection seems to develop with mild, influenza-like symptoms in the vast majority of subjects, i.e., 10%–15% of COVID-19 patients. Since rRT-PCR tests serve as the gold standard method to confirm a SARS-CoV-2 infection, false-negative results could hinder the prevention and control of the epidemic, particularly considering the test plays a key role in the decision for continued isolated medical observation or discharge. Our findings also indicate that a radical increase in the identification and isolation of currently undocumented infections would be needed to fully control SARS-CoV2.

KEYWORDS: Coronavirus. Epidemiology. Signs and symptoms. Diagnosis. Therapeutics.

SUMMARY

O presente estudo teve como objetivo realizar uma revisão sobre epidemiologia, manifestações clínicas, diagnóstico laboratorial, tratamento e perspectivas futuras relacionados à infecção pelo COVID-19. As seguintes bases de dados eletrônicas foram utilizadas MEDLINE, SCIELO e LILACS. Ficou claro que a infecção pelo COVID-19 ocorre por exposição ao vírus, e tanto a população imunossupressora quanto a normal parecem suscetíveis. O curso clínico do COVID-19 ainda não está claro, embora a infecção por SARS-CoV-2 pareça ocorrer com sintomas leves e semelhantes à gripe na grande maioria dos indivíduos, em 10%-15% dos pacientes com COVID-19. Uma vez que os testes rRT-PCR servem como o método padrão-ouro para confirmar a infecção do SARS-CoV-2, os resultados falso-negativos podem dificultar a prevenção e o controle da epidemia, particularmente quando este teste desempenha um papel de referência fundamental na decisão da necessidade de observação médica isolada ou alta. Nossos achados também indicam que seria necessário um aumento radical na identificação e isolamento de infecções não documentadas atualmente para controlar totalmente o SARS-CoV2.

PALAVRAS-CHAVE: Coronavirus. Epidemiologia. Sinais e sintomas. Diagnóstico. Terapêutica.

INTRODUCTION

The coronavirus was initially designated as the 2019-novel coronavirus (2019-nCoV) in January 2020 by the World Health Organization (WHO). The disease caused by it was named coronavirus disease 2019 (COVID-19). The Coronavirus Study Group of the International Committee suggested naming the new coronavirus as SARS-CoV-2, based on taxonomy, phylogeny, and established practice issued in February 2020¹. In December 2019, several acute respiratory illnesses, now called COVID-19, occurred in Wuhan, Hubei Province, China. A total of 509,164 cases of COVID-19 have been confirmed, including 23,335 deaths as of 27 March 2020. The pathogen of this disease was confirmed as a novel coronavirus by molecular methods, and to date, COVID-19 has affected people in more than 172 countries and has become a global pandemic².

Coronaviruses are enveloped single-stranded RNA viruses that are zoonotic in nature and cause symptoms ranging from those similar to the common cold to more severe respiratory, hepatic, enteric asymptomatic carrier, pneumonia of varying degrees of severity and neurological symptoms^{3,4}.

There are relevant factors associated with COVID-19; therefore, the present study aimed to review the epidemiology, clinical manifestation, laboratory diagnosis, treatment, and future perspectives related to the COVID-19 infection epidemiology.

METHODS

The following electronic databases were included in this review: Medical Literature Analysis and Retrieval System Online (MEDLINE) via PubMed (1966 to January 2020),

available through the following link: <https://www.ncbi.nlm.nih.gov/pubmed/>; Scientific Electronic Library Online (SCIELO), available at <https://www.scielo.org/> and Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), available through the following link: <https://bvsalud.org/>; (1982 to January 2020). The electronic search resulted in 908 articles. Among them, thirteen were duplicates. After selecting the title and abstract, 74 articles were identified for a complete evaluation of the text. From those, 24 were used for the final review. There was no date and language restriction. Records were managed by EndNote X 9.0 software.

Epidemiology

It became evident that the COVID-19 infection occurs through exposure to coronavirus, and both the immunosuppressed and healthy population appear to be susceptible. Some studies have documented an age distribution of adult patients between 25 and 89 years old. Most adult patients were between 35 and 55 years old⁵. A study on early transmission dynamics of the virus reported the average age

of patients to be 59 years old, ranging from 15 to 89 years, with the majority (59%) being male. It was suggested that the population most at risk might be people with a poor immune function, such as older people and those with renal and hepatic dysfunction⁶.

Figure 1 shows the distribution of COVID-19 cases as of 25 March 2020, 23,59 (CET), per WHO.

The epidemic of unknown acute respiratory tract infections broke out first in Wuhan, China, in December 2019. This is possibly linked to the seafood market. Several studies suggested that bats may be the potential source of SARS-CoV-2. However, there is no evidence to date that the origin of SARS-CoV-2 is from the seafood market⁷.

Currently, person to person transmission from patients with pneumonia or asymptomatic patients during the incubation period is the main source for the spread of the virus. Respiratory droplets are the main route of transmission, but the virus can also be transmitted through interpersonal contact or through the fecal-oral route based on a study that demonstrates the presence of the virus in rectal swabs^{8,9}. Prevention

and control strategies and methods are reported at three levels: national level, case-related population level, and general population level¹⁰.

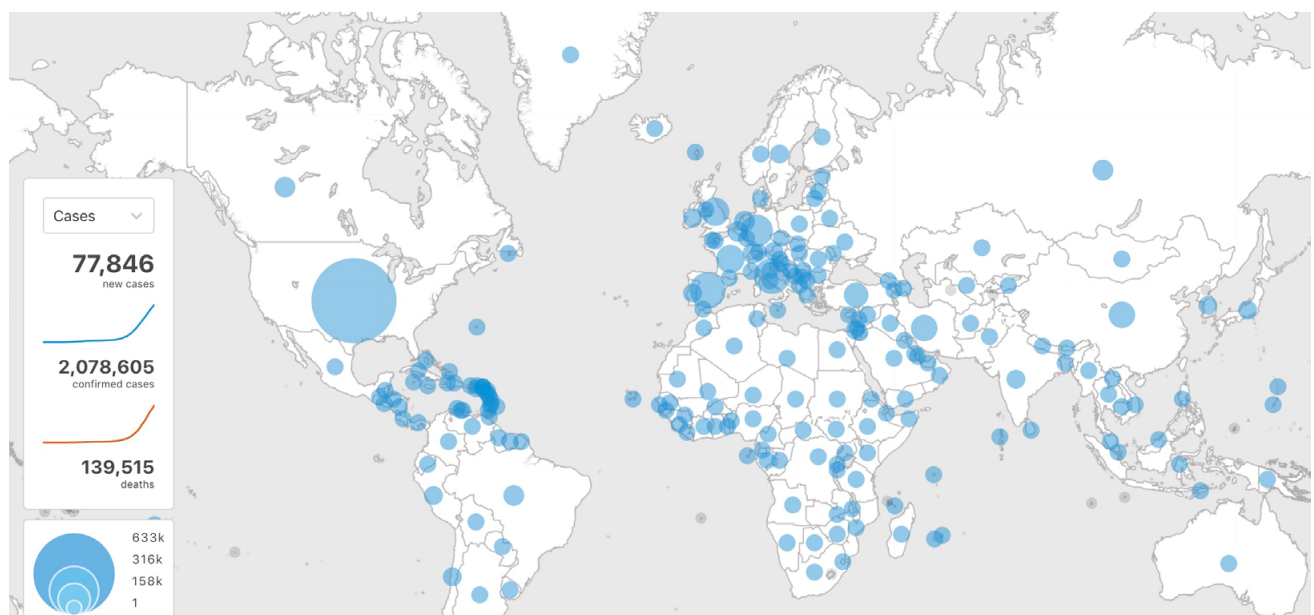
Airborne precautions and other protective measures have been discussed and proposed for prevention. Infection preventive and control measures that may reduce the risk of exposure include the following: use of face masks; covering coughs and sneezes with tissues that are then safely discarded¹¹.

Presently, there are four endemic coronavirus strains currently circulating in human populations: 229E, HKU1, NL63, OC43. If the novel coronavirus follows the pattern of the 2009 H1N1 pandemic influenza, it will also spread globally and become a fifth coronavirus pandemic in the human population¹². Table 1 shows data as reported by national authorities on 27 March 2020.

Clinical manifestation

The clinical course of COVID-19 is still unclear. Although the SARS-CoV-2 infection seems to occur with mild, influenza-like symptoms in the vast majority of subjects, i.e., 10%–15% of COVID-19 patients (especially older

FIGURE 1. GLOBALLY, AS OF 2:00AM CEST, 17 APRIL 2020, THERE HAVE BEEN 2,078,605 CONFIRMED CASES OF COVID-19, INCLUDING 139,515 DEATHS, REPORTED TO WHO.



Source: World Health Organization, 2020.

TABLE 1. DATA AS REPORTED BY NATIONAL AUTHORITIES ABOUT SARS-COV-2 ON MARCH 27 2020.

	Confirmed	Deaths
Western Pacific Region	100 018 confirmed	3567 deaths
European Region	286 697 confirmed	16105 deaths
South-East Asia Region	2932 confirmed	105 deaths
Eastern Mediterranean Region	35249 confirmed	2336 deaths
Region of the Americas	81 137 confirmed	1176 deaths
African Region	2419 confirmed	39 deaths
Globally	509 164 confirmed	23335 deaths

Source: World Health Organization, 2020

ones and those with relevant comorbidities), the disease may progress to severe interstitial pneumonia, which may then evolve to acute respiratory distress syndrome and death in 2%–5% of cases¹³.

Reliable evidence suggests that the incubation period of SARS-CoV-2 is approximately 6 days and that the average period between symptom onset and hospitalization is 7 days, while the average period of symptom duration is approximately 13 days, or slightly longer in patients with severe disease (16 days)¹⁴.

In a study involving 108 patients (38 men, 70 women; age range, 21–90 years old), the manifestations observed were fever in 94 of 108 patients (87%), dry cough in 65 of 108 (60%), and fatigue in 42 of 108 (39%). The laboratory results were normal white blood cells (WBC) count in 97 of 108 patients (90%) and normal or reduced lymphocyte count in 65 of 108 (60%). High-sensitivity C-reactive protein level was elevated in 107 of 108 patients (99%). Most patients have lymphopenia and bilateral ground-glass opacity changes on chest computed tomography (CT) scans¹⁵.

Laboratorial diagnosis

The nucleic acid test or genetic sequencing for SARS-CoV-2 was considered the gold standard method for confirmation of infection. Since rRT-PCR tests serve as the gold standard method to confirm a SARS-CoV-2 infection, false-negative results could

hinder the prevention and control of the pandemic, especially since the test plays a key role in the decision for the need of continued isolated medical observation or discharge. The accuracy of RT-PCR can be substantially affected by the lack of harmonization of primers and probes, as well as by a variety of technical and analytical errors¹⁶.

Studies on COVID-19 have generally been limited to the description of the epidemiology characteristics, initial clinical, hematological, and radiological findings. Laboratory results also found that SARS-CoV-2 is similar to some of the beta (β) coronaviruses generally identified in bats¹⁷, which are part of a group of SARS/SARS-like CoV viruses. Case definition guidelines mention the following symptoms: decreased lymphocytes and white blood cells, new pulmonary infiltrates on chest radiography, and lack of improvement of symptoms after 3 days of antibiotic treatment⁶. For patients with a suspected infection, the following procedures have been suggested for diagnosis: real-time fluorescence RT-PCR to detect the positive nucleic acid of SARS-CoV-2 in sputum, throat swabs, and secretions of the lower respiratory tract samples¹⁸.

In the advanced phase of SARS-CoV infection, rapid reduction of lymphocytes in peripheral blood, mainly T lymphocytes, was observed, and both CD4 and CD8 T lymphocytes decreased. The loss of lymphocytes precedes even the abnormal changes

on the chest X-ray. SARS-specific IgG antibodies are produced in the late advanced stages (about 2 weeks) and gradually increase with the course of the disease. The sustainable existence of IgG makes the patients acquire immune function after the infection. The IgG level of mild patients was significantly higher than that of severely infected patients¹⁹.

Treatment and futures perspectives

Suspected and confirmed cases need to be treated in designated hospitals under effective quarantine conditions. Suspected cases need to be treated separately in a single room, with confirmed cases admitted to the same ward, and critical cases should be admitted to ICU as soon as possible²⁰.

Unfortunately, there is no known specific treatment against COVID-19. Because of this, identifying effective antiviral agents to combat the disease is urgently necessary. However, chloroquine phosphate has shown apparent effectiveness in the treatment of COVID-19 associated pneumonia in clinical studies. Chloroquine is a 9-aminoquinoline discovered in 1934; it is used to prevent and treat malaria and is effective as an anti-inflammatory agent for the treatment of rheumatoid arthritis and lupus erythematosus. The drug also has many interesting biochemical properties, including an antiviral effect. Studies revealed that it also has potential against viral infection. Moreover, chloroquine was also found to be a potent inhibitor of SARS coronavirus infection by interfering with ACE2, one of cell surface binding sites for S protein of SARS-CoV²¹.

The development of attenuated-virus vaccines is also possible by carefully screening the serially propagated SARS-CoV-2 with reduced pathogenesis such as induced minimal lung injury, diminished limited neutrophil influx, and increased

anti-inflammatory cytokine expressions compared with the wild-type virus²².

At least five vaccine technologies will be reviewed: inactivated vaccine, subunit protein vaccine, nucleic acid vaccine, adenoviral vector vaccine, and recombinant influenza viral vector vaccine²³. Traditional vaccine technologies have been improved, and a wide variety of new technologies have emerged in the past two decades²⁴.

CONCLUSION

Our findings also indicate that a radical increase in the identification and isolation of currently undocumented infections would be necessary to control SARS-CoV2 fully. An estimation

of the prevalence and contagiousness of undocumented novel coronavirus (SARS-CoV2) infections is critical for understanding the overall prevalence and pandemic potential of this disease. These findings explain the rapid geographic spread of SARS-CoV2 and indicate containment of this virus will be particularly challenging. No specific antiviral treatments or vaccines are available because it is a new and emerging viral disease. The development of SARS-CoV-2-based vaccines is urgently required.

CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest that may have influenced this work.

Authors' contributions

ARVSC, MLCF, PCPA, and RNSF searched the databases. TJMR, CFSR, FTB, and FWSR selected the articles to be included in the research. FWSR corrected the writing in English. All authors performed the other parts of the research in an equally. All authors have reviewed and approved the final text of this article and are responsible for its content. ■

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