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What do we know about SARS-CoV-2 virus and COVID-19 disease?

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Abstract

Introduction. Emerging viral diseases are a serious public health problem, especially with such a dynamically changing epidemic situation, in which we are observers and participants. Coronaviruses are present in our lives almost constantly. Currently, the world is struggling with a pandemic caused by the new SARS-CoV-2 coronavirus, which is the etiological factor of COVID-19 disease.

Objective. The aim of the study is to review scientific reports and systematize current knowledge about SARS-CoV-2 coronavirus and the COVID-19 disease it causes in the face of the ongoing pandemic.

State of knowledge. The course of SARS-CoV-2 infection is similar to cases caused by coronaviruses of the severe acute respiratory syndrome (SARS-CoV) and the Middle East respiratory syndrome (MERS-CoV). Symptoms vary from mild to viral pneumonia, including fever, difficulty breathing, bilateral infiltrative pneumonia, and multi-organ failure in the most severe cases. COVID-19 disease also leads to complications, such as pulmonary fibrosis, neurological disorders, an increased risk of heart attack, thrombosis, and liver dysfunction. The review presents information about the taxonomy, structure, pathomechanism, clinical symptoms, complications, number of cases, diagnostics, and treatment of COVID-19 disease caused by the SARS-CoV-2 virus.

Conclusions. The SARS-CoV-2 virus has spread quickly around the world, causing a rapidly increasing number of infections and deaths among patients. There is currently no effective vaccine or targeted treatment. The only way to prevent the spread of the virus remains quarantine, the isolation of sick people, and the use of a sanitary regime.

Key words

coronavirus, SARS-CoV-2, 2019-nCoV, COVID-19, pandemic, pneumonia

INTRODUCTION

It is believed that coronaviruses have existed since about 8,000 BC. Bats and birds are considered to be involved in the evolution and spread of CoV because they are their main hosts. There have been reports in the past of diseases caused by CoV in cattle and equidae (1800), and cattle and dogs (1950s) [1]. Information about human coronaviruses dates from the 1960s and concerns two pathogens, HCoV-229E and HCoV-OC43, which have been isolated and described [2]. They can cause colds and self-limiting upper respiratory tract infections in immunocompetent people, while the elderly and immunocompromised individuals may experience lower respiratory tract infections. In 2002 – 2003, there occurred a worldwide epidemic of disease caused by the previously unknown and highly infectious SARS-CoV (severe acute respiratory syndrome) species. The first case of SARS virus infection was recorded at the end of 2002 in the Guangdong Province of southern China. Due to the natural seasonality of coronaviruses and then countermeasures taken, the virus disappeared from among the human population after a few months [2]. In 2012, ten years after the SARS-CoV epidemic, for the first time in Saudi Arabia appeared cases of a new, severe, and often fatal respiratory disease caused by the MERS-CoV coronavirus. The world is currently struggling with the new SARS-CoV-2 coronavirus, first identified in December 2019 the city of Wuhan with a population of 11 million, in China. Since January 2020, the dynamic spread and increase in infections and deaths due to SARS-CoV-2 have been observed. More than 80,000 cases and several thousand deaths have been reported in China alone, as well as thousands of cases in other countries [3, 4, 5]. Although the SARS-CoV-2 mortality rate is currently lower than for SARS-CoV, the virus appears to be highly contagious, given the number of infected cases to-date. On 11 March 2020, the WHO announced that the SARS-CoV-2 coronavirus-induced disease COVID-19 has been declared a pandemic [6].

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OBJECTIVE

The aim of the study is to review scientific reports and systematize current knowledge in the field of SARS-CoV-2 coronavirus and the COVID-19 disease caused by it.

Source of infection. The first COVID-19 cases concerned the Huanan marine food market in Wuhan, China. The first patients re infected with the new type of coronavirus were employees or customers of this market which sells meat from various animal species, including donkeys, pigs, sheep, camels, foxes, badgers, and multiple species of reptiles. Researchers who have determined the genetic code of the virus have shown that COVID-19 can be derived from snakes that often hunt bats. Two species were distinguished: many-banded krait *Bungarus multicinctus* and Chinese cobra *Naja atra* [7]. The WHO report states that SARS-CoV-2 was

detected in environmental samples taken from the seafood market. A study by Ji et al. [8] showed that SARS-CoV-2 is a chimeric virus between bat coronavirus anda coronavirus of unknown origin. Then, comparing the homology of other animal coronavirus glycoproteins, they found that snakes were the most likely reservoir for SARS-CoV-2 [8]. Studies by Benvenuto et al. [9] showed that SARS-CoV-2 was closely related to isolated coronavirus from Chinese bats in 2015. Their research confirmed the theory of transmission from bats to humans. Chan et al. [10] and Hui et al. [11] confirmed that SARS-CoV-2 was a new coronavirus closely related to bat SARS-CoV. Zhou et al. [12] and Wu et al. [13] found that the sequence homology between SARS-CoV-2 and SARS-CoV was 79.5%. They also found that SARS-CoV-2 showed high homology with bat coronaviruses. Current evidence therefore strongly indicates that SARS-CoV-2 is derived from bats, although indirect SARS-CoV-2 hosts remain to be determined. These observations suggest that bats are indeed a source of origin. At the same time, the animals sold at the Wuhan seafood market, e.g. snakes, may represent an intermediate host to facilitate the appearance of the virus in humans [14]. The new coronavirus is transmitted directly – through contact with the secretions of the infected person (droplet route, but also faeces and urine) or indirectly – through contact with surfaces on which there are secretions of an infected person, e.g. from sneezing and coughing [15].

Taxonomy. Initially, the new virus was called 2019-nCoV because it belongs to the coronaviruses (CoV) and appeared at the end of 2019. Then, a group of experts from the International Committee on Virus Taxonomy (ICTV) described it as SARS-CoV-2 because it is very similar to the virus that caused SARS-Co-Vs [8, 16]. CoVs have become significant pathogens of emerging respiratory disease in the last twenty years. COVID-19 is the name of an infectious disease caused by the SARS-CoV-2 virus. Coronaviruses (CoV) are positive single-strand RNA viruses with a nucleocapsid with helical symmetry and a crown-like appearance [17]; the CoV effect is due to the presence of barbed glycoproteins on the envelope, which is visualized by electron microscopy. Coronaviruses hold the largest genome among RNA viruses. SARS-CoV-2 belongs to the family Coronaviridae (order Nidovirales), the sub-family Coronavirinae, which is classified into four genera of CoV: Alphacoronavirus (alphaCoV), Betacoronavirus (betaCoV), Deltacoronavirus (deltaCoV) and Gammacoronavirus (gammaCoV). The betaCoV genus is additionally divided into five subspecies. Studies of genetic sequencing have shown that SARS-CoV-2 is a betaCoV virus closely related to the SARS virus [18], which was also confirmed by the research of Zhu et al. [19]. The genus BetaCoV-2 includes SARS and MERS. Both Alpha- and Beta-CoV infect bats and can infect other species, including humans, camels, rabbits, and other animal species.

Structure of SARS-CoV-2. In the SARS-CoV-2 structure, several functionally essential components have been distinguished, especially major structural proteins: spike protein (S), nucleocapsid protein (N), membrane glycoprotein (M), and envelope protein (E) (Fig. 1). Protein S usually mediates the entry of the virus into host cells. It facilitates attachment to surface receptors of the host cell and then promotes fusion between viral membranes and host cells. The S protein is also a crucial determinant of viral host range and tissue tropism, and a significant factor inducing host immune responses. The N protein primarily acts on binding to the RNA genome, forming a nucleocapsid. The M protein defines the shape of the viral envelope. It is also considered a central virus assembly organizer that interacts with the E protein to produce and release viruses. Protein E is mainly involved in virus formation, maturation, and budding [9, 16].

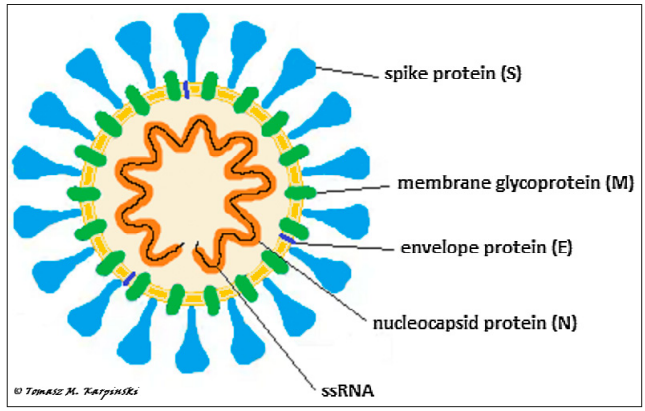

Figure 1. Structure of the SARS-CoV-2 virus.

Pathomechanism. The mechanisms of SARS-CoV-2 infection are not precise, but structural analysis suggests that the likely entry of the virus into human cells is via the ACE2 receptor [12]. Epithelial cells in the respiratory tract and gastrointestinal tract are the primary target cells for SARS-CoV-2 [20, 21, 22]. Zhanh et al. [23] found that the angiotensin-converting enzyme 2 (ACE2) is a receptor for SARS-CoV-2. ACE2 is expressed on type I and II alveolar epithelial cells which occur in the normal human lung. Among type II alveolar cells, 83% of these show ACE2 expression. Researchers indicate that men have higher levels of ACE2 in alveolar cells than women. Asians have higher levels of ACE2 expression in alveolar cells than Caucasian and African American populations. This proves that Asians are more susceptible to SARS-CoV-2 infection. Wrapp et al. [24] also found that the SARS-CoV-2 receptor binding capacity is 10 – 20 times stronger than the SARS-CoV capacity, and the density of this enzyme is higher in adults than in children. Therefore, a greater predisposition to both infection as well as severe disease is observed in adults. Scientists argue that it is a enzyme common in both humans and bats. In addition to the lungs, this receptor is found in the heart and kidneys. The binding of SARS-CoV-2 to ACE2 causes increased expression of ACE2, which can lead to follicular cell damage. Injury to alveolar cells, in turn, can cause several systemic reactions and even death. Current treatment concepts include the administration of angiotensin receptor blockers (such as losartan) instead of inhibitors [25].

Clinical symptoms. According to the World Health Organization (WHO), COVID-19 is a respiratory infection. Most people with COVID-19 develop only mild, uncomplicatedform of the disease, while about 14% develop a severe illness requiring hospitalization and oxygen support, and 5% require admission to an intensive care unit [18]. In severe cases, COVID-19 can complicate acute respiratory distress syndrome (ARDS), leading to sepsis and septic shock, multiple organ failure, including acute damage to

the kidneys and heart [26, 27, 28]. Older age and coexisting illnesses are considered as risk factors for death. In children with COVID-19, the symptoms are usually less severe than in adults, and mainly occur with cough and fever (fewer ACE2 receptors) [29, 30]. Relatively few cases of babies with confirmed COVID-19 infection have been registered. Previous reports indicate a mild course of the disease among infants. There were also no differences in the course of the disease in pregnant women, compared to non-pregnant women with childbearing potential [31].

Number of cases. In the face of a pandemic, the situation is changing very dynamically, and the inflowing data is updated regularly. The WHO estimates the mortality rate of the new coronavirus at about 3.4%: influenza – 0.1%, SARS – 9.6%, and MERS – 34%) [32]. However, these values vary depending on the region, age group, and chronic disease burden. Currently, the largest number of infections and deaths is observed in two large outbreaks, i.e. in Western Europe and the United States (Figs. 2–4) [33, 34].

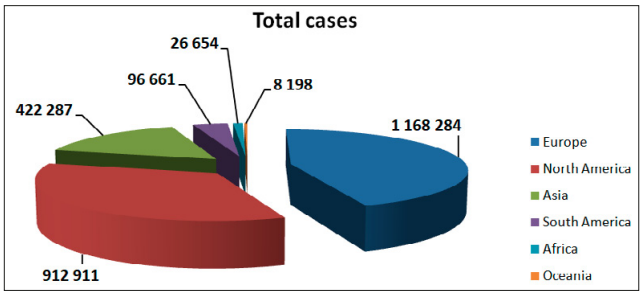

Figure 2. Distribution of cases SARS-CoV-2 until 22 April 2020.

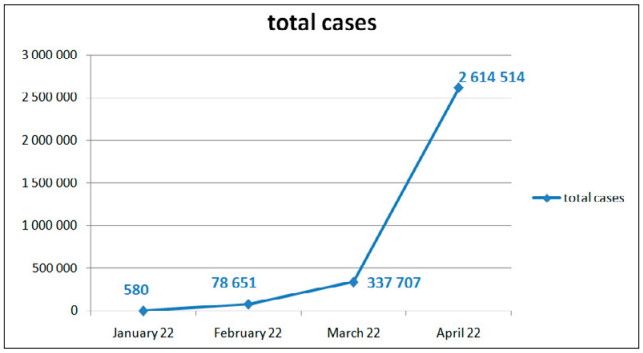

Figure 3. Number of confirmed cases of SARS-CoV-2 infection from 22 January – 22 April 2020 worldwide.
Source: **ECDC** [34].

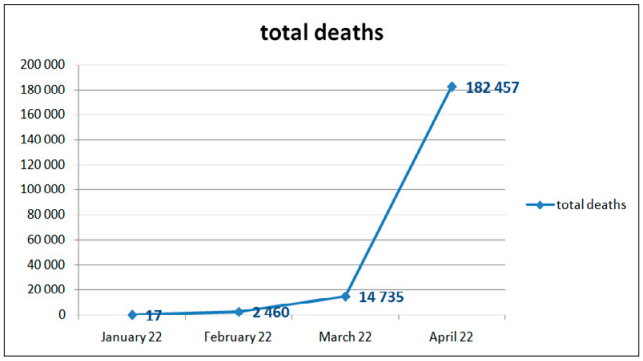

Figure 4. Evaluation of the number of deaths worldewide from 22 January – 22 April 2020 as a result of SARS-CoV-2 infection.
Source: ECDC [34].

Diagnostics. Confirmatory diagnostics are directed to people based on clinical symptoms, such as fever, cough, and shortness of breath. Imaging diagnostics (CT) are a crucial element in the diagnosis of SARS-CoV-2, which indicates bilateral interstitial pneumonia. RT-PCR remains the gold standard for the diagnosis and confirmation of SARS-CoV-2 [35]. According to the WHO and CDC guidelines for SARS-CoV-2 diagnostics, as far as possible samples should be taken from the lower and upper respiratory tract [36].

Table 1. Samples of clinical material for SARS-CoV-2 testing, according to the WHO [36]

Lower respiratory tract	Upper respiratory tract
broncho-alveolar lavage (BAL)	nasopharyngeal swab
endotracheal aspirate (ETA)	oropharyngeal swab
sputum	nasopharyngeal aspirate

Samples of clinical specimens (Tab. 1) from the lower respiratory tract, broncho-alveolar lavage (BAL), bronchoaspirate and expectorated sputum, have greater diagnostic value than these from the upper respiratory tract (e.g. nasopharyngeal swab). A single positive test should be confirmed in a second RT-PCR test targeting another SARS-CoV-2 gene. A single negative SARS-CoV-2 test (especially if it is from an upper respiratory tract sample) or a positive test for another respiratory pathogen result, does not rule out SARS-CoV-2 infection. If SARS-CoV-2 infection is suspected, another sample should be tested using primary and secondary RT-PCR assays (WHO) [37, 38].

It has been proven that over time since the first clinical symptoms of SARS-CoV-2 infection, the sensitivity of RT-PCR genetic tests decreases, which is observed already after the first week. They can generate false-negative results due to a reduction in the number of virus particles in the respiratory epithelium. In this situation, an essential place in the diagnosis of SARS-CoV-2 is occupied by serological tests that detect antibodies in the IgM, IgG, and some even IgA class, which are the body's response to virus infection [39]. Antibody detection tests available on the market are based on the enzyme-linked ELISA method, chemiluminescence and immunochromatography [40]. Serological tests for the detection of SARS-CoV-2 virus antigens use immunochromatography ('quick' cassette tests) and ELISA methods.

Many manufacturers offer so-called rapid 'cassette' tests based on lateral-flow (LFIA) immunochromatography, e.g. 2019-nCoV IgG / IgM Rapid Test Cassette BioMaxima. Whole blood, serum or plasma are used for the tests. If antibodies are present in the sample, they are combined with viral antigens labeled, e.g. with gold particles. The resulting complex migrates through the nitrocellulose membrane under the influence of capillary forces, and is eventually captured by membrane-attached antibodies to human immunoglobulins, forming a coloured line. The reaction result appears after 15 – 30 minutes. These tests do not require laboratory facilities, hence they are used in so-called mobile download points 'Drive-Thru; or 'Go-Thru' for quick diagnostics. However, any positive result always requires genetic confirmation [41].

In chemiluminescent tests, a luminophore or enzymatic reaction indicator is used, and the technique requires specialized equipment. The time to obtain a result is up to

30 min. [42]. An example is the DZ-Lite SARSCoV-2 IgM CLIA Diazyme Laboratories test. By comparing the effects of chemiluminescence tests with genetic tests, the authors rated the test sensitivity in both classes of antibodies at over 90% [43]. ELISA enzyme immunoassay testing allows the detection of specific IgA, IgG, and IgM antibodies against SARS-CoV-2 in serum samples [44]. Some research teams are developing their ELISA (in-house tests), e.g. the team of Zhang et al. [45]. Many authors suggest combining the RT-PCR technique with a serological test [46, 47] to eliminate the risk of false-negative results.

Serological tests to identify anti-SARS-CoV-2 IgG may form the basis of population-based epidemic studies to retrospectively determine the prevalence of infection in the population. Identification of IgG also enables the detection of convalescents who undergo asymptomatic or scanty-symptomatic infection. They also allow finding the sources of infection and confirming the result in patients with atypical symptoms [48]. Although many rapid serological tests are currently available, there are no scientific research results confirmed by experts that would indicate the usefulness of selected diagnostic test kits. The use of rapid serological tests in routine diagnostics requires many independent tests and validations. Considering the aspects mentioned above, it seems that the combination of the selected, validated serological test with the RT-PCR genetic analysis will avoid false-negative results, especially at a later stage of infection.

Treatment. Currently, the treatment of patients with SARS-CoV-2 infection is mainly symptomatic. The study by Huang et al. [49] indicates that the most common complications in patients with SARS-CoV-2 infection are acute respiratory distress syndrome, followed by anaemia, acute heart trauma, and secondary infections; therefore, empirical antibiotics, antiviral therapy (oseltamivir) and systemic corticosteroids are often used. Patients with uncontrolled hypoxaemia are receiving invasive mechanical ventilation. Remdesivir, a nucleotide analog, and chloroquine, an anti-malarial drug, are promising drugs against COVID-19 because they are known to inhibit the SARS-CoV-2 virus *in vitro* [50]. Chloroquine is widely used, safe, and inexpensive, effective in viral infections, and these conclusions come from preclinical studies, which should be confirmed in clinical studies [51]. Preclinical studies have shown that remdesivir (GS5734) may be useful in both preventing and treating HCoV infection. Remdesiviris an RNA polymerase inhibitor with *in vitro* activity against many RNA viruses, including Ebola [52]. This drug has been successfully tested on the animal model of MERS-CoV infection [53]. Currently, full clinical trials are needed to confirm the efficacy and safety of the preparations mentioned above in the treatment of COVID-19. Current treatment concepts include the administration of angiotensin receptor blockers (e.g. losartan) instead of inhibitors [54]. In some centres, in cases of severe SARS-CoV-2 infection, patients are treated with convalescents' plasma containing high levels of virus-neutralizing antibodies [55]. This approach leads to a rapid reduction in the viral load by binding of the virus particles by antibodies, and consequently to clinical improvement of the patient. Research conducted by Shen et al. and Duan et al. show that this effect can be achieved after a single dose of plasma is administered to patients with severe COVID-19. Such preparations must be compatible with the blood group of the plasma donor, and the patient to whom it is administered. At the same time, it must be emphasized that the optimal dose of the plasma preparation, time of administration, and real benefits for the patient require further clinical research. It should be borne in mind that the blood-derived preparation, which is the healers' plasma, does not fulfill the role of a drug that can be widely used [55, 56].

Prevention. In the absence of effective treatment, the best way to deal with the SARS-CoV-2 epidemic is to control the sources of infection. Strategies include early diagnosis, reports, isolation and supportive care, epidemic information, and social order. Standard recommendations for the prevention of the infection spread among those in affected areas include regular hand washing, covering the mouth and nose while coughing and sneezing, and avoiding close contact with people showing signs of respiratory disease. Many experts point out that immediate quarantine and immediate action to control infection are the best tools to prevent further spread of infection [57].

Many scientists around the world are working intensively to develop a SARS-CoV-2 vaccine, with individual centres studying various experimental models. Several proposals are in Phase I or Phase II of clinical trials, among them Inovio Pharmaceuticals from Coalition for Epidemic Preparedness Innovations (CEPI), which is developing a vaccine based on plasmid DNA encoding SARS-CoV-2 antigens [58]. The mRNA-1273 vaccine from Moderna and Vaccine Research Center is targeted to the coronavirus spike (S) protein. The mRNA carriers in this vaccine are lipid nanoparticles [59]. The Chinese Institute of Biotechnology of the Military Medical Academy and the CanSino Biologics Company are working on a recombinant vaccine based on the not replicable adenoviral vector (type 5 adenovirus). Genes encoding SARS-CoV-2 main antigens were introduced into the vector [60]. The team at the Jenner Institute in Oxford, UKI, is also using a replication-defective adenovirus vector. The resulting construct is: "ChAdOx1 nCoV-19" with S glycoprotein expression [61]. Researchers in China are working on inactivated vaccines. One of the products obtained is Pi-CoVacc containing a virus inactivated by ß-propionolactone and aluminum adjuvant [62]. Obtaining an effective and safe vaccine preparation has now become a priority; however, it takes time to conduct all the tests and clinical trials that will guarantee effectiveness and safety.

Survival in the environment. Research conducted by scientists indicates that the virus can survive in the air for more than three hours (recommendations of epidemiologists to limit leaving home). It can survive longer on various surfaces; e.g. on paper and cardboard it survives for 24 hours, on plastic and stainless steel – 2–3 days, on copper objects – 4 hours, and will still be able to infect [63]. These data indicate that no contact with an infected person is required to become infected with the coronavirus. Currently, available data indicate that the virus can survive several hours on surfaces. The virus can be ousted from the environment, as with most microorganisms, with the help of alcohol-based disinfectants. All coronaviruses are sensitive to ultraviolet rays and heat [64, 65]. According to the WHO, they can be effectively inactivated with lipid solvents, including ether (75%), ethanol (70%), a chlorine-containing disinfectant, peroxyacetic acid and chloroform [66, 67].

Complications. The authors point to the problem of pulmonary fibrosis arising in the context of SARS-Cov-2 infection. Sheng et al. [68] stated that infections may increase the risk of pulmonary fibrosis. Therefore, pulmonary fibrosis can be one of the severe complications after curing patients from COVID-19 disease. Prevention of pulmonary fibrosis in patients cured of 2019-nCoV infection is a problem that requires urgent action. Another complication is mild to moderate liver damage reported in patients with COVID-19. Increased transaminases levels, hypoproteinaemia, and prolonged prothrombin time have been observed in patients. Up to 60% of patients with SARS had liver problems, and it is believed that hepatic toxicity may also be associated with the action of antiviral drugs, antibiotics, steroids, and the immune system [69]. Numerous neurological pathologies following SARS-CoV-2 infection have also been documented, such as encephalopathy, encephalitis, stroke, epileptic seizures, rhabdomyolysis and Guillain-Barre syndrome [70]. Complications can also affect the cardiovascular system, including myocardial damage, myocarditis, acute myocardial infarction, heart failure, arrhythmias and thrombosis [71].

CONCLUSIONS

The study reviewed scientific reports and systematized current knowledge about SARS-CoV-2 coronavirus and the COVID-19 disease it causes in the face of the ongoing pandemic. Emerging viral diseases are a serious public health problem, especially with such a dynamically changing epidemic situation of which we are observers and participants. Coronaviruses are present in our lives almost constantly and are responsible, among others, for colds and runny nose. The last twenty years have brought several epidemics to the world involving coronaviruses: SARS-CoV in 2002–2003, MERS-CoV in 2012, and COVID-19, which is the cause of the current pandemic that broke out in Wuhan, the largest metropolitan area in the Chinese province of Hubei. The current pandemic was first reported to the WHO National Office in China on 31 December 2019. When analyzing previous cases of lower respiratory tract infections from this region, classified as 'pneumonia of unknown etiology', it should be presumed that the onset of the pandemic occurred in the first days of December 2019. The course of SARS-CoV-2 infection is similar to the cases caused by coronaviruses of severe acute respiratory syndrome (SARS-CoV) and the Middle East respiratory syndrome (MERS-CoV). Signs are present in patients of viral pneumonia, including fever, breathing difficulty, and bilateral infiltrative pneumonia or multi-organ failure in the most severe cases. COVID-19 disease also carries the risk of developing complications, such as pulmonary fibrosis, neurological disorders, an increased risk of heart attack, thrombosis, and liver dysfunction. This review has presented information about the taxonomy, structure, pathomechanism, clinical symptoms, complications, number of cases, diagnostics and treatment of the COVID-19 disease caused by SARS-CoV-2 virus.

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