IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
June 2021 Vol.:21, Issue:3

Overview on Human COVID-19: Symptoms and Treatment

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Tanaya Pawar*, Mayur Sarode, Akshay Ade, A. R. Dhole, C.S.Magdum, V.C. Yeligar

A/P-Rajarambapu College of Pharmacy, Kasegaon, Tal- Walwa, Dist- Sangli, India.

Submitted: 22 May 2021
Accepted: 29 May 2021
Published: 30 June 2021

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: COVID-19, coronavirus disease, anti-viral, vaccines, respiratory tract

ABSTRACT

Coronavirus disease 2019 has spread throughout the world and received worldwide attention. Scientists and physicians are racing to find out a new infectious agent and therefore the pathophysiology of COVID-19 to discover controllable treatment regimens and find out efficient remedy and immunizing agent. It is transmitted from bat via unknown intermediate organisms to human beings. It is more serious and hard to correct for a patient with hypertension, metabolic acidosis, respiratory distress syndrome, cardiovascular disease, septic shock, COPD, diabetes, multiple organ failure, and coagulation dysfunction. Nucleic acid detection in nasal and throat swab sampling is the diagnosis process used for the detection of another respiratory tract sampling by real-time PCR. There is currently no vaccine to guard against COVID-19. The best solution to stay away from infection is to take preventive action, like stay away from the public who are ill and washing your hands with soap, handwash and if water is not available then wash with a sanitizer, use the mask. There is no single antiviral treatment for COVID-19. People with COVID-19 can seek medical aid to assist relieve symptoms. Most of the anti-viral drugs are under experimental conditions. Existing drugs are used to control COVID-19 which decreases the symptoms.

INTRODUCTION

History:

December 2019: The World Health Organization is aware by Chinese officials regarding many pneumonia-like cases in the area of Wuhan city in China, as celebrations for the New Year take place across the country.

January 2020: A seafood marketplace in Wuhan is recognized by the Centers for Disease Control and Prevention (CDC) of U. S. as the focus of the outbreak.

7 January 2020: China reports its first well-known death from disease because of the novel coronavirus. The patient was a 61-year-old man in Wuhan.

13 January 2020: The WHO informs a case in Thailand, the first time it has been discovered outside china.

16 January 2020: Japan upholds the first case of infection with the novel coronavirus.

20 January 2020: In the first reported case of the latest coronavirus, South Korea records.

21 January 2020: The United States announces its first confirmed coronavirus case, a guy in his thirties in the Washington state.

22 January 2020: The death in China jumps to 17, with more than 550 infections. North Korea closes borders to all foreign tourists. Many airports begin to step up checks on flights from Wuhan.

23 January 2020: China is bringing Wuhan under quarantine. All flights and trains originating from the city are stopped and subways buses and ferries are suspended throughout the city. The WHO says the epidemic is not yet a globally concerned public emergency and there is "no evidence" of one human to another human transmission outside of China.

25 January 2020: The first case in Canada is confirmed after a man traveling from the city of Wuhan in China confirms positive for the infection of novel coronavirus. Australia and Malaysia declare their first confirmed cases of the new coronavirus. 27 January 2020: Germany has confirmed the new coronavirus in its first instance.

30 January 2020: The WHO declares the outbreak a global public health emergency as more than 9000 cases are reported worldwide, including in 18 countries beyond China.

1 February 2020: Princess Cruises confirms that a passenger who was onboard the Diamond Princess from Yokohama, Japan, tested positive for the virus.

2 February 2020: The first of coronavirus is reported outside China, a 44-year-old Wuhan resident who died in the Philippines.

3 February 2020: China reports 57 new deaths, bringing the death toll in China to at least 361. An increase in the number of cases to 17,205 across the country.

4 February 2020: The Diamond Princess cruise ship is quarantined off the coast of Japan with about 3700 people, including passengers and crew, on board.

7 February 2020: Dr. Li Wenliang, a Chinese doctor who issued a notice regarding the increase in the spreading of a new virus similar to the SARS virus before it was officially documented, dies from the new covid-19 in Wuhan. In China, Dr. Li became a hero and his death caused a period of national mourning.

8 February 2020: The first U.S. citizen dies from the virus in Wuhan.

9 February 2020: Mainland China's death toll is rising to 811, exceed the death toll from the 2003 SARS outbreak.

11 February 2020: The WHO announces the infection caused by the novel coronavirus will be known by the official name COVID-19. It means the coronavirus disease that was found in 2019.

14 February 2020: Egypt reported the first patient of COVID-19, becoming the first country to be affected by the outbreak in Africa. Outside of Asia, the first COVID-19 death was reported. The patient is a Chinese tourist aged 80 who died in France.

19 February 2020: Iran reports two COVID-19 cases. Hours later, officials confirmed that both patients have died.

24 February 2020: Italy becomes the worst-hit country in Europe as cases spike. The U.S. stock market plummets over coronavirus fears later the Dow Jones Industrial Average experienced its worst day in two years. An Iranian minister appears ill at a news conference before being diagnosed with COVID-19.

29 February 2020: The U.S. announces extra travel limitations involving Iran and increased warnings about traveling to Italy and South Korea. The first COVID-19 death in the U.S., a guy in his 50s in Washington state, is recorded.

6 March 2020: As the number of global cases approaches 100,000, Trump is signing an $8.3 billion emergency spending package to tackle it.

7 March 2020: Recently nominated MP Fatemeh Rahbar died because of the novel coronavirus in the country Iran, one of the worst-hit countries, with 4747 confirmed cases and 124 deaths.

9 March 2020: All of Italy and its 60 million residents are placed under lockdown. Canada announces its first COVID-19 related death, The elderly man lived at a North Vancouver nursing home.

10 March 2020: Lebanon and Morocco both report first deaths from the virus, while the Democratic Republic of the Congo, Panama, and Mongolia confirms the first cases of infection. 11 March 2020: The WHO declares the new coronavirus outbreak pandemic. Turkey, Lvory Coast, Honduras, and Bolivia confirm cases. The NBA announces it will suspend games until further notice as it deals with the COVID-19 pandemic.

12 March 2020: The NHL also suspends its season.

16 March 2020: The Indian government shut down the schools and colleges. Canada closes its borders to most foreign travelers and imposes tougher screening measures for visitors as the number of cases in the country increases to approximately 320. New York City Mayor Bill de Blasio orders the city's bars, theatres, and cinemas to close down as the number of cases keeps rising in the U.S. Egypt suspends all flights from its airports to control the new coronavirus spread.

17 March 2020: Thousands of stores, restaurants, cinemas, and bars across New York City, Chicago, Los Angeles, and San Francisco are ordered to shut down.

18 March 2020: Canada, U.S. temporarily close the boundary to non-essential transportation. The U.K. government shuts down schools.

19 March 2020: China reports zero latest local coronavirus cases for the first time while the outbreak began. The U.K. faces a shortage of medical equipment, which could lead to a

higher number of COVID-19 related deaths. Australia and New Zealand close the country's borders to stop the outspread of the virus. Italy surpasses China within the number of coronavirus-related deaths.

20 March 2020: California issues statewide live at home order, urging residents to only leave home when necessary.

22 March 2020: The Indian government declares lockdown all over the country.

Transmission:

The COVID-19 virus is likely to have originated from an animal source but is now spreading from one person to another person. It is supposed that the virus spreads mostly through respiratory droplets created while an infected one coughs or sneezes between public who make contact with each other (within about 6 feet). It can also be probable for an individual to get a corona virus through touching a plane or object that is in contact with their mouth, nose, or probably their eyes with the virus, but this is not known to be the primary way the virus spreads. [1]

Symptoms of COVID 19:

Patients with COVID-19 have had mild to severe respiratory disease with symptoms of fever, cough, and shortness of breath.

Prevention from COVID-19:

Stop touching unwashed hands with your nose, eyes, mouth, and wash your hands repeatedly for a minimum of 20 seconds with soap and water. Make use of an alcohol-based hand sanitizer that includes a minimum of 60% alcohol when soap and water are not available, avoid contact with sick peoples. Initially, coronavirus was named as the 2019 novel coronavirus on January 12, 2019, by WHO (World Health Organization), and WHO officially named a disease coronavirus disease 2019 (COVID-19). The coronavirus study group (CGS) of the international committee planned the name of a new coronavirus as SARS-COV-2. [2]

Origin and Transmission:

It is a coronavirus that is enveloped by non-segmented positive-sense RNA virus having subgenus: sarbecovirus, sub-family: orthocoronavirinae. Coronaviruses are divided into 4 genera including g α–/ β–/γ–/δ-CoV. Among that α- and β-CoVcan infect mammals and γ-

and δ-CoV are infecting to birds. Previously, six CoVs are identified as a human-susceptible virus, among which α-CoVs HCoV-229E and HCoV-NL63, and β-CoVs HCoV-HKU1 and HCoV-OC43 with low pathogenicity, cause mild respiratory symptoms similar to a common cold, respectively. The other two known β-CoVs, SARS-CoV and MERS-CoVcause severe and potentially fatal respiratory tract infections. It was found that the genome sequence of SARS-CoV-2 is 96.2% just like a bat CoV RaTG13, whereas it shares 79.5% identity to SARS-CoV. The bat has been supposed on the basis of virus genome sequencing results and evolutionary examination because the natural host of virus origin and SARS-CoV-2 could be transported from bats to infect humans through unknown intermediate hosts. It is now clear that angiotensin-converting enzyme 2 may be used by SARS-CoV-2 (ACE2), an equivalent receptor as SARS-CoV to infect humans. The primary route of transmission of SARS-CoV-2 was believed to be direct interaction with intermediate host animals or consumption of wild animals. [2,3]

Structure and key viral factors:

- Viral Factors:

1) S proteins: Attaching to host receptor ACE2 including two sub-units S1 and S2, 2) The virus-host range and cellular tropism are determined by S1 by RBD 3) S2 mediates virus-cell membrane fusion by HR1 and HR2, 4) M Protein: It is responsible for the transmembrane transport of nutrients, the bud release and formation of enveloping 5) N, E proteins and several accessory proteins, interfered with host immune response or unknown function.

Other unknown molecules facilitated membrane invagination.

- Receptors:

1) Bat: ACE2 binding, 2) Swine: ACE2 binding, 3) Civet: ACE2 binding, 4) Mouse: ACE2 no binding

Host Factors: SARS –COV-2 receptor: Human angiotensin-converting enzyme 2

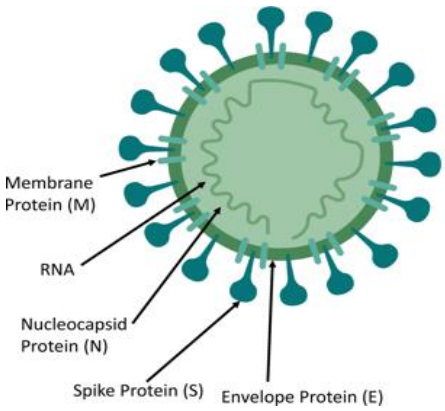
- Individual who are more susceptible to severe disease:

Elderly (>65 years of age) and the public with underlying diseases include hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular diseases.

- Severe Complications:

Respiratory distress syndrome, Metabolic acidosis, Coagulation dysfunction, Multiple organ failure, Septic shock.

Structure:



Structural Protein	Function of Protein
Nucleocapsid Protein (N)	• Bound to RNA genome to make up nucleocapsid
Spike Protein (S)	• Critical for binding of host cell receptors to facilitate entry of host cell
Envelope Protein (E)	• Interacts with M to form viral envelope
Membrane Protein (M)	• Central organiser of CoV assembly • Determines shape of viral envelope

- It has been noted that some CoVs do not need to have the full ensemble of structural proteins to make virions, highlighting that certain proteins may be dispensable or compensated by the function of non-structural proteins.

Figure No. 1: Corona Virus

Coronavirus Replications and Pathogenesis:

ACE2, which is present in humans in the lower respiratory tract, is known as the SARS-CoV cell receptor and controls both cross-species and human-to-human transmission, isolated from a COVID-19 patient's bronchoalveolar lavage fluid (BALF), Zhou et al. They also verified that SARS-CoV-2 utilize the same receptor for cellular entry, ACE2, as SARS-CoV. Virion S-glycoprotein can bind to the receptor on the surface of the coronavirus, and ACE2 can bind to the surface of human cells. The viral genome RNA is free into the cytoplasm after membrane fusion, and the uncoated RNA translates two polyproteins, pp1a and pp1ab, which encode non-structural proteins, into the double-membrane vesicle and forms the replication transcription complex (RTC). A nested set of subgenomic RNAs, encoding accessory proteins and structural proteins is continuously replicated and synthesized by RTC. Mediating endoplasmic reticulum (ER) and Golgi, newly formed genomic RNA, nucleocapsid proteins, and covering glycoproteins bring together and form viral particle buds. Lastly, the virion-containing vesicles attach to the plasma membrane to release the virus. Because the binding of SARS-CoV-2 Spike (S) glycoprotein and ACE2 receptor is a difficult step for virus entry. [4,5]

Clinical Characteristics:

As a growing acute respiratory infectious disease, COVID-19 spreads primarily through the respiratory tract, through droplets, through respiratory secretions, and direct contact with a

low dose of infection. The ACE2 protein is abundant in pulmonary alveolar epithelial cells and small intestine enterocytes, which can help to clarify the routes and manifestations of infection. The period is 1–14 days, mostly 3–7 days, based on current epidemiological studies. And during the latency period, COVID-19 is contagious. It is highly infectious in humans, particularly in the older and public with underlying diseases. The median age of patients is 47–59 years, and 41.9–45.7% of patients were females. As it is selected SARS-CoV-2, COVID-19 patients presented similar symptoms like fever, malaise, and cough. The majority of adults and children infected with SARS-CoV-2 have minor flu-like effects, but a few patients experienced acute respiratory distress syndrome, respiratory failure, multiple organ failure, and even death. [6,7]

Diagnostic criteria:

The viral research institution in China has conducted preliminary identification of the SARS-CoV-2 through the classical Koch's postulates and observing its morphology through electron microscopy. So far, the golden clinical diagnosis method of COVID-19 is nucleic acid detection in the nasal and throat swab sampling or another respiratory tract sampling by real-time PCR and further confirmed by next-generation sequencing.[8]

Clinical Symptoms:

Clinical symptoms like- Fever (88.7%), shortness of breath (18.6%), cough (67.8%), headache (13.6%) fatigue (38.1%), sore throat (13.9%), sputum production (33.4%), sore throat (13.9%), and headache (13.6%). Also, a part of patients manifestation gastrointestinal symptoms, vomiting (5.0%) with diarrhea (3.8%). The elderly and those with underlying disorders (i.e., hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular disease), developed rapidly into acute respiratory distress syndrome, metabolic acidosis, septic shock, difficulty to correct, and coagulation dysfunction, even leading to death. In laboratory test results, the majority of patients had lymphocytopenia and white blood cell levels that were normal or reduced. However, the neutrophil count, D-dimer, blood urea, and creatinine levels were slightly higher in the extreme patients, while lymphocyte numbers continued to decline, additionally, inflammatory factors (interleukin (IL)-6, IL-10, tumor necrosis factor-α (TNF-α) increase, indicating the immune status of patients. The data showed that patients with ICU had higher plasma levels of IL-2, IL-7, IL-10, granulocyte colony-stimulating factor (GCSF), 10 kDinterferongamma-induced protein (IP-10), monocyte chemoattractant protein-1 (MCP-1), macrophage inflammatory protein 1-α (MIP-1α), and

TNF-α. In addition, the CT imaging showed that factor-α (TNF-α) increases, indicating the immune status of patients. [9,10]

Why Coronavirus Spread so fast?

Protein on the surface of the virus explains why it is so easy to infect human cells. It spread much more readily than the one that caused severe acute respiratory syndrome/ SARS & has infected more than 10 times the number of people who contracted SARS. Coronavirus uses a spike protein that attaches to the cell membrane, it is activated by specific cell enzymes, to infect the cell. Genomic analyses of the latest coronavirus have revealed that its spike proteins vary from those of close relatives and suggest that proteins have a site thereon which is activated by host cell enzyme called furin. This is important because furin is present in many human tissues including lungs, liver, small intestine which means that virus can attack multiple organs, SARS, and other coronaviruses within the same genus. After all, the new virus doesn't have furin activation sites. The furin activation site "In terms of its entry into cells, set the virus up very differently to SARS & possibly impact virus stability & therefore transmission. Spike proteins attach to a receptor on a human cell known as (angiotensin-converting enzyme2 ACE2). At least 10 times more tightly than does the spike protein in the SARS virus. The reproduction number is an important property of infectious diseases. Reproduction numbers ranged from 1.4 to 6.49 in 12 studies of the coronavirus epidemic in china& had an average of 3.28. If we compare coronavirus with SARS which has a reproduction number of 2.8, coronavirus is significantly more infective. Another reason is it's a new virus & so the human immune system hasn't seen that virus before and then people are more likely to be contagious because they don't have an innate immunity already built up from prior exposure. So that new coronavirus moving quickly through different populations.

TREATMENT:

More effective drugs in the treatment:

Management of severe COVID-19 is not different from the management of most viral pneumonia-causing respiratory failure. Remdesivir, Chloroquine/ hydroxychloroquine, HIV combination drug like Ritonavir/ Lopinavir which is safe for use for COVID-19. Remdesivir was originally developed to treat Ebola by blocking the replicase system. It was found to be safe for humans. The molecules in remdesivir look like molecules that the replicase system used to make RNA. When a drug gets into a cell the virus tries to use the drug molecule to

replicate then it doesn't manage to replicate properly. It is an adenosine analog. It is incorporated into nascent viral RNA chains and leads to early termination. There's also another drug called Kaletra (Lopinavir/ Ritonavir combination) which is used to treat HIV. It was tried during the original SARS outbreak in2003 and seemed to offer some benefits. The target of that drug is the enzymes that chop up big proteins into smaller proteins during the replication process of a virus. Both remdesivir and Kaletra are now being tested as a part of the global mega trial set up by the World Health Organization in March. Chloroquine which is widely used as an anti-malarial and autoimmune disease drug recently reported as a potential broad-spectrum antiviral drug. It blocks virus infection by enhancing the endosomal pH require for virus or cell fusion as well as it is interference with glycosylation of cellular receptor of SARS-COV. Besides this antiviral activity chloroquine has an immune-modulating activity that may synergistically enhance the anti-viral effect in vivo. It is a cheap and safe drug that has been used for more than 70 years and it is potentially clinically applicable against the 2019 coronavirus. A person who fully recovers from COVID-19 donates blood plasma for possible use for the treatment of the virus. This is known as hyperimmune globulin therapy.

Common and Potent Anti-viral Drugs:

Table No. 1: Common Potent Anti-viral Drugs:

Status	Drug	Action Mode	Anti-infective Mechanism	Target Disease
Investigational	Nafamostat	Synthetic serinprotease inhibitor	Prevent membrane fusion by reducing the release of cathepsin B ; anticoagulant activity	Influenza, MERS, Ebola
Investigational	Favipiravir (T-705)	Nucleoside analoge: Viral RNA polymerase inhibitor	Action on viral genetic copying to stop its reproduction, without affecting host cellular RNA or DNA synthesis	Ebola, Influenza, A(H1N1)
Approved	Ribivirin	Synthetic guanosine nucleosides	Inferring with synthesis of viral mRNA (a broad spectrum activity against several RNA and DNA viruses)	HCV, SARS, MERS
Approved	Oseltamivir	Neuraminidase inhibitor	Inhibiting the activity of the viral neuraminidase enzyme, preventing budding from the host cell, viral replication and infectivity	Influenza viruses A
Approved	Penciclovir/ Acyclovir	Nucleoside analog	Asynthetic acyclic guanine derivative, leading to chain termination	HSV, VZV

Table 2. Key Proteins and Their Roles during the Virus Infection Process

Target Candidate	Full name	Role during viral infection	Drug Candidate
3CLpro	Corona virus main protease	A protease for the proteolysis of viral polyproteininto functional unit	Lopinavir
RdRp	RNA-dependent RNA polymerase	RNA dependent RNA polymerase for replicating the viral genome	Remdesivir, Ribavirin
TMPRSS2	Transmembrane protease, serine2	A host cell produced protease that primes S protein to facilitate its binding to ACE2	Camostat mesylate
AT2	Angiotensin AT2 receptor	An important effect or involved in the regulation of blood pressure and volume of the cardiovascular system	L-163491
PLpro	Papain like protease PLpro	A protease for the proteolysis of viral polyprotein into functional units	Lopinavir
Sprotein	Viral spike glycoprotein	Avirus surface protein for binding	Arbidol

REFERENCES:

1. CDC.gov/COVID19 Fact sheet.
2. Yan-Rong, Qing-Dong Cao, Zhong-Si Hong, Yuan-Yang Tan, Shou-Deng Chen, Hong-Jun Jin, Kai-Sen Tan, De-Yun Wang , Yan Yan The origin transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. Millitary Medical Research. (2020); 2-5.
3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J. A novel coronavirus from patients with pneumonia in China . N Engl J Med. (2020);382(8): 727–33.
4. Jia HP, Look DC, Shi L, Hickey M, Pewe L, Netland J. ACE2 receptor expression and severe acute respiratory syndrome coronavirus infection depend on differentiation of human airway epithelia. J Virol. 2005;79(23): 14614–21.
5. Tortorici MA, Veesler D. Structural insights into coronavirus entry. Adv Virus Res. 2019;105:93–116.
6. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004;203(2):631–7.
7. Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019- nCoV) infected pneumonia (standard version). Mil Med Res. 2020;7(1):4.
8. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: the mystery and the miracle. J Med Virol. 2020;92(4):401–2.
9. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020.
10. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497–506.
11. Hsieh HP, Hsu JT. Strategies of development of antiviral agents directed against influenza virus replication. Curr Pharm Des.2007;13(34):3531–42.
12. Furuta Y, Gowen BB, Takahashi K, Shiraki K, Smee DF, Barnard DL. Favipiravir (T- 705), a novel viral RNA polymerase inhibitor. Antivir Res. 2013;100(2):446–54.
13. Tchesnokov EP, Feng JY, Porter DP, Gotte M. Mechanism of inhibition of ebola virus rna -dependent rna polymerase by remdesivir. Viruses. 2019;11(4).
14. McQuade B, Blair M. Influenza treatment with oseltamivir outside of labeled recommendations. Am J Health. 2015;72(2):112–6.
15. V\McQuade B, Blair M. Influenza treatment with oseltamivir outside of labeled recommendations. Am J Health. 2015;72(2):112–6v.