

Review Article

An Overview of COVID-19 outbreak -Diagnosis, treatments, and prevention

Dr. Vikram Sarbhair

MBBS, MD, DNB, FCCP, FACP, FISDA, FNCCP,
Senior Consultant, Department of Pulmonology, Critical care and Sleep medicine, National heart institute, New Delhi.

ABSTRACT:

The recent spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its associated coronavirus disease has affected the entire world and caused widespread public health concerns. The outbreak of coronavirus disease 2019 escalated into the world as pandemic creating global health and economic crisis. Despite of global efforts to stop the spread of the disease, the outbreak is still on a rise. This is a zoonotic infection similar to other coronavirus infections which were believed to have originated in bats and pangolins, later transmitted to humans. Once entry into the human body, this coronavirus (SARS-CoV-2) is abundantly present in nasopharyngeal and salivary secretions of affected patients and its spread is predominantly thought to be respiratory droplet / contact in nature. This Virus can have direct or indirect transmission either directly from person to person or by respiratory droplets. Emerging evidence suggested that it may also be transmitted through contact and fomites. The novel Coronavirus -2019 (2019-nCoV) can also be transmitted directly or indirectly through saliva. The aim of this article is to provide a brief overview of epidemiology, symptoms, and routes of transmission of this novel infection. In addition, specific recommendations suggested for patient screening, infection control strategies and patient management protocols.

Key words: Coronavirus; COVID-19; severe acute respiratory syndrome; Coronavirus-2; SARS=Cov2 symptoms, treatment.

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Corresponding Author: Dr. Vikram Sarbhair, MBBS, MD, DNB, FCCP, FACP, FISDA, FNCCP, Senior Consultant, Department of Pulmonology, Critical care and Sleep medicine, National heart institute, East of Kailash, New Delhi-110065.

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INTRODUCTION:

Coronaviruses are a large family of viruses causing disease in animals and humans. Until now, seven coronaviruses are identified that can produce infection in humans around the world (1). The four most common ones are: 229E, NL63, OC43 and HKUI. These viruses can cause sicknesses such as common colds to more severe respiratory diseases such as the Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) and even death. Most recently discovered infectious coronavirus (COVID-19) can cause the entire spectrum of such diseases in humans. WHO originally called this infectious disease the Novel Coronavirus-Infected Pneumonia (NCIP) and the virus was named the 2019

novel coronavirus (2019-nCoV). On 11th February 2020, the WHO officially renamed the condition as COVID-19 (Coronavirus Infectious Disease -19) which was announced via Twitter. The outbreak of Covid-19 caused by 2019-nCoV or SARS-CoV-2 began in the city of Wuhan in Hubei province in China in December 2019. The current outbreak was officially announced as pandemic by WHO.

The virus is typically spreading from one person to another via respiratory droplets produced during coughing and sneezing. When people are symptomatic, it is the most contagious, although transmission may be possible before symptoms appear in patients. Time from exposure and onset of symptoms may range between 2 and 14 days. Common symptoms include fever, cough, sneezing, shortness of breath, anosmia and loss of taste.

Complications may include rapidly progressive pneumonia, and acute respiratory distress syndrome with Acute Respiratory failure widespread micro and macro thrombo-embolism including pulmonary embolism. Currently there is no specific antiviral treatment or a vaccine. Efforts consist of supportive therapy to relieve the symptoms. Recommended preventive measures include repeated hand washing with soap, covering the mouth while coughing or sneezing by a mask, maintain social distancing of more than 1-meter interpersonal distance and monitoring self-isolation for fourteen days for people suspected of infection (2). The standard tool of diagnosis is by reverse transcription-polymerase chain reaction (rRT-PCR) from a throat swab or nasopharyngeal swab or other Respiratory secretions. The infection can also be diagnosed from a combination of symptoms, risk factors and a chest CT scan showing features of pneumonia and pulmonary thrombo-embolism (3). As of early September 2020, 210 countries and territories around the world have reported over 26.5 million SARS-CoV2 cases with nearly 875,000 COVID-19 related deaths and counting (4). Though it's relieving that there are also more than 18.7 million recoveries (4)

Origin and Transmission of Covid-19

The first case was reported from Wuhan, city of Hubei province in China, in December 2019. It has been linked to the Hunan seafood market from where the infection spread up to 109 countries. The market has been linked with sales of raccoons, dogs, snakes, and other animals (5).

The sequence-based analysis suggested bats are the main reservoir. The recommendation of DNA was found to be involved at spike glycoprotein which assorted SARS-COV (COVZXC21 or COVZC45) with RBD of another Beta COV, thus could be the reason for cross species transmission and rapid infection (6).

The virus is mainly transmitted through contact or inhalation of respiratory droplets from cough, sneezing or talking by the infected people rather than through air (6). A single cough can circulate up to 3000 droplets when it lands on other people, covering surfaces around them and several smaller particles will stay in the air from infected individual's upper respiratory tract secretions (7). That is why it is advisable to stay 3 feet away from a person who is infected. The virus can also be transmitted through surface contamination when respiratory secretions droplets land on objects and surfaces around the infected person and normal individual touches these objects or surfaces and further on touching their eyes, nose or mouth these normal people catch COVID-19 (8,9).

Virus Replication

Infection begins when the virus enters the host cell, virus particles uncoated and spike protein attaches to its complimentary host cell receptor. Proteolytic enzyme of host cell cleaves and activates the receptor- attached spike macromolecule, enabling cell entry through endocytosis or direct fusion of the viral envelope with the host membrane. The chemical structure of coronavirus RNA consists of 5' methylated head and a 3' polyadenylated tail through which the RNA attaches to the free ribosomes of the host cell. This leads to the process of translation and formation of a long polypeptide chain. This protein has its enzyme (proteases) which breaks the poly protein into multiple non-structure proteins.

Coronaviruses have prickly spikes that project from their surface. They are enveloped RNA viruses, are characterized by club – like spikes that project from their surfaces they have a unique replicatory process. These viruses can cause upper respiratory infections in humans which may even be fatal (10).

COVID-19 Symptoms

Maximum patients when infected with virus experience common cold and 'flu' while a big majority of them remain asymptomatic. 80% of the patients show mild symptoms of the disease. Though young adults have best immunity to fight against the infections, they are more likely to spread the infection since many of them are asymptomatic unknowing carriers of COVID-19 Disease.

A study on 140 patients at Zhangnan hospital of Wuhan University identified different types of symptom varying from fatigue, dry cough, very high fever and difficulty in breathing (11). Research from the Chinese CDC observes that around 80% coronavirus cases are mild, around 15% cases are severe infected cases and 5% were critically ill. A day by day breakdown of corona symptoms shows how symptoms progress among typical patients, how the disease, Covid-19, goes from bad to worse (11).

Day 1: The patient suffers from fever with fatigue, muscle pain, dry cough. Few of them may experience nausea and diarrhea before the appearance of symptoms.

Day 5: Patients may suffer from breathing problems especially in elderly with some pre-existing health condition.

Day 7: According to Wuhan University study patients get admitted to the hospital.

Day 9: 15% of the patients develop acute respiratory distress syndrome (ARDS), where fluid fills up in the lungs and becomes fatal.

Day 10: The progression of the disease leads to worsening of the symptoms and patient is shifted to ICU. The current mortality rate is around 2%.

Day 17: On average after two and a half weeks patients who recover are discharged from the hospital.

Emergency warning signs of COVID-19 needs medical attention immediately, continuous pain or pressure in the chest, include trouble in breathing, confusion and bluish lips or face. The progressive condition leads to pneumonia (2,12). As per the new information, symptoms could appear as early as three days after exposure to as delayed as 13 days later. Recently published research found the average incubation period is about five-day post exposure (12).

Diagnosis of COVID-19

If the person develops symptoms of coronavirus 2019 disease, he should consult the doctor. The doctor considers whether an individual had close contact with someone diagnosed with COVID-19 or lived in any areas with ongoing community spread of COVID-19 within last 14 days. To test for COVID-19 doctor or health practitioner may take samples including a sample of saliva, a nasal swab and throat swab to send to a lab for testing or follow the directions of your local health authority (13).

Paper based test COVID-19

As COVID-19 cases increased all over the world required fast easy to handle diagnostic test procedure. Massachusetts Institute of Technology (MIT) is working on a paper-based test which may deliver results in less than half an hour. In this test a strip of paper, this is coated with antibodies which bind to a particular (COVID-19) protein. A second antibody is attached to gold nanoparticles, and patient's sample particles. Then test strip is dipped in this solution. A colored spot appears on the strip if any viral protein is present in sample within 20 minutes.

Currently two primary types of COVID diagnostic methods are available. First is screening patient blood sample for antibodies against the virus. Drawbacks of this test is that antibodies are often not detectable until a few days after symptoms begin. The second type in checking for viral DNA in the sample which is polymerase chain reaction (14).

Molecular Assays to Diagnose 2019-nCoV

Commercially several assays have been prepared to detect only novel virus and few can also detect other strains (e.g.SarS-CoV) that are genetically similar(15).

Treatment Strategy of COVID 19

It is important to caution the readers that new data gets updated nearly every hour regarding clinical characteristics, diagnosis, treatment options and

outcome for COVID-19. Optimized supportive care remains the backbone of therapy. The clinical efficacy for these agents is still under investigation or in clinical trials (16). Mostly clinical and preclinical data on antiviral therapy is taken from the other viruses, including SARS-CoV-1(17), Middle East Respiratory syndrome (18), and non-coronaviruses (Ebola) (8,19).

General treatment

A confirmed patient of COVID 19 needs bed rest and supportive treatment with adequate food and fluid intake to reduce the risk of fluid dehydration. Water electrolyte balance and homeostasis need to be maintained along with monitoring of vital signs and oxygen saturation; keeping respiratory tract unobstructed and inhaling oxygen in more severe cases; measuring blood count, C-reactive protein, urine test, and other blood biochemical indexes including liver kidney function, myocardial enzyme spectrum, and coagulation function. Chest imaging should be continuously re-examined and blood gas analysis should be performed when required.

Symptomatic Treatment

Control measures are needed for patients with a high fever. Antipyretic drug treatment should be given if the temperature exceeds 38.5 degrees centigrade. Warm water bath and anti-pyretic patches are preferred as preventive measure to reduce the temperature. Common drugs include Acetaminophen or Paracetamol 10-15mg/kg every time. NSAIDs should be avoided as far as possible.

Oxygen therapy

The chances of hypoxia increase as the virus target the lungs. Nasal catheter, mask oxygen should be immediately provided to the patient. In emergency conditions, Non-invasive or invasive mechanical ventilation should be provided to the patient (20).

Antiviral drugs

Group of antiviral drugs such as interferon a (IFN-a), lopinavir/ritonavir, chloroquine phosphate, ribavirin, and arbidol are therapeutically useful for prevention and treatment of Novel Coronavirus -induced Pneumonia by the National Health Commission (NHC) of the People's Republic of China for tentative treatment of COVID-19.

IFN-a is administered in the form of vapors inhalation at a dose of 5 million U (and 2 ml of sterile water for injection) for adults, two times/day. The dosage of lopinavir /ritonavir is 400mg /100 mg for adults 2 times/ day. Ribavirin should be administered via intravenous infusion at a dose of 500 mg for adults, 2 to 3 times/day in combination with IFN-a or Lopinavir /Ritonavir. Chloroquine phosphate is orally

administered at a dose of 500 mg (300mg for Chloroquine) for adults, 2 times/day. Arbutol is orally administered at a dose of 200 mg for adults, 3 times /day. The duration of treatment is no more than 10 days.

Favipiravir is new drug that is now approved after clinical trials for treatment of COVID-19. On February 15, 2020, China approved it as an useful drug for treating Novel Influenza. It acts by inhibiting the enzyme RNA dependent RNA Polymerase. The drug is capable of blocking the replication of flavi-,alpha-, filo-, bunya-, arena-,noro-, and other RNA viruses. Favipiravir is converted into an active phosphoribosylated form (favipiravir-RTP) in cells and is recognized as a substrate by viral RNA polymerase, thus inhibiting RNA activity. Therefore, favipiravir may have potential antiviral action on SARS-CoV-2, which is an RNA virus.

Remdesivir is another drug that is now approved after clinical trial for treatment of COVID -19. It is a nucleoside analogue and broad- spectrum antiviral. Animal studies proved Remdesivir can effectively reduce the viral load in lung tissue of infected mice with MERS-CoV, also helps in improving the lung function, and alleviate pathological damage to lung tissue.

A team of researchers from Shanghai Institute of Materia Medica and Shanghai Tech University performed drug screening and enzyme activity test, and reported 30 agents have potential antiviral activity against SARS -CoV-2 on January 25,2020. These agents are indinavir, saquinavir, lopinavir, carfilzomib, ritonavir, remdesivir, atazanavir, darunavir, tipranavir, fosamprenavir, enzaplatovir, pesatovir, abacavir, bortezomib, elvitegravir, maribavir, raltegravir, montelukast, deoxyrhapontin, polydatin, chalcone, disulfiram, carmofur, shikonin, ebselen, tideglusib, PX-12, TDZD-8, cyclosporin A, and cinanserin (21).

According to the new survey it is discovered that Chloroquine Phosphate is more effective in control treatment in inhibiting the progression of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course. This anti-malarial molecule would represent to be a successful drug and good choice in the treatment of acute viral infection as the drug is easily available and cost effective. However, still large number of research data needs to be collected before drawing any conclusion (22).

Prevention & Precaution of COVID -19

People should be aware of WHO latest information about the COVID-19 outbreak and follow the local health authority to prevent secondary infection,

interrupt human to human transmission to close contacts precautions by health care workers can prevent further spread by following the subsequent steps (24,25).

Boost your immune system

Real defense in any illness prevention is strong immune system. Dr. Tom Moorcroft, an osteopathic doctor who specializes in infectious disease says start daily activities and food choices that support people's health which will lead to lifelong improvements in health by eating enough micronutrients getting adequate sleep and some fresh air and sunlight daily what they can try their best during this time now (23).

RNA Vaccines

The Cambridge-based biotech company Moderna, prepared an experimental vaccine to diagnose coronavirus. Daniel Anderson, MIT professor in chemical engineering says a key advantage of messenger RNA is that the speed with which you can identify a new sequence and can be used to come up with a new vaccine.

Traditional vaccines consist of an inactivated form of a viral protein that induces an immune response. Usually, take longer time to manufacture, and they have inherent risks for few diseases. Vaccines that consists of messenger RNA is an appealing alternative because they induce host cells to produce many copies of the proteins they encode, promoting a stronger immune response than proteins delivered on their own.

Messenger RNA can encode the viral antigens, but to work, we seek out the simplest way to deliver these antigens to a particular part of the body so that they generate an immune response. It also makes sure that the vaccine causes appropriate immune stimulation to get a strong response.

RNA vaccines can also quickly target the viral proteins once the sequence encoding of the proteins is understood. Such vaccines are effective and safe to deliver at the site of action. A recent study showed that packing such vaccines into a special type of lipid nano particles can enhance the immune response (14).

Take steps to protect yourself:

Wash your hands regularly and thoroughly with soap and water for at least 20 seconds or with an alcohol based hand rub until they dry especially after you have been visited a public place, or after blowing your nose, sneezing or coughing .

Avoid touching many surfaces as you can pick up viruses and virus can enter the body causing the sickness.

Maintaining social distancing (1 meter or 3 feet) and avoid close contact with people which stop the spread of droplet infection (25, 26).

Take steps to protect others:

Wear a face mask when you are around other people.

Stay home if you are feeling unwell

If you have cough, fever and difficulty in breathing, seek medical help. If you're sick avoid taking public transportation.

Cover the nose and mouth while coughing or sneezing.

Throw the used tissues in the trash and wash your hands immediately with soap and water.

Clean the surfaces with disinfectant before and after the usage, which include desks, phones key boards, light switches, countertops, door handles.

Avoid direct physical contact to respiratory and other body secretions.

Protection to health workers by wearing Personal Protective Equipment (PPE) as additional protection (26).

Conclusion:

In conclusion, COVID -19 is dynamic and continues to rapidly evolve. Chest CT in recent cases showed similar to SARS as ground- glass and consolidations., SARS had a mortality rate of 9.5% whilst the novel coronavirus appears to have a mortality rate around 2%, based on confirmed cases and deaths.

It is important to consider the following points in the long term: Preparedness and contingency planning for modifying clinical practice of medicine.

Optimization of cross-infection protocols.

Patient empowerment and education.

Increased role of e-consultancy and tele-medicine.

Sanitizing and social distancing will help to an extent.

References:

1. WHO Q&A on coronaviruses (COVID-19) March 2020. <http://www.who.int/news-room/q-a-coronaviruses>.
2. Center for disease control and prevention, coronavirus disease 2019 (COVID-19). <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html>.
3. Velavan TP, Meyer CG. The COVID-19 epidemic. *Trop Med Int Health*. 2020; 25(3): 278-280. doi:10.1111/tmi.13383. <https://pubmed.ncbi.nlm.nih.gov/32052514/>.
4. <https://www.worldometers.info/coronavirus/> (as accessed on 05 September, 2020).
5. Murphy A and Bell D.J, et al.COVID-19, Radiopedia. <https://radiopaedia.org/articles/covid-19-2?lang=us>.
6. Shereen M.A, Khan S, COVID-19 infections: origin, transmission and characteristics of human corona viruses. *Journal of Advanced research*,16 March 2020. <https://www.sciencedirect.com/science/article/pii/S2090123220300540>.
7. Gray R, COVID-19: How long does the coronavirus last on surfaces? BBC 17 March 2020. <https://www.bbc.com/future/article/20200317-Covid19-how-long-does-the-coronavirus-last-on-surfaces>
8. WHO Q&A on corona viruses (COVID-19). <https://www.who.int/news-room/q-a-detail/q-a-coronaviruses>.
9. Alaska department of Health and Social Services. Human coronaviruses. <https://dhss.alaska.gov/dph/Epi/id/pages/Human-coronavirus.aspx>
10. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. *Methods Mol Biol*. 2015; 1282:1-23. doi:10.1007/978-1-4939-2438_1
11. Bendix A, A day-by-day breakdown of coronavirus symptoms show how the disease, COVID-19, goes from bad to worse. *Business Insider* Feb 2020. <https://www.businessinsider.in/science/news/a-day-by-day-breakdown-of-coronavirus-symptomd-shows-how-the-disease-covid-19-goes-from-bad-to-worse/articleshow/74257460.cms>
12. Coronavirus Resource Centre, Harvard Medical School, Harvard Health Publishing, Mar2020. <https://www.health.harvard.edu/diseases-and-condition/coronavirus-resource-center#COVID>
13. Coronavirus disease 2019 (COVID-19) Mayo clinic <https://www.mayoclinic.org/diseases-conditions/coronavirus/diagnosis-treatment/drc-20479976>
14. Trafton A, Chu J, CoVid-19 diagnostic based on MIT technology might be tested on patient samples soon, MIT News Office March,2020. <https://news.mit.edu/2020/covid-19-diagnostic-test-prevention-0312>
15. WHO Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans. <https://www.who.int/emergencies/novel-coronavirus-2019/technical-guidance/laboratory-guidance>
16. Erin K. Mc Creary E.K and Pogue J.M, COVID -19 Treatment: A Review of Early and Emerging Options, on behalf of the Society of Infectious Diseases Pharmacists. <https://watermark.silverchair.com/>
17. O'Keefe BR, Giomarelli B, Barnard DL, et al. Broad - spectrum in vitro activity and in vivo efficacy of the antiviral protein graffithsin against emerging viruses of the family Coronaviridae. *Journal of Virology*.2010;84(5):2511-2521.
18. Arabi YM, Shalhoub S, Mandourah Y, et al. Ribavirin and Interferon Therapy for critically Ill patients with Middle East Respiratory Syndrome: A Multicenter observational Study. *Clinical infectious disease: an official publication of the infectious Diseases Society of America*. 2019.
19. Siegel D, Hui HC, Doerffler E, et al. Discovery and synthesis of a Phosphoramidate Prodrug of a Pyrrolo[2,1-f][triazine-4-amino] Adenine C-Nucleoside (GS -5734) for the treatment of Ebola and Emerging Viruses. *Journal of medicine chemistry*.2017; 60(5):1648-1661.
20. Shen K, Yang Y. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: expert's World Journal of Paediatrics, February 2020. <https://doi.org/10.1007/s12519-020-00343-7> .
21. Liying Dong, Shasha Hu, Jianjun Gao, discovering drugs to treat corona virus disease 2019(COVID-19), *Drug Discoveries and Therapeutics* 2020 DOI:10.5582/ddt.2020.0102

22. Franck Touret, Xavier de Lamballerie, Commentary of Chloroquine and COVID-19, www.elsevier.com/locate/antiviral
23. Amanda Capritto How to protect yourself from the coronavirus March 19, 2020. <http://www.cnet.com/how-to/how-to-protect-yourself-from-coronavirus/>
24. WHO Coronavirus disease 2019 (COVID-19) Situation Report -53, March 2020 https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200313-sitrep-53-covid-19.pdf?sfvrsn=adb3f72_2
25. WHO Corona virus disease (COVID-19) advice for the public. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public>
26. How to protect Yourself, Coronavirus Disease 2019 (Covid-19), Centre for disease control and prevention. <https://www.cdc.gov/coronavirus/2019-ncov/prepare/prevention.html>