

WORLD JOURNAL OF PHARMACEUTICAL RESEARCH

SJIF Impact Factor 8.084

Volume 9, Issue 8, 373-391.

Review Article

ISSN 2277-7105

AN OVERVIEW ON SARS-COV-2 OUTBREAK: PANDEMIC OF THE CENTURY

¹*Ahire Saurabh Nandkumar, ²Panchave Rutuja Tukaram, ³Dr. Mahaparale Sonali, ⁴Khadse Shubham and ⁵Pagar Roshani Rajendra

¹M. Pharm Research Scholar, ²M. Pharm Research Scholar, ³Associate Professor, ⁴M. Pharm Research Scholar, ⁵M. Pharm Research Scholar

Dr. D. Y. Patil College of Pharmacy Akurdi, Pune.

Article Received on 26 May 2020,

Revised on 16 June 2020, Accepted on 06 July 2020

DOI: 10.20959/wjpr20208-18074

*Corresponding Author Ahire Saurabh

Nandkumar

M. Pharm Research Scholar, Dr. D. Y. Patil College of Pharmacy Akurdi, Pune.

1. ABSTRACT

Whole world is facing new invisible enemy SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus 2). This world health crisis begins in December 9, when SARS-CoV- 2 emerged at seafood wet market of Wuhan, Hubei province, South China and then it rapidly spread throughout the whole world. Virus then declare as a Public health emergency of International concern by WHO (World Health Organization). This coronavirus generally affects the lower respiratory tract and manifests as pneumonia in humans. The incubation period is around 2-14 days. Many patients are asymptomatic and they may act as carrier of virus some of them may be super spreaders. Diagnosis of disease is done by RT-PCR test by using nasopharyngeal swabs. CT of

chest is also abnormal in those with no symptoms or mild disease. Currently there is no any cure or vaccine is available to treat this SARS-CoV-2 and by using some drug like remdesivir, hydroxychloroquine the severity of disease is decreases. WHO and CDC advice to keep social distancing and avoid public places and close contact with infected person. This article is all about the publicly available information related to this new virus and summarize the knowledge about the pathogen and the current pandemic. In this literature review, the introduction of SARS-CoV-2, condition all over the world, pathogenesis, symptoms, treatment and management and prevention strategies all are reviewed.

KEYWORDS: SARS-CoV-2, RT-PCR, pneumonia, coronavirus.

2. INTRODUCTION

There are various pandemics are observed in the history of mankind among them some pandemics are more disastrous than the others to the humans. And now the human beings are again facing a very tough situation of an invisible enemy that is Novel Corona Virus Disease (nCOVID-19). The COVID-19 was initially observed in Wuhan city of china which is now spread at very faster rate all around the global world. According to reports from china the first infected person and other which are comes in contact with that infected person are had links to an animal and seafood market which is also known as wet market of Wuhan. From this information scientist concluded that this coronavirus may transmitted from the animals to human.

On December 31, 2019, The China Health Authority alerted the WHO (World Health Organization) about some cases of pneumonia with unknown etiology in Wuhan city of Hubei province in Central China. The cases had been reported since Dec. 8, 2019 and many of them are lived around or worked at the local Huanan seafood wholesale market while some of the other early cases had no exposure to this seafood market.^[1] On Jan. 7, 2020, a new type of coronavirus also called as novel coronavirus original abbreviated by WHO as 2019-nCoV was identified from a throat sample obtain from a patient having a disease with unknown etiology. ^[2] The pathogen then renamed as Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) by the international Committee on Taxonomy of Viruses (ICTV)^[3] and disease was named by WHO as Corona Virus Disease 2019 (COVID-2019). As of Jan. 30, 2020, 7736 confirmed cases of COVID-19 with 12,167 suspected cases had been reported in china alone while 82 confirmed cases had been reported in other 18 countries. Hence on Jan. 30, 2020, WHO declared SARS-CoV-2 outbreak as a Public Health Emergency of International Concern (PHEIC)^[4] and on Mar. 11, 2020 the WHO announced the rapidly spreading SARS-CoV-2 outbreak as a pandemic viral disease. As of today, Jun 24, 2020 there are total 9,394,595 infected patients of SARS-CoV-2, almost 4.8 lakh peoples lost their lives while 5 million patients are recovered from disease. Following figures shows how the number of cases is increased along with deaths.^[5]

COVID-19 is highly infectious which is spread at very high rate having relatively mortality rate at around 5.12% and the information available in public reports and published literatures is rapidly increasing day by day. The aim of our review is to summarize the current pandemic situation which includes the basic information about the coronavirus, current situation of world

facing this pandemic, pathogenesis of disease, diagnosis treatment with prevention and control of disease.

2.1 Types

Coronaviruses Types belong to the family *Coronaviridae* with subfamily *Orthocoronavirinae*. Human coronavirus having different types according to severity of disease and how far they can spread. Until now scientists recognize seven different strain of coronavirus that can infect human:

Common types

- A. 229E (alpha coronavirus)
- B. NL63 (alpha coronavirus)
- C. OC43 (beta coronavirus)
- D. HKU1 (beta coronavirus)^[6]

In the past 2 decades two different instances are occurred related to coronavirus where there is crossover of animal beta corona virus to humans has resulted in severe diseases. The first instance was occurred in between 2002-2003 when a new strain of beta coronavirus having origin in bats crossed over to human through intermediate host palm civet cats in Guangdong province of China. This virus was named as Severe Acute Respiratory Syndrome (SARS) which affect 8422 people mostly from China and Hong Kong also killed almost 916 infected peoples with mortality rate 11%.^[7] After this incidence almost 10 years later in 2012, A new strain emerged in SaudiArabia named as Middle East Respiratory Syndrome (MERS) also having bat origin with dromedary camels as an intermediate host which affect 2494 people and responsible for 858 deaths with mortality rate 34%.^[8] A dangerous new strain of coronavirus in December 2019 called SARS-CoV-2 started circulating, causing the disease COVID-19.

3. CONDITION OF COVID-19 ALL OVER THE WORLD

COVID-19 total cases

According to the site of worldometers.info, As of Jun 24, 2020, the total corona virus cases around word are 9,394,595. Among which more than 5 million peoples are cured while 4.8 lakh peoples died due to pandemic. China was the first country got infected by COVID 19 and reached the number of total cases 83,430 as of Jun 24, 2020. However, USA shows the highest number of infection (2,425,507), followed by Brazil (1,152,066) then Russia and India with cases 606,881 and 461,828 respectively (Figure 1).^[5]

Death Rate in Different country

Worldwide death rate is around 5.12%. Amongst all infected countries, the death rate as of Jun 24, 2020 in Italy (14.51%) is the highest followed by UK (13.96%). This virus is showing a 5% death rate in the USA.^[5]

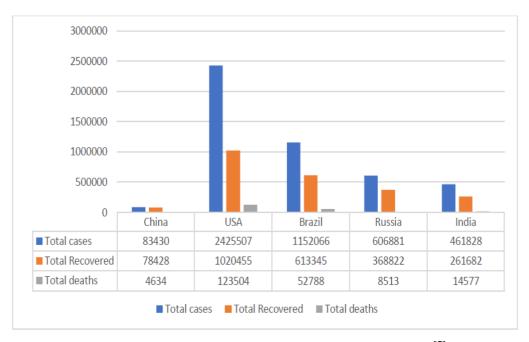


Figure 1: COVID-19 total cases up to Jun 24, 2020.^[5]

4. Pathogenesis

Coronavirus is the single stranded positive sense RNA enveloped virus with a diameter of 60 nm to 140 nm, which is having spike-like projection on its surface gives it Crown-like appearance under the electronic microscope. Corona is the Latin term for crown hence the virus is named as Coronavirus. Coronavirus belongs to family coronaviridaewith subfamily Orthocoronavirinae, order Nidivirales. These are genome composing of positive-sensed single-stranded RNA. Currently there are 4 generations of coronaviruses which are α -CoV, β -CoV, γ -CoV, and δ -CoV. So according to phylogenetic analysis based on the viral genome, SARS-CoV-2 belongs to β -CoV generation. The α -CoV and β -CoV infect mainly the central nervous system, respiratory system and gastrointestinal system of humans and mammals, whereas γ -CoV and δ -CoV infect mainly birds.

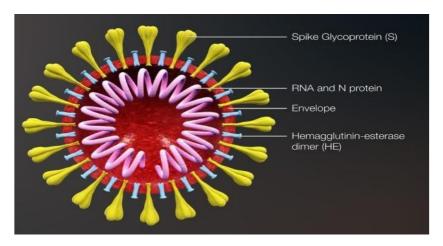


Figure 2: Structure of Coronavirus.

Studies shows that there is highest load of virus in nasal cavity as compared to throat with no difference in viral burden between symptomatic and asymptomatic infected people.^[19] Some people are act as super spreader who spreads the disease rapidly. The virus can remain on surface for days in favorable atmospheric conditions but it can be destroyed easily within a minute with the help of common disinfectant like Hydrogen peroxide, Sodium hypochloriteetc.^[20] Studies suggested that angiotensin receptor 2 (ACE2) is the receptor through which the virus enters in the respiratory mucosa.^[21]

Based on the cells that are likely infected, COVID-19 can be divided into three phases that correspond to different clinical stages of the disease.^[22]

Stage 1- Asymptomatic state: Which is occurs in initial 1–2 days of infection. Initially the inhaled virus attached to epithelial cells present in nasal cavity and starts to replicate. ACE is receptor site for SARS-CoV-2 and SARS-CoV.^[23,24] According to *Invitro* data with SARS-CoV ciliated cell are initially infected in conducting airways.^[25] At this stage virus is detected with help of nasal swab. Nasal swabs may be more sensitive than that of throat swabs. There is local propagation of the virus but a limited innate immune response.

Stage 2- Upper airway and conducting airway response: which occurs in next few days of infection where the virus propagates themselves and moves downward in the respiratory tract along conducting airways. In this stage, more innate immunity response is generated. Nasal swab or sputum gives indication of presence of SARS-CoV-2 and markers of innate immunity response. At this stage, the disease COVID-19 is clinically manifest. CXCL10 which is an interferon responsive gene which has superb signal to noise ratio in alveolar type 2 cell response to influenza and SARS-CoV. [26,27]

Around 80% infected patients the disease is restricted to upper respiratory tract and conducting airways and the disease will be mild.^[22] These patients may be handled at home with conservative symptomatic therapy.

Stage 3- Hypoxia, ground glass infiltrates, and progression to Acute Respiratory Distress Syndrome: around 80 % patients have mild symptoms and stays in stage 2 while 20% are infected patients will have entered to stage 3 and will develop Pulmonary infiltrate and some of these may develop very aggressive severe disease. The mortality rate also initially 2% but now it is around 6.9 % which may vary according the country. The virus reaches to gas exchange units of the lung and infects alveolar type II cells. Both SARS-CoV and influenza preferentially infect type II cells compared to the type I cells. SARS-CoV propagates into the type II cells, number of viral particles are get released and cells undergoes apoptosis process and die (figure 3). The pathological result of SARS and COVID-19 is diffuse alveolar damage with fibrin rich hyaline membranes and a few multinucleated giant cells. The abnormal wound healing may cause more severe scarring and fibrosis than other forms of ARDS. Recovery must require an acquired and innate immunity response and epithelial regeneration. Elder people are generally at risk because of their reduced immune response and also reduced the ability to repair the damaged epithelium.

There is no any evidence of pathogenesis of SARS-CoV-2 and there will be many assumptions are made for the next few months related to pathogenesis. So according to some research the viral entry of SARS-CoV-2 is same as that of receptors for SARS-CoV. [33]

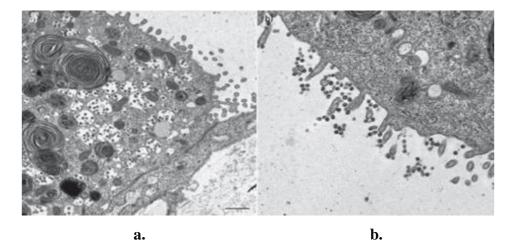


Figure 3: Human type II cells were isolated, cultured *in vitro*, and then infected with SARS- CoV. Viral particles are seen in double membrane vesicles in the type II cells (a) and along the apical microvilli (b).^[26]

5. Symptoms

The symptoms of COVID-19 infections are generally appears after the incubation period of approximately 5 days. [34] The period from onset of COVID symptoms to the death ranged from 6 to 14 days with median period of 14 days known as incubation period. [35] This incubation period is affected by age of the patient and the immune system of patient as it was shorter in patients which are more than 70 years old. [35] The very common symptoms of COVID-19 illness are sneezing, Runny nose, Sore throat, cough, fever, myalgia and fatigue, while other symptoms include headache, sputum production, lymphopenia, diarrhea, hemoptysis and dyspnea. [35-38] Clinical features from a chest CT scan Showsbilateral pneumonia, however, there were abnormal features such as acute cardiac injury, RNAaemia, acute respiratory distress syndrome, and incidence of grand-glass opacities that led to death. [37]

Table 1: Frequency of Symptoms in COVID-19.

Symptoms	Patients in percent with symptoms
Fever	85% (only 45% febrile on presentation)
Cough	50-80%
Fatigue	69.6%
Dyspnea	20-40%
URI symptoms	15%
GI symptoms (nausea, vomiting, diarrhea)	10%

COVID-19 shows symptoms similar to beta coronavirus such as fever, dry cough, Dyspnea and bilateral ground- glass opacities on chest CT scans but COVID-19 also shows some unique Clinical features includes targeting the lower airway as evident by upper respiratory tract symptoms such as sneezing, rhinorrhea and sore throat. Some of the cases shows infiltration in upper lobe of lung causes due to dyspnea with hypoxia.

Clinical features

SARS-CoV-2 manifest with a wide clinical spectrum ranging from asymptomatic patients to multiorgan dysfunction and septic shock. SARS-CoV-2 may classified based on severity of disease into mild, moderate, severe and critical.^[41]

i. Mild disease

Patients having mild illness may having symptoms related to upper respiratory tract viral infection. It includes mild fever, dry cough, sore throat, headache, nasal congestion, muscle pain.^[42] It is also characterized by absence of serious symptoms like dyspnea. Majority of SARS-CoV-2 cases (81) % are either mild or asymptomatic.^[41]

ii. Moderate disease

These patients have respiratory symptoms like shortness of breathing, cough and tachypnea. [42]

iii. Severe disease

Severe patients have severe pneumonia, Acute respiratory distress syndrome (ARDS), septic shock. Diagnosis is done by clinical manifestation. Clinical presentation includes presence of tachypnea (respiratory rate > 30/min), severe dyspnea, respiratory distress, SpO2 $\le 93\%$, PaO2/FiO2 <300, and more than 50% lung infiltrates within 24 to 48 hours. Patients can develop critical disease with features such as RNAaemia, respiratory failure, septic shock, cardiac injury or organ dysfunction. Acute respiratory distress syndrome (ARDS), septic shock, cardiac injury or organ dysfunction.

Table 2: The Director-General noted that the risk of serious complications increases with age. According to the WHO.

Stage of severity	Rough percentage of people with SARS-CoV-2
Mild stage from which a person can recover	More than 80%
Severe stage in which breathlessness and pneumonia	Around 14%
Critical stage including respiratory failure, septic shock and the failure of more than one organ	About 5%
Fatal stage	2%

6. Diagnosis

According to China Health Commission, COVID-19 disease is identified by patient's epidemiological history and clinical manifestation along with verification of SARS-CoV-2 infection by one subsequent method: real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay, high-throughput genome sequencing, and serological evaluation of anti-viral immunoglobulin M (IgM) and G (IgG) antibodies. [43,44]

RT-PCR: SARS-CoV-2 RNA is identified by RT-PCR technique. Samples use for diagnosis are throat swab (nasopharyngeal of children), lower airway secretions, sputum, blood and stool selected to diagnose of SARS-CoV-2 ribonucleic acid. Studies suggested that there is higher level of virus in nasal cavity than that of throat with no distinction in viral burden between symptomatic asymptomatic individuals.^[19] If an oropharyngeal swab is taken then it should also have kept in the nasopharyngeal swab specimen. Negative RT-PCR results from oropharyngeal swabs and CT indicates viral pneumonia, have been demonstrated in certain cases that ultimately shown to be positive for SARS-CoV-2. So nasopharyngeal should preferred to analyze SAR-CoV-2. Sputum should only be obtained from cases should be productive and do not force the patient to induce the sputum. If the test is negative is there any

doubt for COVID-19, WHO advices to recollect the samples and analyze them from several airways sites. Sometimes testing of SARS-CoV-2 ribonucleic acid shows false negative results, then another diagnosis method serological analysis method which analyze virus specific IgG and IgM antibodies should be selected as an alteration.^[44]

The CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel contains:

- i. 2019-nCoV_N1 and 2019-nCoV_N2 probes and primers which target regions of virus nucleocapsid (N) gene. The panel specifically designed for detection of SARS-CoV-2.
- ii. RP probes and primers which targets the Human RNase P gene.
- iii. nCoVPC, the 2019-nCoV positive control used in the assay. [46]

Imaging findings

Following are the abnormalities have been reported by imaging finding techniques of COVID-19 patients:

The chest X-ray (CXR) of COVID-19 patients usually shows bilateral infiltrates as shown in figure 4 but it could be normal in early disease.^[47]

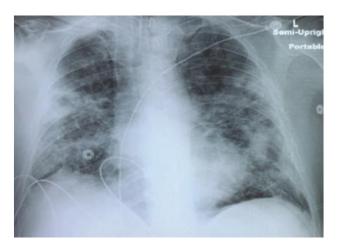


Figure 4: COVID-19 imaging of chest X-ray shows bilateral peripheral opacities.

The CT scan is more sensitive and specific for diagnosis. CT scan of lung of COVID-19 Patients shows infiltrates, ground glass opacities and sub segmental consolidation as shown in figure 5. CT is also abnormal in the patients which are asymptomatic or patients who have no clinical evidence of lower respiratory tract involvement. In fact, abnormal CT can be used to diagnose COVID-19 suspected cases with negative molecular diagnosis. [47,48]

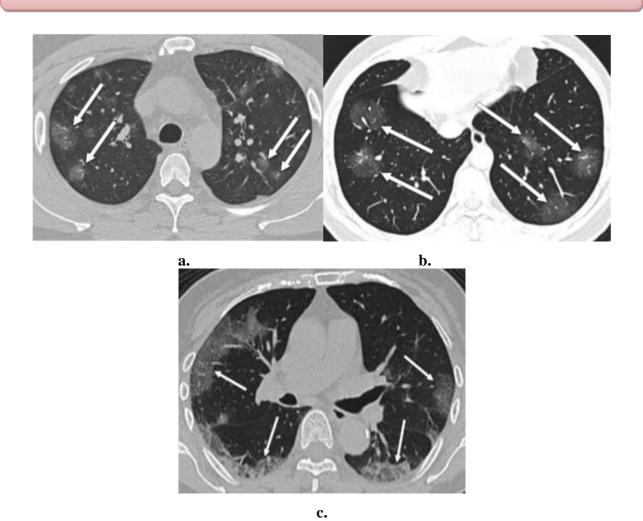


Figure 5. (a): Axial CT scan image obtained without intravenous contrast material of a 36-year-old male patient shows ground-glass opacities in upper lobes with round morphology (arrows). (b) Axial CT scan image of a 44-year-old male patient with round morphology (arrows). (c) Axial CT scan image of 65- year-old female patient shows bilateral ground-glass and consolidative with a striking peripheral distribution (arrows). [48]

Treatment

There is no any specific therapy for SARS-CoV-2 also not any type of vaccine is available currently to increase the immunity against disease. Treatment is symptomatic and oxygen therapy represents major part of treatment for patients having severe infection. Mechanical ventilation can also be required when respiratory failure in unmanageable by oxygen therapy, while hemodynamic support is necessaryfor managing the septic shock. Home management is suitable for asymptomatic or paucisymtomatic patients. They only required daily checking of body temperature, blood pressure, respiratory saturation and respiratory symptoms for atleast 14 days. Management of this asymptomatic patients should be specially

focus on the prevention of transmission to others.

Following are the pharmacological experimental options with potential clinical benefit for coronavirus which cannot completely cure the SARS-CoV-2 but helps to decrease the severity of the disease:

i. Remdesivir (GS-5734)

Remdesivir is an investigational monophosphoramidate prodrug of adenosine analogue which is discovered by Gilead Science, Inc. for the Ebola outbreak in west Africa from 2014-2016. Remdesivir activated in the form of triphosphate nucleoside and then remdesivir binds to RNA-dependent RNA polymerase and acts as a RNA chain terminator. It also shows potent *in vitro* activity against SARS-CoV-2 withan EC50 at 48 hours of 0.77 µM in Vero E6 cells. ^[52] The dose investigated for treatment of SARS-CoV-2 is 200mg intravenously (IV) on first day followed by 100mg for 10 days. Emerging clinical evidence and available *in vitro* showsremdesivir is promising agent for SARS-CoV-2 treatment. ^[52]

ii. Lopinavir-Ritonavir

These two antiviral drugs acts as protease inhibitor which are used mainly in HIV infection. The combination shows effective action against SARS-CoV infection *in vitro* and some activity against MERS-CoV in animals.^[53] In a case study, using this combination of Lopinavir-Ritonavir 5 cases are treated which shows 3 cases properly recovered while 2 cases worsened; 4 cases have gastrointestinal side effects. So, this combination is now currently tried in treatment of adults SARS-CoV-2 patients with pneumonia.^[54]

iii. Chloroquine and Hydroxychloroquine

Chloroquine is an antimalarial drug with an immunomodulatory and anti-inflammatory activity which gained much more attention for the management of SARS-CoV-2. In February, Wand and his colleaguesdemonstrates a potent *in vitro* activity of chloroquine against COVID-19 with an EC50 at 48 hours of 1.43 µM in Vero E6 cells. These researches have supported the clinical use of chloroquine at a dose of 500 mg orally two times daily in numerous clinical trials in chine during outbreak. Chloroquine phosphate have good results in inhibiting the exacerbation of pneumonia, improves lung imaging findings, promoting a virus negative conversion and shortening the course of disease. But the use of chloroquine phosphate is limited because of its cardiovascular toxicity, for this as an alternate, Hydroxychloroquine, a compound which is different from chloroquine by a single hydroxyl group has gained

interest. Hydroxychloroquine has better tolerability than chloroquine.

iv. Ribavirin

Ribavirin is used in combination with Lopinavir-Ritonavir to treat the SARS-CoV-2 cases shows better results as compared to the cases used ribavirin only. But *in vitro* activity of ribavirin against SARS-CoV-2 shows EC50 of 109 µM which is 100 times less potent than Remdesivir. However, ribavirin has the high risk of hematologic toxicity at high dose, hence ribavirin was not considered viable candidate to treat the SARS-CoV-2 due to lack of *in vitro* efficacy, toxicity profile and poor outcomes.

v. Tocilizumab

Tocilizumab is a humanized monoclonal antibody which inhibits soluble interleukin-6 (IL-6) and membrane-bound receptors. Interleukin-6 is generally secreted by monocytes and macrophages. It drives immunogenic responses and symptoms in Cytokine-Release Syndrome (CRS) patients. It was first approved in 2010 by FDA to treat the Rheumatoid Arthritis, then it gained attention for the treatment of CRS.^[57] Immunotherapy of tocilizumab is used to treat the severe or critical cases of SARS-CoV-2 with elevated IL-6 in 7th edition of the National Health Commission of the People's Republic of China COVID-19 Diagnosis and Treatment Guide.^[58] The recommended dose of Tocilizumab is 4-8 mg/kg or 400 mg standard dose IV once with an option to repeat a dose in 12 hours (not to exceed total dose of 800mg).

vi. Faripiravir

Favipiravir is selectively inhibiting RNA dependent RNA polymerase (RdRP) which is an enzyme required for RNA viral replication inside the human cell. Favipiravir functions as purine analogue which is incorporated instead adenine and guanine terminates the elongation of viral RNA.^[59] The Science and Technology Ministry of China officially stated few months ago that Favipiravir is clearly effective for SARS-CoV-2 treatment.

Along with the medicines there are some therapies are also used to treat the SARS-CoV-2 such as,

i. Convalescent plasma therapy

There is no any effective drug of vaccine is available right now to treat the COVID-19, convalescent plasma therapy could be an effective way to treat the severely infected patients.^[60] Plasma therapy is more useful than severe doses of hormonal shock in patients with severe SARS, shortening the hospital stay and reducing mortality.^[61] In convalescent plasma

therapy, the patients which are recovered from SARS-CoV-2 produces specific antibody against the virus in their blood and serum. This blood from people recovered from disease is known as convalescent plasma. This plasma is then injected to the patient having severe SARS-CoV-2. This plasma containing antibodies use to prevent re-infection. This antibody also reduces the reproduction of virus in acute phase of infection and help to clear the virus, this causes the rapid recovery of patient from disease.

ii. Auxiliary blood purification treatment

According to some recent studies, kidneys could be another main target to attack for SARS-CoV-2. Many patients with severe SARS-CoV-2 might suffer from cytokine storm. Immune damage can could be occurring due to imbalance of pro-inflammatory and inflammatory factors. Hence, Blood purification technique could be used to eliminate the cytokine storm and inflammatory factors, correcting imbalance and maintaining acid-base balance.^[62]

iii. Oxygen therapy

The virus mainly targets the lungs so there are chances of development of hypoxia. Nasal catheter, mask oxygen should immediately provide to the infected patient. In emergency, invasive or noninvasive mechanical ventilation should provide to the diseased patient. [43]

7. Prevention

Since there is no any cure for the infection of COVID-19, prevention is also crucial part. As of now, there is no any vaccine is available and best prevention is to avoid exposure to the virus. Some properties of this SARS-CoV-2 make it difficult to prevent from spreading, like lack of symptoms in patients so the patients himself act as carrier to the virus and spread the virus, long incubation period, tropism for mucosal surfaces like conjunctiva, prolong duration of illness and transmission of virus even after recovery.

Following are some preventive guidelines provided by WHO, CDC and OSHA

- Wash your hands regularly and thoroughly with water and soap for at least 20 seconds or
 pour alcohol-based hand rub sanitizer (contains at least 60 % alcohol) on your hands and
 rub them together until they do not dry especially after you blowing your nose, sneezing or
 coughing or after you had been visited a public place.
- Avoid touching of your unwashed hands to your nose, eyes or mouth because hands touch
 many surface and may pick up virus from contaminated area. These are the routes of
 entry of virus in the body.

- Maintain social distancing. Keep 3 feet or 1 meter distance between yourself and anyone.
- Avoid close contact to the sick peoples who are coughing or sneezing, they spray small
 droplets from mouth or nose which may contain SARS-CoV-2 virus
- Apply disinfectant daily on frequently touched surfaces such as desks, light switches, phones, keyboards, tables, faucets, doorknobs, handles, countertops, toilets and sinks.
- Before clinical care started, identify the potential cases as soon as possible and isolate the suspected cases from confirmed infected patients with COVID-19 to prevent the transmission of infection to other patients and health care staff.
- Health care staff should use Personal Protective Equipment (PPE) while treating the COVID-19 patients
- Keep up to date about the latest information related to SARS-CoV-2 from trusted sources like WHO or national or local health authorities. [63-65]

If you feel sick then

- Stay at home if you feeling unwell then don't get out of house unless there is emergency.
- If you have fever, cough or difficulty in breathing then contact immediately the doctor.
- Cover your mouth and nose with tissue whenever you sneeze or cough.
- Isolate yourself from the other family members and pets. wear face mask when you are around the people also the peoples who comes in contact with should also wear face mask.
- Avoid sharing bedding, glasses, dishes and other household items. If possible, use a separate toilets and bathroom from the family. [63-65]

8. CONCLUSION

This new virus outbreak is clearly an international public health problem and it has now challenged medical, economic and public health infrastructure of whole world. SARS-CoV-2 spread by human to human transmission by close contact with infected person via airborne droplets generated while sneezing, coughing, smooching or kissing. In case any suspect of SARS-CoV-2, infection control action should be immediately executed and a nasopharyngeal swab should be sent for RT-PCR testing. Social distancing and regularly sanitization is the only preventive action from this virus and prevention is the only cure to the virus as there is no any cure or vaccine is available as of now. Researchers work so hard to find the cure for this virus until then we have to take care of ourselves by following the rules and regulations provided by health authorities like WHO or CDC or the government of that respected country.

9. REFERENCES

- 1. 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: 401-402.
- 2. Hui DS, Madani TA, Ntoumi F, Kock R, Dar O, *et al*. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health the latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis., 2020; 91: 264-266.
- 3. Gorbalenya AE, Baker SC, Baric RS, *et al.* Severe acute respiratory syndrome-related coronavirus: the species and its viruses a statement of the Coronavirus Study Group, 2020; 1-15.
- 4. Burki TK. Coronavirus in China. Lancet Respir Med., 2020; 8: 238.
- 5. https://www.worldometers.info/coronavirus/
- 6. Unhale SS, Bilal Q. A review on corona virus (COVID 19). Int J of Pharmaceutical and Life Sci., 2020; 6: 109-115.
- 7. Chan-Yeung M, Xu RH. SARS: epidemiology. Respirology, 2003; 8: S9–S14.
- 8. Middle East Respiratory Syndrome Coronavirus. Available at: https://www.who.int/emergencies/mers-cov/en/.
- 9. Richman DD, Whitley RJ, Hayden FG (Eds.). Clinical virology. John Wiley & Sons, 2016.
- 10. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol., 2015; 1282: 1–23.
- 11. Gorbalenya A, Enjuanes L, Ziebuhr J, Snijder E. Nidovirales: evolving the largest RNA virus genome. Virus Res., 2006; 117(1): 17–37.
- 12. Nakagawa K, Lokugamage KG, Makino S. Advances in Virus Research. Editor-John Ziebuhr, 2016; 96: 165–192.
- 13. Fan Y, Zhao K, Shi ZL, Zhou P. Bat coronaviruses in China. Viruses, 2019; 11(3): 210.
- 14. Zhou P, Yang XL, Wang XG, Ben Hu, Zhang L, Zhang W, *et al.* A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature, 2020; 579(7798): 270-273.
- 15. Perlman S, Netland J. Coronaviruses post-SARS: update on replication and pathogenesis. Nat Rev Microbiol, 2009; 7(6): 439–450.
- 16. Weiss S, Leibowitz J. Coronavirus pathogenesis. Adv Virus Res., 2011; 81: 85–164.
- 17. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. Respirology, 2018; 23(2): 130–137.
- 18. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, *et al*. A new coronavirus associated with human respiratory disease in China, Nature, 2020; 579: 265-269.

- 19. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, *et al.* SARSCoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med., 2020; 382(12): 1177–1179.
- 20. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents. J Hosp Infect, 2020; 104(3): 246-251.
- 21. Cheng ZJ, Shan J. 2019 novel coronavirus: where we are and what we know. Infection, 2020; 48(2): 155-163.
- 22. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA., 2020.
- 23. Wan Y, Shang J, Graham R, *et al.* Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS. J Virol, 2020; 94(7): e00127- 20.
- 24. Hoffmann M, Kleine-Weber H, Schroeder S, *et al.* SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell., 2020; 181: 271-280.
- 25. Sims AC, Baric RS, Yount B, *et al.* Severe acute respiratory syndrome coronavirus infection of human ciliated airway epithelia: role of ciliated cells in viral spread in the conducting airways of the lungs. J Virol, 2005; 79: 15511–15524.
- 26. Qian Z, Travanty EA, Oko L, *et al*. Innate immune response of human alveolar type II cells infected with severe acute respiratory syndrome-coronavirus. Am J Respir Cell Mol Biol., 2013; 48: 742–748.
- 27. Wang J, Nikrad MP, Phang T, *et al.* Innate immune response to influenza A virus in differentiated human alveolar type II cells. Am J Respir Cell Mol Biol., 2011; 45: 582–591.
- 28. Mossel EC, Wang J, Jeffers S, *et al.* SARS-CoV replicates in primary human alveolar type II cell cultures but not in type I-like cells. Virology, 2008; 372: 127–135.
- 29. Weinheimer VK, Becher A, Tonnies M, *et al.* Influenza A viruses target type II pneumocytes in the human lung. J Infect Dis., 2012; 206: 1685–1694.
- 30. Gu J, Korteweg C. Pathology and pathogenesis of severe acute respiratory syndrome. Am J Pathol, 2007; 170: 1136–1147.
- 31. Xu Z, Shi L, Wang Y, *et al.* Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med., 2020; 8: 420–422.
- 32. Ho JC, Chan KN, Hu WH, et al. The effect of aging on nasal mucociliary clearance, beat

- frequency, and ultrastructure of respiratory cilia. Am J Respir Crit Care Med., 2001; 163: 983–988.
- 33. Jeffers SA, Tusell SM, Gillim-Ross L, *et al.* CD209L (L-SIGN) is a receptor for severe acute respiratory syndrome coronavirus. Proc Natl Acad Sci USA., 2004; 101: 15748–15753.
- 34. Q Li, X Guan, P Wu, X Wang, L Zhou, Y Tong, *et al.*, Early transmission dynamics in Wuhan, China of novel coronavirus-infected pneumonia, N Engl J Med., 2020; 382: 1199-1207.
- 35. W Wang, J Tang, F Wei. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. J Med Virol., 2020; 94: 441–447.
- 36. LL Ren, YM Wang, ZQ Wu, ZC Xiang, L Guo, T Xu, *et al.* Identification of anovel coronavirus causing severe pneumonia in human: a descriptive study. Chinese Med J., 2020; 133: 1015-1024.
- 37. C Huang, Y Wang, X Li, L Ren, J Zhao, Y Hu, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet., 2020; 395: 497–506.
- 38. WG Carlos, CS Delacruz, B Cao, S Pasnick, S Jamil. Novel Wuhan (2019-nCoV) coronavirus. Am J Respir Crit Care Med., 2020; 201: 7–8.
- 39. N Lee, D Hui, A Wu, P Chan, P Cameron, GM Joynt, *et al.* A major outbreak of severe acute respiratory syndrome in Hong Kong. N Engl J Med., 2003; 348: 1986–1994.
- 40. LT Phan, TV Nguyen, QC Luong, TV Nguyen, HT Nguyen, HQ Le, *et al.* Importation and human-to-human transmission of a novel coronavirus in Vietnam. N Engl J Med., 2020; 382: 872-874.
- 41. Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. J Med Virol, 2020.
- 42. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Napoli RD: Features, Evaluation and treatment Coronavirus (COVID-19). Treasure Island (FL): Stat Pearls Publishing, 2020.
- 43. Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R, *et al.* Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. World J Pediatr, 2020.
- 44. Dong X, Cao YY, Lu XX, Zhang JJ, Du H, Yan YQ, *et al.* Eleven Faces of Coronavirus Disease 2019. *Allergy.*, 2020.
- 45. Interim guidelines for collecting, handling, and testing clinical specimens from persons under investigation (PUIs) for coronavirus disease 2019 (COVID-19). Available from:

- https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html.
- 46. https://www.cdc.gov/coronavirus/2019-ncov/lab/rt-pcr-panel-primer-probes.html
- 47. Huang P, Liu T, Huang L, *et al.* Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology, 2020; 295: 22-23.
- 48. A Bernheim, X Mei, M Huang, Y Yang, ZA fayad, *et al.* Chest CT findings in Coronavirus disease 2019 (COVID-19). Radiology, 2020; 295: 685-691.
- 49. Wang H, Wang S, Yu K. COVID-19 infection epidemic: The medical management strategies in Heilongjiang Province, China. Crit Care, 2020; 241: 07.
- 50. Chan KW, Wong VT, Tang SC. COVID-19: An update on the epidemiological, clinical, preventive and therapeutic evidence and guidelines of integrative Chinese-Western medicine for the management of 2019 novel coronavirus disease. Am J Chin Med., 2020; 13: 1–26.
- 51. Chinese Association of Rehabilitation Medicine; Respiratory rehabilitation committee of Chinese Association of Rehabilitation Medicine; Cardiopulmonary rehabilitation group of Chinese society of physical medicine and rehabilitation. Zhonghua Jie He Hu Xi Za Zhi., 2020; 43: 308-314.
- 52. Wang M, Cao R, Zhang L, *et al*. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell research, 2020; 30(3): 269-271.
- 53. Chan JF, Yao Y, Yeung ML, Deng W, Bao L, Jia L, *et al.* Treatment with Lopinavir/Ritonavir or interferon-β1b improves outcome of MERS-CoV infection in a nonhuman primate model of common marmoset. J Infect Dis., 2015; 212(12): 1904–1913.
- 54. Lim J, Jeon S, Shin HY, Kim MJ, Seong YM, Lee WJ, *et al.* Case of the Index Patient Who Caused Tertiary Transmission of COVID-19 Infection in Korea: The Application of Lopinavir/Ritonavir for the Treatment of COVID-19 Infected Pneumonia Monitored by Quantitative RT-PCR. J Korean Med Sci., 2020; 35(6): e79.
- 55. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Bioscience trends, 2020; 14: 72-73.
- 56. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, *et al*. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak an update on the status. Mil Med Res., 2020; 7: 11.
- 57. Kotch C, Barrett D, Teachey DT. Tocilizumab for the treatment of chimeric antigen receptor T cell-induced cytokine release syndrome. Expert review of clinical immunology,

- 2019; 15(8): 813822.
- 58. National Health Commission (NHC) of the People's Republic of China. The diagnosis and treatment guide of COVID-19 pneumonia caused by new coronavirus infection. 2020; 7. Translanted to English.
- 59. Furata Y, Komeno T, Nakamura T. Favipiravir (T705), a broad spectrum inhibitor of viral RNA polymerase. Proc Jpn Acad Ser B Phys Biol Sci., 2017; 93(7): 449–463.
- 60. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, Cleary P, Khaw FM, Lim WS, Makki S, Rooney KD, NguyenVan-Tam JS, Beck CR. Convalescent Plasma Study Group. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. J Infect Dis., 2015; 211: 80-90.
- 61. Soo YO, Cheng Y, Wong R, Hui DS, Lee CK, Tsang KK, Ng MH, Chan P, Cheng G, Sung JJ. Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients. Clin Microbiol Infect, 2004; 10: 676-678.
- 62. Lim CC, Tan CS, Kaushik M, Tan HK. Initiating acute dialysis at earlier Acute Kidney Injury Network stage in critically ill patients without traditional indications does not improve outcome: a prospective cohort study. Nephrology (Carlton), 2015; 20: 148-154.
- 63. WHO Coronavirus disease (COVID-19) advice for the public. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public
- 64. How to Protect Yourself, Coronavirus Disease 2019 (COVID-Coronavirus Disease 2019 (COVID-19)19), Centre for disease control and prevention. https://www.cdc.gov/coronavirus/2019-ncov/prepare/prevention.html
- 65. COVID-19, Occupational Safety and Health Administration, United State Department of labor, https://www.osha.gov/ SLTC/covid-19/controlprevention.html