**Title: COVID-19: A Conundrum to Decipher**

**Authors: Vishwajit Deshmukh[1†], Satyendra Chandra Tripathi[2†*], Arvind Pandey[3], Vaishnavi Deshmukh[4], Ashlesh Patil[5], Bharat Sontakke[1]**

[1]Department of Anatomy, [2]Biochemistry, [4]Physiology, All India Institute of Medical Sciences, Nagpur, Maharashtra, India

[4]Department of Microbiology, All India Institute of Medical Sciences, Bhubaneswar, Orrisa, India

[3]Department of Neurosurgery Research, Houston Methodist Centre, Houston, Texas, USA

[†]Contributed equally

[*]Corresponding Author: Satyendra Chandra Tripathi **(**sctripathi@aiimsnagpur.edu.in)

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**Abstract**

**OBJECTIVE:** Recent outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), another member of coronavirus family is an ongoing worldwide life-threatening crisis. The early diagnosis and management of the disease remains a major challenge. In this review, we aim to summarize the updated epidemiology, causes, clinical manifestation and diagnosis, as well as prevention and control of the novel coronavirus SARS-CoV-2.

**MATERIALS AND METHODS:** A broad search of the literature was performed in "PubMed" "Medline" "Web of knowledge", and "Google Scholar" World Health Organization-WHO" using the key words "severe acute respiratory syndrome coronavirus", "SARS", "SARS-CoV-2" "Epidemiology" "Transmission" "Pathogenesis" "Clinical Characteristics". We reviewed and documented the information attained from literature on epidemiology, pathogenesis and clinical appearances of SARS-CoV-2 infection.

**RESULTS:** The global cases of COVID-19 till 30$^{th}$ March 2020 have rose more than 700,000 and morbidity has gone more than 37,000. The infection rate for COVID-19 has been predicted to be higher than the previous outbreaks of same family members, that includes the SARS-CoV and Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The main clinical presentation ranges from asymptomatic stages to

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severe lower respiratory infection in the form of pneumonia. Most of the patients also presented with fever, cough, sore throat, headache, fatigue, myalgia and breathlessness. High risk includes elderly people and patients with weak immune system or suffering from chronic medical condition like hypertension, diabetes, cancer, respiratory illness and cardiovascular diseases.

**CONCLUSIONS:** SARS-Cov-2 has emerged as a worldwide threat, affecting almost each and every country on globe. As there is still growing understanding of SARS-CoV-2 in relation to its virology, epidemiology and clinical management strategies, we need to learn our lessons to conceive comprehensive measures to prevent such outbreaks in future.

## 1. Introduction: -

The recent outbreak of novel coronavirus is of grave international concern. Although zoonotic in its origin, an evolved strain of coronavirus can be fatal for humans. So far SARS-CoV, MERS-CoV were the recognized coronavirus, which caused detrimental effects on humans. Recently identified Novel Coronavirus (2019-nCoV or SARS-Co-V-2) is the seventh coronavirus known to infect humans [1]. The origin of the 2019-nCoV was in the Wuhan City of Hubei Province of China, which now has spread over to the rest of the world.

Majority of the patients in local hospitals of China presented with the severe infection of the lower respiratory track in the form of pneumonia of unknown etiology [2]. Many of these patients were confronted to the Huanan seafood market in Wuhan City, known to have lot of exotic live animals and their parts. It is suspected that coronavirus must have cross over from this market to humans. On December 31$^{st}$ 2019, China notified World health organization about the outbreak of virus and soon after the seafood market was closed [2]. On 7$^{th}$ January, the infected organism was identified as a strain of corona virus with >95% homology to bat coronavirus and > 70% similarity with SARS-CoV-1. (Figure 1) Although, origin of COVID-19 has been postulated from bat coronavirus, still the intermediary carrier from which it has crossed over to humans is uncertain. Current suspects as intermediary carrier for transmission of this virus to human includes pangolins and snakes. Series of events for progression of COVID-19 [3] to become a pandemic are shown in figure 1.

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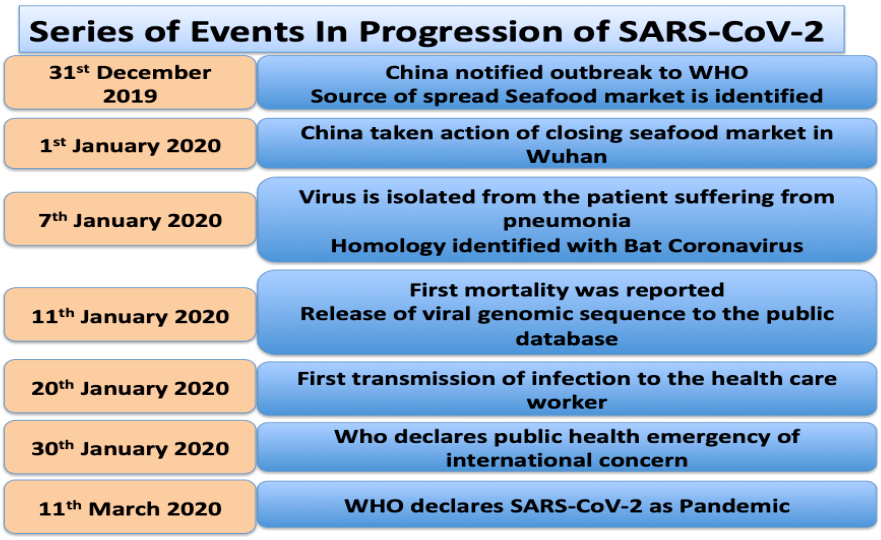


**Figure 1: - Series of events in progression of COVID-19**

Many patients were put under surveillance with similar complications of severe respiratory distress and an exponential increase in number of cases was reported thereafter. Modeling studies had reported 1.8 days for the epidemic doubling [4]. It was identified that the people who were not exposed to the seafood market also presented with similar type of symptoms, raising doubt about transmission of the virus via human-to-human contact [5]. Constant surveillance is necessary to contain the human-to-human transmission, which can increase the chances of viral genome mutation making it more virulent in nature. The outbreak has spread substantial to in most of the countries all over the world to infect > 700,000 people including >37,000 deaths up to March 30, 2020 (Figure 2).

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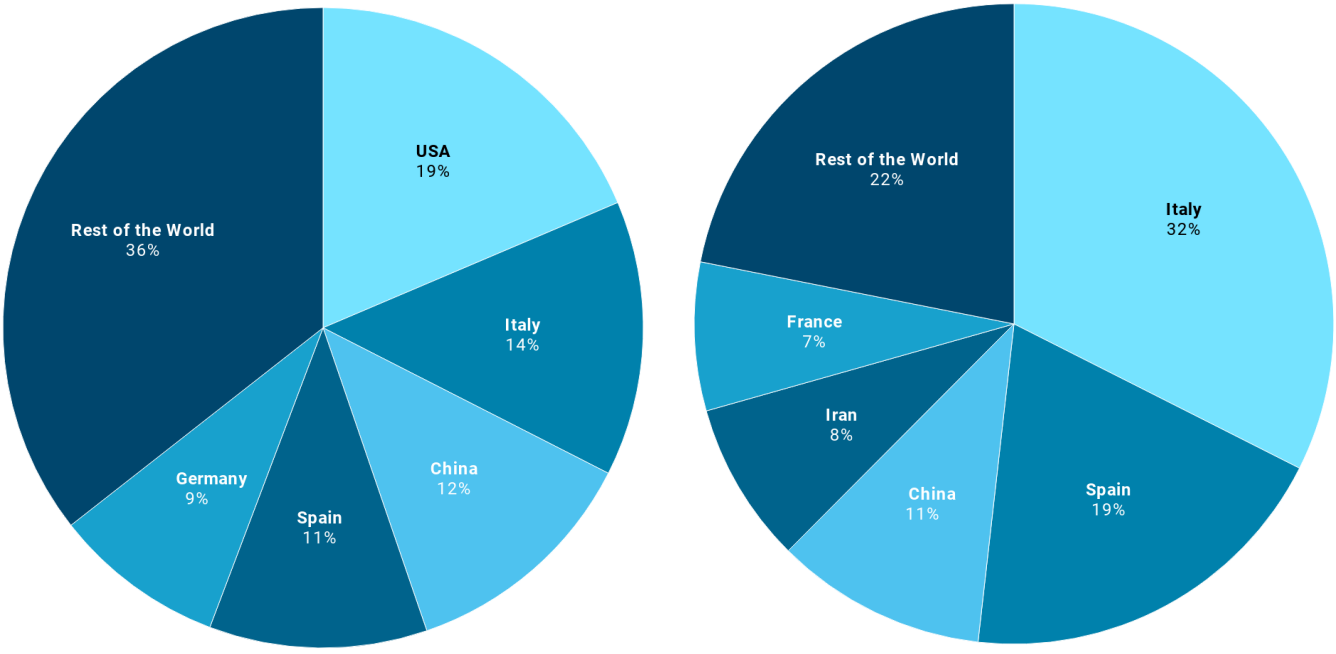


**Figure 2: - Global distribution of Positive cases and death due to COVID-19.**

## 2. Basic reproductive number (Ro) of SARS-CoV-2: -

Basic reproductive number is average number of secondary cases produced by one infected individual introduced into population of susceptible individuals, where an infected individual has acquired the disease, and susceptible individuals are healthy but can acquire the disease. Here, in relation to COVID-19 cases, it will be difficult to precisely estimate the BRN for the SARS-CoV-2, as it is difficult to identify exact number of infected cases during the epidemic. The other factors affecting the BRN are environmental circumstances, demography and statistical methodologies. So far, the estimated $R_0$ for SARS-CoV-2 has been estimated of 2.4 – 3.58 days in comparison to other deadly viruses (Table 1).

**Table 1: - Basic reproductive number for various viruses.**

| Sr No | Disease | Year | Ro |
|---|---|---|---|
| 1 | Small pox [6] | 1968-1973 | 3.5-6 |
| 2 | SARS [7] | 2002-2003 | 2-5 |
| 3 | H1N1 [8] | 2009 | 1.3-1.7 |
| 4 | MERS [9] | 2012 | 2.7- 3.9 |
| 5 | Ebola haemorrhagic fever [10] | 2014 | 1.5-2.5 |
| 6 | Novel Coronavirus [11] | 2019-2020 | 2.4-3.58 |

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## 3. Structure of the SARS-CoV-2: -

Coronavirus family was initially discovered in 1960s. They were classified under the family coronaviridae, which is the largest family within the order Nidovirales. Family coronaviridae includes two subfamilies: Orthocoronavirinae and Torovirinae. Orthocoronavirinae encompasses four genera; alpha, beta, gamma and delta coronavirus[12].

Corona virus are spherical, enveloped (lipid bilayer derived from the host cell membrane) positive sense single-stranded RNA viruses ranging from 60nm to 140nm in diameter with spikes like projection on its surface giving it a crown like appearance under the electronmicrosopic examination [13]. The major factor in the structure of the corona virus is the presence of spikes on the surface containing glycoprotein, which attaches to the host cell membrane, and is hypothesized to play a major role in order to enter the host cell. The CoV spike glycoprotein is a key target for vaccine, therapeutics and diagnostics. The spread of corona virus infection to humans is mainly achieved by the domestic animals with modified genomic recombination. While the recently identified SARS-CoV infects the type 2 pneumocytes and non-ciliated bronchial epithelial cells and uses the angiotensin converting enzyme 2 as a receptor to cause the effects [14].

Previous to the onset of SARS-CoV-2, two such incidences were reported where the transmission of the animal viruses to the human caused severe disease and mortality. The first instance was in 2002-2003 when the B-coronavirus, which was originated in bats, crossed over to humans via the palm civet cats in the Guangdong province of China. It was designated as SARS-Co-V-1 and almost affected majority of population with mortality rate of around 11% before being contained [15]. After a decade in 2012, another outbreak of corona virus with Bat origin (MERS-CoV) emerged in Middle East and affected more than 200 peoples with approximately 34% of mortality rate [16]. The identified receptor for the MERS-CoV is depeptidyl peptidase 4 (DPP4), a transmembrane glycoprotein and also affects type 2 pneumocytes and non-ciliated bronchial epithelial cells [17].

## 4. Comparison of various coronavirus infective to humans: -

Till date, only seven coronaviruses were identified to infect human via zoonotic transmission. SARS-CoV-1 MERS-CoV, SARS-CoV-2 can cause severe respiratory

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diseases in human while others such asHKU1, NL63, OC43, 229E were associated with mild symptoms [18]. Human infection from coronavirus revealed that the transmission of the virus is through bats, which acts as a primary host for the virus. SARS-CoV-1 has been identified to act on ACE 2 Receptors present in lungs causing respiratory symptoms. The intermediate hosts in the SARS-CoV-1 were identified as Civets and raccon dogs [19]. MERS-CoV acts on human DPP4 (CD26) with similar primary host as SARS-CoV-1 but the intermediate hosts were identified as camels in the Middle East part of the world [17]. The current SARS-CoV-2, not surprisingly also acts probably on the ACE2 receptors causing severe respiratory distress and pneumonia. The SARS-CoV-2 binds to the ACE 2 receptors with high affinity as compared to the SARS-CoV-1. With humans as terminal host, the primary host for SARS-CoV-2 again was identified as bat and suspected intermediate host incudes pangolins and snakes (Figure 3) [2]. The incubation period identified for the entire human infection-causing viral group is from 2-14 days. Therefore at least 14 days of quarantine is mandatory for avoiding the transmission. The mode of transmission is through the large droplets generated during coughing and sneezing. But the fatality rate for the current SARS-CoV-2 (3-4%) is fortunately less as compared to SARS-CoV-1 (10%) and MERS-CoV (approx. 35%) [20]. However, new cases have been added every day, the fatality percentage may keep changing and will not be accurately calculated until the containment of the disease.

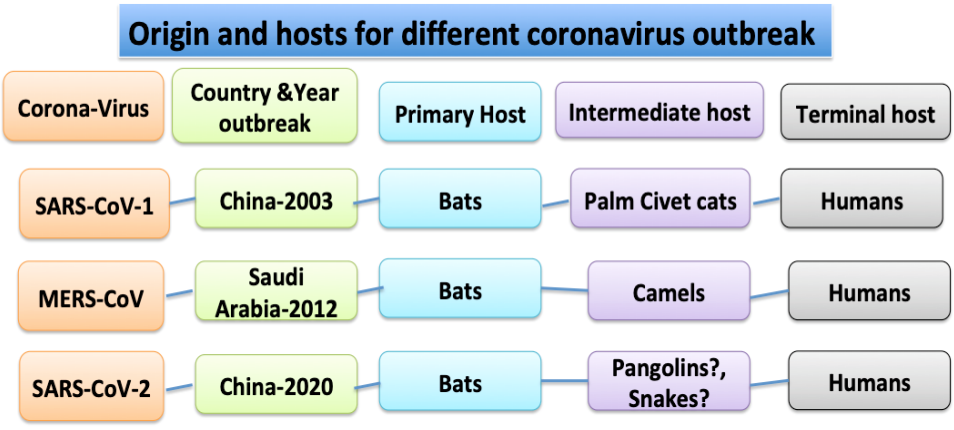


**Figure 3: - Origin and hosts of various Corona-viruses.**

## 5. Presenting features of COVID-19 patients: -

Individual of all ages are susceptible to the infection. Diseases in neonates, infants and children have also been reported but the disease is significantly milder as

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compared to adult counterpart. The infection and symptoms were significantly less in children below 12 years of age. Chances are there that in children more than 12 years the overall immune status is stronger than adults [21]. Vaccinations may play an important role in case of children, as they will be more updated with the vaccines, which may prevent them from other secondary infections often triggered by the primary infection [22].

Varied signs and symptoms were observed in patients infected with SARS-CoV-2. The presentation ranges from asymptomatic stages to severe lower respiratory infection in the form of pneumonia. Most of the patients presets with fever, cough, sore throat, headache, fatigue, myalgia and breathlessness [23]. Observations showed that most of the infected patients were progressing to pneumonia at the end of first week followed by respiratory failure and death. In many patient's recovery starts at the second or third week of infection. The positive patients for SARS-CoV-2 can be discharged from the hospital or discontinued from the quarantine based on the following criteria: -1. Normal body temperature lasting longer than 3 days, 2. Resolved respiratory symptoms, 3. Substantially improved acute exudative lesion on chest CT images, 4. Two consecutive negative RT-PCR test result separated by at least 1 day. Negative patients should be correlated with the history of contact, clinical observation and epidemiological information.

## 6. Primary Diagnosis for SARS-CoV-2: -

Diagnosis is based upon the suspicion of the patients depending upon the clinical features such as fever, sore throat, headache, fatigue, myalgia, respiratory distress and breathlessness. In suspected cases, specific molecular tests should be done on the respiratory samples collected from throat, nasopharynx, sputum, endotracheal aspirates and bronchoalveolar lavage in more critical patients [24]. The definitive diagnosis is based on the PCR analysis [25] of various type of samples from symptomatic patient such as:

- Throat swab , nasal swab- dacron or polyester swab transport to laboratory $4^0$ - in viral transport medium in cold chain , both the swab should placed in same tube to increase viral load
- Broncho-Alveolar lavage- collection in sterile container – transported to laboratory at $4^0$

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- Tracheal aspirate , nasal wash, nasopharyngeal aspirate- collection in sterile container- transported to laboratory at $4^0$
- Sputum - collection in sterile container- transported to laboratory at $4^0$
- Tissue / biopsy- sterile container with saline- transported to laboratory at $4^0$
- Serum 2 samples- 3 to 5 ml- transported to laboratory at $4^0$ - collect paired samples – acute- first week of illness, convalescent – 2 to 3 weeks later

Chest X-rays usually show bilateral infiltrates but findings may not be present in early stages of the infection. CT is more reliable, sensitive and specific investigation. CT images generally show infiltrates, ground glass opacities and subsegmental opacities. The current scenario is to perform the CT investigation for the diagnosis of COVID-19 in suspected cases with negative molecular results [26].

## 7. Emerging Challenges and Treatment strategies for the treatment of COVID-19 infection -

The exponential increase in cases of COVID-19 (SARS-CoV-2) infection, causing respiratory illness pose threat and challenges to global public health, medical and research communities all over the world. In the response to the outbreak, many affected countries have enforced travel restriction and lockdown to prevent further transmission of this disease. Many asymptomatic patients still can transmit and later become symptomatic for COVID-19 infection. Currently major challenge with COVID-19 infection is the treatment of patient with weak immune system (immune-compromised) and suffering from chronic medical condition like cancer, respiratory illness, cardiovascular diseases etc.

### 7.1 COVID-19 infection in hypertensive, diabetic and cardio-vascular disease patients-

Recent reports suggest higher risk of COVID-19 infection related mortality in-patient with hypertension, diabetes and cardio-vascular diseases. He XW et al. Conducted a study in 54 patients and reported highest mortality in patients with hypertension (44.4%), diabetes (24.1%) and coronary heart disease (14.8%)[27]. Another study from China confirmed the same on lager cohort consisting 191 patients and established that the risk factor for mortality was high in the patients with hypertension (30%), followed by diabetes (19%) and coronary heart disease (8%) [28]. In the third study related to morbidity of 140 cases of COVID-19 infections, 30% had

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hypertension and 12% had diabetes [29] . These reports indicate that severe or critically ill COVID-19 patients with any ailment like hypertension, diabetes and cardio-vascular disease have significantly higher risk of mortality and require special attention on their safety during hospitalization.

**7.2 COVID-19 infection during pregnancy-**

The pregnant woman is susceptible to severe illness after COVID-19 infection because of physiological changes in their immune and cardiopulmonary systems[30]. A report suggest that vertical transmission can be prevented by delivering an infant by cesarean section in a negative-pressure operating room [31]. Another study on 13 COVID-19 infected pregnant women showed that delivery in 38% women were done by emergency cesarean section due to pregnancy complications including fetal distress, premature rupture of the membrane and stillbirth. However, 46% women had preterm labor. These perinatal complications could be attributed to the virus infection as well as the physiologic changes that render the woman intolerant to hypoxia during late pregnancy. However, this study showed no severe neonatal asphyxia in the nine live births and no vertical transmission overall [32]. An analysis of 38 Pregnant Women with COVID-19 showed that unlike coronavirus SARS and MERS infections, these 38 pregnant women COVID-19 did not lead to maternal deaths and no report of intrauterine transmission of SARS-CoV-2 from COVID-19 infected mothers to their fetuses[33].

In a recent study, key recommendations were provided for the management of COVID-19 infections in pregnancy considering the optimal delivery timing, the safety of vaginal delivery or cesarean delivery to prevent vertical transmission at the time of delivery. As an initial management, women with confirmed COVID-19 infection should be admitted and isolated in an intensive care unit with negative pressure rooms. When possible, these women could have better uteroplacental oxygenation while lying in a lateral-decubitus position, regardless of the mother's respiratory status. The perinatal care could be managed by electronic fetal heart rate monitoring, lowering or early the delivery timing, mode of delivery in a negative pressure isolation ward and an appropriate disposal of placenta of pregnant women. Placenta from infected women should be considered as bio hazardous waste. A quick cord clamping for neonates from pregnant women is recommended and the neonate should be cleaned and dried immediately. To avoid further transmission of virus, women

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should use personal protection and should be in isolation until recover from delivery [34]. Overall, perinatal and neonatal management plan for prevention and control of 2019 novel coronavirus infection are need special consideration due to reduced immune function and possibility of mother-fetal vertical transmission [35].

**7.3 COVID-19 infection in patients undergoing transplantation**

Li et al. reported two microbiologically confirmed COVID-19 cases in heart transplantation detected in the Hubei province in China. These two patients presented with variable severity of disease (one mild and another with more severe manifestations requiring a prolonged hospitalization) however both patients survived after infection [36]. It is now evident that immunosuppressed patients may have higher risk to COVID-19 infection, which may apply to the patient undergoing transplantation. However, transplantation related immunosuppression effects on predisposition to acquire infection with COVID-19 are not known. In lieu of this, the American Society of Transplantation and the Transplantation Society have updated their factual information on COVID-19 and Transplantation [37].

**7.4 COVID-19 infection in patients with digestive disorders-**

In a descriptive, cross-sectional, multi-centric study on 204 patients with COVID-19 infection revealed that digestive disorder symptoms are common in admitted patients. The most common symptoms in these cases were lack of appetite (78.6%), diarrhea (34%), vomiting (3.9%), and abdominal pain (1.9%). However, lack of appetite was excluded from this study for further analysis. These patients also had evidence of longer coagulation, and higher liver enzyme levels. According to this report, in rare cases patient can even present with digestive symptoms in the absence of respiratory symptoms[38]. The mild to moderate liver injury including elevated aminotransferases, hypoproteinemia and prothrombin time prolongation has been reported in clinical investigations of COVID-19. However, there is no clear indication of COVID-19 infection in liver [39] .

**7.5 COVID-19 infection in cancer patients-**

Cancer patients are more susceptible to infection because of their immune-suppressive state caused by malignancy and anti-cancer treatment. An epidemiological study conducted in China during COVID-19 outbreak indicates that

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incidence was higher in-patient with cancer history compared to healthy Chinese population. Among the cancer patients, lung cancer was most frequent type to get infected with COVID-19 [40]. Strict protection to lung cancer patient is required because of difficulty to differentiate lung cancer patients with COVID-19 based on clinical symptoms. These bring the immediate attention to develop the individual clinical management for lung cancer patient during this COVID-19 outbreak [41] [42]. The immunotherapy treatment to lung cancer patients could be postpone for some time considering the potential pulmonary toxicity and adverse effects of lung injury from immunotherapy [43]. Recent report showed that two patients underwent for lung lobectomies for adenocarcinoma revealed apart from tumor it also showed early phase of the lung pathology of COVID-19 pneumonia [44]. Another report suggests continuing use of treatment for lung cancer patient with COVID-19 infection. As clinical management, an intensive care and CT scans were performed in case of pneumonia exacerbation and cancer progression [45].

Till date, there is no original research published showing treatment strategy hepatobiliary, gastrointestinal, colorectal, gynecological and breast malignancies during the outbreak of COVID19 rather discussion and suggestion on clinical management of cancer patient [46–52].

Overall strict safety measurement with standard care should be opted during diagnosis, treatment and follow-up treatment to avoid and minimize the change of COVID-19 infection to cancer patients. It is also necessary to arrange the online medical and psychological counseling after the first consultation between physician and patient. An alternative treatment strategy also required during this pandemic COVID-19 infection to well managed cancer patient needs.

### 7.6 Treatment Strategies for COVID-19

Angiotensin-converting enzyme II (ACE2) has been identified as most likely cell receptor for COVID-19 (SARS-CoV2) as same as found for SARS-CoV and HCoV-NL637 [53,54]. Another study suggests a strong interaction between COVID-19 spike protein and human ACE2 molecule [55], which plays an important role in cellular entry within ACE2 expressing cells. Zou et al identified the organs such as lung, heart, esophagus, kidney, bladder, and ileum, and located specific cell types (i.e., type II alveolar cells (AT2), myocardial cells, proximal tubule cells of the kidney, ileum and esophagus epithelial cells, and bladder urothelial cells that are vulnerable to

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COVID-19 infection [56]. ACE inhibitor has been shown to prompt more ACE2 receptor however there is no current evidence related to worsening of COVID-19 infection in human with ACE inhibitor. More detailed studies are required to assess the effect of ACE inhibitor on COVID-19 infection in human.

The researchers are currently developing the various vaccine candidates for clinical trials as well as therapeutics for lethal COVID-19. However, till date no effective vaccine and therapeutics have been approved for clinical use. Recent reports suggest that many healthcare professionals have tried various combination of previously approved antibiotics, anti-viral, anti-malarial and anti-HIV drug to treat the COVID-19 infected patients. A randomized trial of HIV anti-viral drug lopinavir–ritonavir combination on 199 patients with laboratory-confirmed SARS-CoV-2 infection showed no benefits beyond the standard care [57]. Some clinical trial in China has been initiated based on *in vitro* studies which revealed that anti-malarial drug, chloroquine can significantly reduce the viral replication of coronaviruses [58,59]. However, the safety and efficacy of this drug in relation to COVID19 treatment is still under investigation [60].

Currently, 20 active clinical trials have been registered against COVID-19 infections to study safety and efficacy of various drug and antibody combination (**Table 2**). In these 20 clinical trials various drugs and their combinations like Bromhexine Hydrochloride, Arbidol Hydrochloride, Recombinant Human Interferon 1b & 2b, Methylprednisolone, thymosin alpha 1, Bevacizumab, Fingolimod (0.5 mg), Remdesivir, Darunavir and Cobicistat, Nitric Oxide, Favipiravir combined with Tocilizumab, methylprednisolone, Lopinavir/ ritonavir and Ribavirin as well as many biological agent like Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector), mesenchymal stem cells, mRNA-1273, NK Cells are being tested on COVID-19 infected patients.

**7.7 Precautions to be taken to prevent the spread of COVID-19: -**

There is a great saying that “Prevention is always better than cure”. To prevent the spread of coronavirus international travelling should be limited or avoided if needed. The present SARS-CoV-2 is spreading through human-to-human contact via respiratory droplets that are produced during the sneezing or coughing of infected person. The droplets can spread up to 1-2 meters and gets them deposited on the surfaces. The virus can remain viable on the surface for days but can be easily

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destroyed by the alcohol-based hand rubs, sodium hypochlorite and hydrogen peroxide [61].

Prevention of COVID-19 is very much similar to the other respiratory infections, for example the foremost thing that can be done is to avoid the contact with any sick person. The person who is not affected should use N95 masks in a proper way to prevent any infection. Risk factor for using N95 is the presence of facial hairs, which will not guarantee protection as small droplets particles have the tendency to enter to cause disease more than large air droplets. The use of N95 respirators compared with surgical masks is not associated with a lower risk of laboratory-confirmed influenza. It suggests that N95 respirators should not be recommended for general public and no high-risk medical staff those are not in close contact with influenza patients or suspected patients [62].

Surgical masks can be used but with caution as they will not fit properly to seal the entry for droplets. As the virus is encapsulated one, washing of hands for more than 30 seconds could be beneficial for avoiding the transmission of disease. Lastly, the cleaning of day to day used areas such as door knobs, doors, objects etc. should be cleaned regularly to avoid transmission of infection.

## Conclusion

Currently, CoVID-19 is a life-threatening disease with no current treatment options. Due to lack of any vaccine or anti-viral therapy it poses a higher risk to aged and immune compromised population. It is essential to learn and incorporate the recent scientific knowledge into the current practice and clinical management of this disease to contain or slowdown the spread of SARS-CoV-2. Also, as future outbreaks of viruses and pathogens are inevitable, we need to devise comprehensive measures to prevent and manage such public health emergency.

## Conflict of Interest

The Authors declare that they have no conflict of interests.

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Table 2: Ongoing clinical trials for treatment of COVID-19 patient (Clinicaltrials.gov)

**ClinicalTrials.gov (Search Results 03/24/2020)**

| | NCT Number | Title | Status | Conditions | Interventions | Study type/ Phase | Population | Sponsor/ Collaborators | Funder Type | Dates | Location |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **NCT 04273763** | Evaluating the Efficacy and Safety of Bromhexine Hydrochloride Tablets Combined with Standard Treatment/ Standard Treatment in Patients with Suspected and Mild Novel Coronavirus Pneumonia (COVID-19) | Enrolling by invitation | •Novel Coronavirus Pneumonia 2019-nCoV | •Drug: Bromhexine Hydrochloride Tablets<br>•Drug: Arbidol Hydrochloride Granules<br>•Drug: Recombinant Human Interferon #2b Spray | Study Type: Interventional<br>Phase: Not Applicable | Enrollment: 60<br>Age: 18 Years to 80 Years (Adult, _Older Adult)<br>Sex: All | •Second Affiliated Hospital of Wenzhou Medical University<br>•WanBangDe Pharmaceutical Group Co.,Ltd. | •Other | Study Start: February 16, 2020.<br>Study Completion: April 30, 2020<br>Results Posted: No Results | China |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | **NCT 04252118** | Mesenchymal Stem Cell Treatment for Pneumonia Patients Infected With 2 019 Novel Coronavirus | Recruiting | 2019 Novel Coronavirus Pneumonia | •Biological: MSCs | Study Type: Interventional Phase: Phase 1 | Enrollment: 20 Age: 18 Years to 70 Years (Adult, Older Adult) Sex: All | •Beijing 302 Hospital. •Wuhan Huoshenshan Hospital, Wuhan, China. •Innovative Precision Medicine Group (IPM), Hangzhou, China. •Tianjin Haihe Hospital. •Shenzhen Third People's Hospital. •Fifth Affiliated Hospital, Sun Yat-Sen University | •Other | Study Start: January 27, 2020. Study Completion : December 2021 Results Posted: No Results | Beijing, China |
| 3 | **NCT 04273321** | Efficacy and Safety of Corticosteroids in COV ID-19 | Recruiting | •COVID-19 •Novel Coronavirus Pneumonia | •Drug: Methylprednisolone | Study Type: Interventional Phase: Not Applicable | Enrollment: 400 Age: 18 Years and older (Adult, Older Adult) Sex: All | •Beijing Chao Yang Hospital | •Other | Study Start: February 14, 2020. Study Completion : May 30, 2020 Results Posted: No Results | Wuhan, Hubei, China. |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 4 | **NCT 04313127** | A Phase I Clinical Trial in 18-60 Adults | Recruiting | •COVID-19 | •Biological: Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) | Study Type: Interventional<br><br>Phase: Phase 1 | Enrollment: 108<br><br>Age: 18 Years to 60 Years (Adult)<br><br>Sex: All | •CanSino Biologics Inc. •Institute of Biotechnology, Academy of Military Medical Sciences. PLA of China. •Jiangsu Province Centers for Disease Control and Prevention •Hubei Provincial Center for Disease Control and Prevention. •Tongji Hospital | Industry •Other | Study Start: March 16, 2020. Study Completion : December 20, 2022 Results Posted: No Results | Wuhan, Hubei, China |
| 5 | **NCT 04320238** | Experimental Trial of rhIFN# Nasal Drops to Prevent 2019 nCOV in Medical Staff | Recruiting | 2019 Novel Coronavirus Infection | •Drug: recombinant human interferon Alpha-1b. •Drug: thymosin alpha 1 | Study Type: Interventional<br><br>Phase: Phase 3 | Enrollment: 2944 Age: 18 Years to 65 Years (Adult, Older Adult) Sex: All | •Shanghai Jiao Tong University School of Medicine | •Other | Study Start: January 21, 2020 Study Completion : June 2020 Results Posted: No Results | Hubei, China |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 6 | **NCT 04269525** | Umbilical Cord (UC)-Derived Mesenchymal Stem Cells (MSCs) Treatment for the 2019-novel Coronavirus (nCOV) Pneumonia | Recruiting | •Pneumonia, Viral •Pneumonia, Ventilator-Associated | •Biological: UC- MSCs | Study Type: Interventional Phase: Phase 2 | Enrollment: 10 Age: 18 Years to 75 Years (Adult, Older Adult) Sex: All | •ZhiYong Peng •Tuohua Biological Technology Co. Ltd. •Zhongnan Hospital | •Other | Study Start: February 6, 2020. Study Completion :September 30, 2020 Results Posted: No Results | Wuhan, Hubei, China |
| 7 | **NCT 04305106** | Bevacizumab in Severe or Critically Severe Patients With COVID-19 Pneumonia-RCT | Recruiting | •COVID-19 Pneumonia | •Drug: Bevacizumab | Study Type: Interventional Phase: Not Applicable | Enrollment: 118 Age: 18 Years to 80 Years (Adult, Older Adult) Sex: All | •Qilu Hospital of Shandong University •Renmin Hospital of Wuhan University •Italy Moriggia Pelascini Gravedona Hospital S.p.A. •Wuhan University. •Jiangbei Union Hospital of Huazhong University of science and technology •Shandong Provincial Chest Hospital | •Other | Study Start: March 17, 2020. Study Completion : July 31, 2020 Results Posted: No Results | Jinan, Shandong, China |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 8 | **NCT 04280588** | Fingolimod in COVID-19 | Recruiting | •Coronavirus Disease (COVID-19) | •Drug: Fingolimod 0.5 mg | Study Type: Interventional Phase: Phase 2 | Enrollment: 30 Age: 18 Years to 80 Years (Adult, Older Adult) Sex: All | •First Affiliated Hospital of Fujian Medical University | •Other | Study Start: February 22, 2020 Study Completion: July 1, 2020 Results Posted: No Results | Fuzhou, China |
| 9 | **NCT 04252664** | Mild/Moderate 2019-nCoV Remdesivir RCT | Recruiting | • 2019-nCoV | •Drug: Remdesivir •Drug: Remdesivir placebo | Study Type: Interventional Phase: Phase 3 | Enrollment: 308 Age: 18 Years and older (Adult, Older Adult) Sex: All | •Capital Medical University •Chinese Academy of Medical Sciences | •Other | Study Start: February 12, 2020 Study Completion: April 27, 2020 Results Posted: No Results | Wu Han, Hubei, China |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 | **NCT 04283461** | Safety and Immunogenicity Study of 2019-nCoV Vaccine (mRNA-1273) to Prevent SARS-CoV-2 Infection | Recruiting | •Corona Virus Infection | •Biological: mRNA-1273 | Study Type: Interventional Phase: Phase 1 | Enrollment: 45 Age: 18 Years to 55 Years (Adult) Sex: All | •National Institute of Allergy and Infectious Diseases (NIAID) | •NIH | Study Start: March 3, 2020. Study Completion: June 1, 2021 Results Posted: No Results | Georgia, United States. Seattle, Washington, United States |
| 11 | **NCT 04252274** | Efficacy and Safety of Darunavir and Cobicistat for Treatment of Pneumonia Caused by 2019- nCoV | Recruiting | •Pneumonia, Pneumocystis •Coronavirus | •Drug: Darunavir and Cobicistat | Study Type: Interventional Phase: Phase 3 | Enrollment: 30 Age: Child, Adult, Older Adult Sex: All | •Shanghai Public Health Clinical Center | •Other | Study Start: January 30, 2020. Study Completion: December 31, 2020 Results Posted: No Results | Shanghai, China |
| 12 | **NCT 04257656** | Severe 2019-nCoV Remdesivir RCT | Recruiting | • 2019-nCov •Remdesivir | •Drug: Remdesivir •Drug: Remdesivir placebo | Study Type: Interventional Phase: Phase 3 | Enrollment: 453 Age: 18 Years and older (Adult, | •Capital Medical University | •Other | Study Start: February 6, 2020 Study Completion: May 1, | Beijing, China |

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| | | | | | | | Older Adult) Sex: All | | | 2020 Results Posted: No Results | |
| 13 | **NCT 04280224** | NK Cells Treatment for Novel Coronavirus Pneumonia | Recruiting | •Novel Coronavirus Pneumonia | •Biological: NK Cells | Study Type: Interventional Phase: Phase 1 | Enrollment: 30 Age: 18 Years to 65 Years (Adult, Older Adult) Sex: All | •Xinxiang medical university. •First Affiliated Hospital of Xinjiang Medical University | •Other | Study Start: February 20, 2020. Study Completion : December 30, 2020 Results Posted: No Results | Henan, China |
| 14 | **NCT 04305457** | Nitric Oxide Gas Inhalation Therapy for Mild/Moderate COVID-19 | Recruiting | •Coronavirus Infections •Pneumonia, Viral •Acute Respiratory Distress Syndrome | •Drug: Nitric Oxide | Study Type: Interventional Phase: Phase 2 | Enrollment: 240 Age: 18 Years and older (Adult, Older Adult) Sex: All | •Massachusetts General Hospital •Xijing Hospital •Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico | •Other | Study Start: March 21, 2020. Study Completion : April 1, 2022 Results Posted: No Results | Boston, Massachusetts, United States |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 15 | **NCT 04264533** | Vitamin C Infusion for the Treatment of Severe 20 19-nCoV Infected Pneumonia | Recruiting | •Vitamin C •Pneumonia, Viral •Pneumonia, Ventilator-Associated | •Drug: VC •Drug: Sterile Water for Injection | Study Type: Interventional Phase: Phase 2 | Enrollment: 140 Age: 18 Years and older (Adult, Older Adult) Sex: All | •ZhiYong Peng •Zhongnan Hospital | •Other | Study Start: February 14, 2020. Study Completion :September 30, 2020 Results Posted: No Results | Wuhan, Hubei, China |
| 16 | **NCT 04306393** | Nitric Oxide Gas Inhalation in Severe Acute Respiratory Syndrome in COVID-19 | Recruiting | •SARS (Severe Acute Respiratory Syndrome) •Coronavirus | •Drug: Nitric Oxide Gas | Study Type: Interventional Phase: Phase 2 | Enrollment: 200 Age: 18 Years to 99 Years (Adult, Older Adult) Sex: All | •Massachusetts General Hospital •Xijing Hospital •Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico •Niguarda Hospital | •Other | Study Start: March 21, 2020. Study Completion : March 21, 2022 Results Posted: No Results | Boston, Massachus etts, United States |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 17 | **NCT04310228** | Favipiravir Combined with Tocilizumab in the Treatment of Corona Virus Disease 2019 | Recruiting | •COVID-19 | •Drug: Favipiravir Combined with Tocilizumab •Drug: Favipiravir •Drug: Tocilizumab | Study Type: Interventional Phase: Not Applicable | Enrollment: 150 Age: 18 Years to 65 Years (Adult, Older Adult) Sex: All | •Peking University First Hospital | •Other | Study Start: March 8, 2020. Study Completion: May 2020 Results Posted: No Results | Hefei, Anhui, China. Beijing, China. Wuhan, Hubei, China. |
| 18 | **NCT04244591** | Glucocorticoid Therapy for Novel Coronavirus Critically Ill Patients with Severe Acute Respiratory Failure | Recruiting | •Coronavirus Infections •Respiratory Infection Virus | •Drug: methylprednisolone therapy. •Other: Standard care | Study Type: Interventional Phase: •Phase 2 •Phase 3 | Enrollment: 80 Age: 18 Years and older (Adult, Older Adult) Sex: All | •Peking Union Medical College Hospital. •Zhongda Hospital. •Zhongnan Hospital. •Renmin Hospital of Wuhan University. | •Other | Study Start: January 26, 2020. Study Completion: December 25, 2020 Results Posted: No Results | Beijing, China |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | **NCT 04276688** | Lopinavir/ Ritonavir, Ribavirin and IFN-beta Combination for nCoV Treatment | Recruiting | •Novel Coronavirus Infection | •Drug: Lopinavir/ ritonavir<br>•Drug: Ribavirin<br>•Drug: Interferon Beta-1B | Study Type: Interventional<br>Phase: Phase 2 | Enrollment: 70<br>Age: 18 Years and older (Adult, Older Adult)<br>Sex: All | •The University of Hong Kong<br>•Hospital Authority, Hong Kong | •Other | Study Start: February 10, 2020.<br>Study Completion: July 31, 2022<br>Results Posted: No Results | Hong Kong |
| 20 | **NCT 04280705** | Adaptive COVID-19 Treatment Trial (ACTT) | Recruiting | •Corona Virus Infection | •Other: Placebo<br>•Drug: Remdesivir | Study Type: Interventional<br>Phase: Phase 3 | Enrollment: 440<br>Age: 18 Years to 99 Years (Adult, Older Adult)<br>Sex: All | •National Institute of Allergy and Infectious Diseases (NIAID) | •NIH | Study Start: February 21, 2020<br>Study Completion: April 1, 2023<br>Results Posted: No Results | Alabama, United States. California, United States. Denver, Colorado, United States. •and 27 more |