

# Novel Coronavirus COVID-19 and Its Diagnosis and Treatments

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**Abstract** Recently, at the end of 2019 in Wuhan, China found a novel flu like Corona virus (COVID-related to the severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory syndrome (MERS) in 2012 and so many cases it confirmed that, it transmitted through human-to-human and spread all over world. There is no proper medicine and vaccine on this novel coronavirus COVID-19. The Economy of so many countries going on declined state due to this novel coronavirus COVID-19. It is challenge to scientists to find out actual medicine and vaccine on this novel coronavirus COVID-19. The present review is an attempt made in the respect of highlighting the some important information regarding detection and treatments on Novel coronavirus COVID-19.

**Keywords:** Coronavirus, COVID-19, SARS, MERS

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## 1. Introduction

Recently, at the end of 2019 in Wuhan, China found a novel flu like Corona virus (COVID-19) related to the severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory syndrome (MERS) in 2012. [1,2] and so many cases it confirmed that, it transmitted through human-to-human. [3] Coronaviruses belongs to subfamily Orthocoronavirinae in the family of Coronaviridae in the order Nidovirales. The Orthocoronavirinae subfamily also include Alpha- coronavirus, Beta- coronavirus, Gamma- coronavirus and Delta- coronavirus. [4,5] Severe acute respiratory syndrome-CoV (SARS-CoV) and Middle East respiratory syndrome CoV (MERS-CoV) all belong to the  $\beta$ -coronavirus family. [6] COVID-19 is a novel human coronavirus in addition to coronavirus 229E, NL63, OC43, HKU1, Middle East respiratory syndrome-related coronavirus (MERS-CoV) and severe acute respiratory syndrome-related coronavirus (SARS-CoV). The genome of COVID-19 is enveloped single-stranded positive stranded RNA virus having diameter of 60–140 nm, spherical or elliptical in shape and pleomorphic. The sequence analysis showed that the COVID-19 possessed a typical genome structure of coronavirus and belonged to the cluster of  $\beta$ -coronaviruses including SARS-CoV and MERS-CoV. [7] The nucleotide sequence of spines protein on the envelope of the virus is also highly identical with that of bat-SL-CoVZC45 (84%) and SARS-CoV (78%). [8,9,10] The physicochemical property of COVID-19 has not been clarified clearly yet. It is thought that COVID-19 is sensitive to ultraviolet radiation and heating. According to researches on SARS-CoV and MERS-CoV,

the virus can be inactivated by heating at 56°C for 30 minutes and by using lipid solvents such as 75% ethanol, chlorinecontaining disinfectant, peroxyacetic acid and chloroform, but not by chlorhexidine. [10]

From WHO Data as of 26 march 2020 COVID 19 spread all over the world. Almost 1 million peoples affected by COVID 19 and so many peoples dead, which is mention in below Table 1 [11].

Table 1. WHO data regarding COVID-19

Reporting Country	Total Confirmed Cases	New Cases	Total Deaths	New Deaths
USA	63570	11656	884	211
Italy	74386	5210	7505	658
China	81961	113	3293	6
Republic of Korea	9241	104	131	5
Australia	2799	547	11	3
Japan	1291	98	45	2
France	24920	2895	1331	231
Germany	36508	4954	198	49
Spain	47610	7937	3454	738
Iran	27017	2206	2077	143
Turkey	2433	561	59	15
India	649	87	13	4
UK	9533	1452	463	41
Saudi Arabia	900	133	2	1
Pakistan	1057	66	8	1
Switzerland	9714	925	103	17
Israel	2369	199	5	0
Egypt	456	54	21	1
Netherland	6412	852	356	80
Norway	2916	350	12	2
South Africa	709	155	0	0
Russian federation	840	182	2	2

## 2. Epidemiology [12]

### 2.1. Infection Sources

The main sources of the infection are patients infected by COVID-19 with or without clinical symptoms. In addition, patients in the incubation period may also have potency to transmit the virus based on the case evidence.

### 2.2. Transmission Route

The novel virus is spread through respiratory droplets when patients cough, talk loudly or sneeze. Close contact is also a source of transmission (e.g., contact with the mouth, nose or eye conjunctiva through contaminated hand). Whether transmission can occur through mother–infant vertically or breast milk has not been established yet.

### 2.3. Susceptible Population

There are general susceptibilities in all groups, with the elderly and people with basic diseases more likely to become severe cases. Children may have mild clinical symptoms after infection.

## 3. Detection of COVID-19 [13]

### 3.1. Respiratory Specimens

The respiratory specimen was used to detect the presence of COVID-19 by next generation sequencing or real-time RT-PCR methods. The primers and probe target to envelope gene of COVID were used and the sequences were as follows: forward primer 5'-ACTTCTTTTCTTGCTTTCGTGGT-3'; reverse primer 5'-GCAGCAGTACGCACACAATC-3'; and the probe 5'CY5-CTAGTTACTAGCCATCCTTACTGC-3'BHQ1. Conditions for the amplifications were 50°C for 15 min, 95°C for 3 min, followed by 45 cycles of 95°C for 15 sec. and 60°C for 30 sec.

### 3.2. Cytokine and Chemokine Measurement

To characterise the effect of coronavirus on the production of cytokines or chemokines in the acute phase of the illness, plasma cytokines and chemokines were measured using Human Cytokine Standard 27-Plex Assays panel and the Bio-Plex 200 system (Bio-Rad, Hercules, CA, USA) for all patients according to the manufacturer's instructions. The plasma samples from four healthy adults were used as controls for cross comparison. The median time from being transferred to a designated hospital to the blood sample collection was 4 days.

### 3.3. Detection of Coronavirus in Plasma

Each 80 µL plasma sample from the patients and added into 240 µL of Trizol LS (10296028; Thermo Fisher Scientific, Carlsbad, CA, USA).. Total RNA was

extracted by Direct-zol RNA Miniprep kit (R2050; Zymo research, Irvine, CA, USA) as per the manufacturer's instructions and 50 µL elution was obtained for each sample. 5 µL RNA was used for real-time RT-PCR, which targeted the NP gene using AgPath-ID One-Step RT-PCR Reagent (AM1005; Thermo Fisher Scientific). The final reaction mix concentration of the primers was 500 nM and probe was 200 nM. Real-time RT-PCR was performed using the following conditions: 50°C for 15 min and 95°C for 3 min, 50 cycles of amplification at 95°C for 10 sec. and 60°C for 45 sec.

**Table 2. Characteristics of patients who have been infected with COVID-19, MERS and SARS [14]**

Characteristics	COVID-19	MERS	SARS
Date	December 2019	June 2012	November 2002
Location	Wuhan, China	Jeddah, Saudi Arabia	Guangdong, China
Fever	98%	98%	99-100%
Dry Cough	76%	47%	29-75%
Dyspnoea	55%	72%	40-42%
Diarrhoea	1	26%	20-25%
Sore throat	0	21%	13-25%

## 4. Genral Treatment

### 4.1. Antiretroviral

#### 4.1.1. Ribavirin

Ribavirin is a broad spectrum Anti-retroviral drug, mostly used to treat Hepatitis C. In the treatment of SARS, Ribavirin was used for most cases. [15] Morgenstern et al, reported that Ribavirin and interferon-β synergistically inhibited the replication of SARS-associated coronavirus in animal and human cell lines. [16]

#### 4.1.2. Lopinavir/Ritonavir

The combination of Antiretroviral drugs such as lopinavir (LPV) with ritonavir (RTV) used in treatment on HIV infection as boosted protease inhibitor. [17] Half-life of Lopinavir increased usually combined with Ritonavir through the inhibition of cytochrome P450. [18] Chu et al reported that the combination of LPV/RTV with ribavirin used in the treatment of SARS. [19] Kim et al found that triple combination therapy LPV/RTV, Ribavirin and IFN-α2a in the treatment of MERS in South Korea. Kim's Triple combination therapy should be considered for treatment on COVID-19. [20]

#### 4.1.3. Remdesivir

As per the report, Remdesivir (RDV) is a nucleoside analog GS-5734 which inhibit the human and zoonotic coronavirus in vitro and to restrain severe acute respiratory syndrome coronavirus (SARS) in vivo. [21] In USA, use of Remdesivir (RDV) was administered in COVID-19 affected person at the its severe condition and therefore concluded that the use of RDV with IFN-β could be a better choice for the treatment of COVID-19 comparing with that of the triple combination of LPV/RTV-IFN-β. [22]

#### 4.1.4. Nelfinavir

Nelfinavir is a selective inhibitor of HIV protease antiretroviral drug which is responsible for post translational processing of HIV propeptides. [23] Yamamoto et al reported that nelfinavir strongly inhibit the replication of SARS-CoV. Therefore, Nelfinavir could also be a better choice for the treatment of COVID - 19. [24]

### 4.2. Immunoenhancers

#### 4.2.1. Interferons

Interferons (IFNs) divided into two type which is type I and Type II Interferons. As a member of Type I IFN, IFN- $\alpha$  is produced very quickly as part of the innate immune response to virus infection. IFN- $\alpha$  inhibits the replication of animal and human coronaviruses. [25,26] The investigation in vitro also concluded that the type I interferons including IFN- $\beta$  could inhibit the replication of SARS. [27] However, interferon- $\gamma$  was reported not to possess antiviral activity against SARS coronavirus. [28] These findings suggest that these approved IFN's along with antiretroviral drug for the treatment of COVID-19.

#### 4.2.2. Intravenous Gammaglobulin

Intravenous gammaglobulin (IVIg) was discovered in 1970s use as the safest immunomodulating drug for long term use in all age. [29] In Singapore, IVIg administered in the patients for the treatment of SARS, It was due to the IVIg-induced increase of viscosity in hypercoagulable states of SARS patients. [30]

#### 4.2.3. Thymosin $\alpha$ -1 (Ta1)

Thymosin  $\alpha$ -1 (Ta1) is a thymic peptide hormone first isolated from thymic tissue in the mid-sixties and it has a peculiar ability to restore the homeostasis of the immune system. [31,32] It was also chemically synthesized and used in diseases where the immune system was hindered or impaired. [33] In SARS patients, it enhance the immunity and it is effective in controlling the spread of the disease. [34,35]

#### 4.2.4. Thymopentin (TP5, munox)

Thymopentin (TP5, munox) is a synthetic pentapeptide mostly responsible to the active site of ofthymopoietin and when administered into the old mice, Thymopentin restored the antibody production in it. [36] Thymopentin also enhanced the antibody response in humans when it administered subcutaneously route for three times a week at doses 50 mg. [37]

#### 4.2.5. Cyclosporine A

Cyclosporine A is a very important immunosuppressive drug and it mostly used in transplantation and treatment of autoimmune disorders. [38] Luo et al reported that the nucleocapsid protein (NP) of SARS-CoV played an important role in the replication process

of virus and release. It also binds to human Cyclophilin A. [39] Cyclophilin A play important role in viral

infection either promoting or inhibits their replication. Cyclosporine A act on Cyclophilin A and bloc the replication of coronavirus of all species, including SARS-CoV. [40]

### 4.3. Chymotrypsin-like (3C-like) Inhibitors

#### 4.3.1. Cinanserin

Cinanserin, an old drug, act as a serotonin receptor antagonist. It inhibits the 3 chymotrypsin-like (3C-like) protease which is responsible for inhibition of replication of SARS-CoV. [41] This 3 Chymotrypsin-like protease (3CLpro) was also responsible for replication of COVID-19. Therefore, Cinanserin may be a better choice for the treatment of COVID-19 infection. [42]

#### 4.3.2. Flavonoids

Flavonoids are an important class of natural products having antiviral abilities and divided into several subgroups such as chalcones, flavones, flavonols, and isoflavones. [43] Jo et al reported that the Flavonoids use in treatment on Corono virus activity due to 3 Chymotrypsin-like protease inhibitions. [44]

### 4.4. Papain-like Protease Inhibitors- Diarylheptanoids

Diarylheptanoids is a natural product and is extracted from the stem bark of *Alnus japonica*. It had been found to be able to inhibit papain like protease of SARS-CoV. [42]

### 4.5. Vitamin Treatment

#### 4.5.1. Vitamin C

Vitamin C is a water-soluble vitamin also called as an ascorbic acid means no-scurvy acid. Vitamin C plays an important role in the synthesis of collagen in connective tissues and acts as an antioxidant. Vitamin C also helps immune functions and provides the protection against infection caused by a coronavirus. [45] Vitamin C also use as a weak antihistamine agent to provide relief action from flu-like symptoms such as a running or stuffy nose, sneezing, and swollen sinuses. [46] Atherton et al concluded that vitamin C increased the resistance of chick embryo tracheal organ cultures to avian coronavirus infection. [47] So vitamin C could be preferred for the treatment of COVID-19.

#### 4.5.2. Vitamin D

Vitamin can be synthesized in our body with the help of sunlight. Low level of vitamin D reported in healthy adults mostly in a winter season. Vitamin D plays an important role in bone integration and stimulates the maturation of many cells including immune cell. [48] The attacked of COVID-19 mostly in winter season of 2019. Most of the peoples affected by COVID-19 virus whose have insufficient of Vitamin D in body. Therefore, vitamin D better choice for the treatment of this novel COVID-19 virus. [49]

## 4.6. Antimalarial Drug

### 4.6.1. Chloroquine

Chloroquine mostly use in the treatment of malaria. It is a derivative of 9-aminoquinoline. It also use in treatment of viral infection. [50] Chloroquine play an important role in treatment of SARS-CoV infection due to interfering with ACE2, which is a cell surface binding site for S protein of SARS-CoV. [51]

## 4.7. Anthraquinone Compound-Emodin

Emodine is a Virucidal agent derived from genus *Rheum* and *Polygonum*. It is an anthraquinone compound which blocks the interaction between the S protein of SARS-CoV and ACE2. Therefore Emodine better choice for treatment on COVID-19. [52,53]

## 4.8. Promazine

Promazine is an anti-psychotic drug which inhibits the replication of SARS-CoV by avoiding the binding of S protein to ACE2. Therefore promazine could be used as alternative choices for the treatment of COVID-19. [54]

## 4.9. Convalescent Plasma Treatment

In Convalescent Plasma Treatment, collect the convalescent plasma from recovered patients, which contain the antibody then which is administered to the serious patient. Mostly, this technique is utilized on SARS-CoV, MERS-CoV. COVID-19 Convalescent Plasma collected from recovered patients that contain antibody, and then it is administered into the COVID-19 infected patients. Therefore Convalescent Plasma Treatment could be as alternative choices for the treatment of COVID-19. [55]

## 5. Conclusion

From so many cases it confirmed that, it transmitted through human-to-human and spread all over world. There is no proper medicine and vaccine on this novel coronavirus COVID-19. The Economy of so many countries going on declined state due to this novel coronavirus COVID-19. It is challenge to scientists to find out actual medicine and vaccine on this novel coronavirus COVID-19.

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