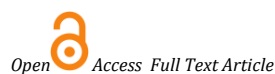
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Review Article

## A Review on the Novel Corona Virus with International and Indian Perspective

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### Abstract

On 31 December 2019, pneumonia of unknown cause was detected in Wuhan, China, and was first reported to the WHO Country Office in China. On 30 January 2020, the outbreak was declared a Public Health Emergency of International Concern. <sup>1</sup>

It was an outbreak of severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) infection that occurred in Wuhan, Hubei Province, China and got spread across China and beyond. WHO officially named the disease - Corona virus Disease 2019 (COVID-19) on February 12, 2020. <sup>2</sup>

It has been spreading worldwide for a period of at least a year & half <sup>3</sup> This review article addresses the current scenario caused by the SARS- Co V along with the treatment protocols and ongoing vaccines.

**Keywords:** Corona virus, COVID-19, m RNA, current therapy, vaccines, clinical symptoms, review

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## Introduction

### Common flu and Covid 19

Corona viruses as the name suggests are called so due to the crown-like projections on their surfaces. "Corona" in Latin means "halo" or "crown." first identified in the 1960s, followed by SARS-Co V IN 2003, HCoV- NL63 in 2004, HKU1 in 2005, MERS-CoV in 2012 respectively. The human corona viruses are currently classified into seven types, which include, HCoV-229E, HCoV-OC43, HCoV-NL63, SARS-CoV, HKU1, MERS-CoV and 2019-nCoV. The corona virus (MERS-CoV and SARS-CoV) are more dangerous among all the

coronaviruses. <sup>4</sup> COVID-19 and influenza have a similar clinical presentation since they both cause respiratory disease and primarily both viruses are transmitted by contact, droplets and fomites<sup>5 6</sup>

### SARS CoV-2

Corona viruses have naturally and evolutionarily, shaped and hosted by the bats. Indeed, it is postulated that most of the corona viruses that are found in humans are derived from the bat reservoir. <sup>7</sup>The recent studies have confirmed the genetic similarity of SARS-CoV-2 and a bat beta corona virus of the sub-genus Sarbecovirus. <sup>7,8</sup>

SIGNS AND SYMPTOMS	COLD	FLU (INFLUENZA)	COVID-19 (WUHAN CORONA VIRUS)
Fever	Mild if present	Often	Often
Fatigue, Tiredness	Occasional, mild	Common	Occasional
Sneezing	Common	Infrequent	Infrequent
Body Aches	Common	Common	Occasional
Headache	Very infrequent	Common	Occasional
Sore Throat	Common	Occasional	Occasional
Stuffy or Runny Nose	Common	Occasional	Infrequent
Diarrhoea	No	Occasional	Infrequent
Watery eyes	Common	Common	Infrequent
Cough	Mild	Dry cough	A dry cough, often severe
Shortness of Breath	No	Rare	With mild/moderate infection

The genome sequence of the novel corona virus is 96.2% similar to the bat SARS-related coronavirus (SARSr-CoV; RaTG13) collected from Yunnan province, China, but is not similar to the genomes of SARS-CoV (about 79%) or MERS-CoV (about 50%). It is been confirmed that the SARS-CoV-2 uses the same receptor, the angiotensin-converting enzyme II (ACE2), same as that of SARS-CoV. But the route of transmission from natural reservoirs to humans remains blinded, studies have been showing the pangolins providing a partial spike gene to SARS-CoV-2. (the crucial functional sites in the protein of SAR-CoV-2 are identical to one of the viruses that were isolated from a pangolin).<sup>7,9</sup>

## Aetiology and pathophysiology

CoVs are positive-stranded RNA viruses that have a spikey appearance due to the presence of glycoproteins on the outer surface. It belongs to the family *Coronaviridae*, which has the subclass *Orthocoronavirinae* that classifies the viruses into four genera of CoVs that include Alphacoronavirus (alphaCoV), Betacoronavirus (betaCoV), Deltacoronavirus (deltaCoV), and Gammacoronavirus (gammaCoV).<sup>10,11</sup>

The SARS-CoV-2 belongs to the betaCoVs category. It has a round/elliptical structure with a pleomorphic form. It has a diameter of 60–140 nm. This novel corona virus is sensitive to ultraviolet rays and heat and also these viruses can get inactivated by lipid solvents that include ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform except for chlorhexidine.<sup>10,12</sup>

## Virion structure

Coronavirus virus mainly contains 4 structural proteins, i.e. spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins, which are all encoded within the 3' end of the viral genome.

**S protein:** The S protein with a mass of ~150 kDa uses an N-terminal signal sequence to gain access to the ER and is heavily N-linked glycosylated. The spikey structure on the surface of the virus is due to the encodement of the homotrimers.<sup>11,13</sup> It is a trimeric S glycoprotein that is a class I fusion protein that mediates the attachment to the host receptor. In some coronaviruses, S is cleaved by a host cell into two separate polypeptides noted S1 and S2. S1 forms the large receptor-binding domain of the S protein and S2 forms the stalk of the spike molecule.<sup>11</sup>

**M protein:** It is small in mass with ~25–30 kDa and has 3 transmembrane domains and is observed to give the virion its shape.<sup>11</sup>

**E protein:** The E protein has a mass of ~8–12 kDa and is found in small quantities. E protein in coronaviruses are specifically different but have a common architecture. The

significant topology of E protein is not completely studied but data suggest that it is a transmembrane protein.<sup>11</sup>

Patients infected with COVID-19 had higher leukocyte numbers, high blood levels of cytokines and chemokines, increased levels of plasma pro-inflammatory cytokines and abnormal respiratory findings. The common symptoms included dry cough, coarse breathing sounds of both lungs, body temperature, fever, sore throat and fatigue.<sup>14</sup>

The pathogenesis of COVID-19 infection being a respiratory system targeting virus is considered to be severe pneumonia, RNA anaemia, along with the incidence of ground-glass opacities, and acute cardiac injury.<sup>15</sup>

## Clinical presentation and transmission

### Incubation period

The incubation period for COVID-19 is observed to vary between 7-14 days, with a median time of 4-5 days from exposure to symptoms onset. Certain studies have reported 97.5% of patients with COVID-19 are developing symptoms within 11.5 days of SARS-CoV-2 infection.<sup>16</sup>

### Clinical symptoms

The prevalence of symptoms of COVID 19, based on over 55,000 lab cases shows fever(88%), dry cough(67%), sore throat (14%) and fatigue(38%). COVID 19 is more contagious and less severe when compared to other SARS & MERS.<sup>14</sup>

### Implications of mutations on the virus

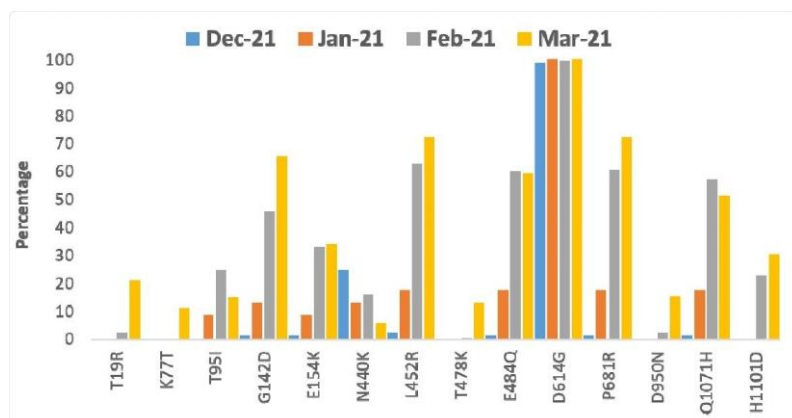
Over 1 year & 6 months, 1200 variants of the novel coronavirus have been identified, of which 1000 strains have been studied.<sup>17</sup> The current scenario rates 11 mutations per sample, which accounts for more than the national average (8.4) and the global average(7.3).<sup>18</sup>

Scientists have observed three major mutations of the COVID-19 virus so far:

- D614G
- VUI2020-12/01
- N501Y

D614G was responsible for the fast spread of the virus in Europe, the US and the rest of the world. VUI 2020-12/01 and N501Y are the current ones spreading in the UK. And the 'South Africa drift', where three mutations happened in the genetic make-up of the virus.<sup>19</sup> Also, B.1.167 Covid variant being recognised as Singapore strain is believed to affect the younger children.<sup>20</sup>

Currently, the exponential increase of the cases in India is attributed to the mutations -L452R, E484Q, and P681R. With other mutations being recognised over as:



Another variant Delta (B.1.617.2), belongs to a viral lineage first recognised in India during the second wave, that seemed to be around 60% more transmissible than the already highly infectious Alpha variant (also called B.1.1.7). Delta is found to be partially resistant to vaccines, A study published on 22 May found that a single dose of either AstraZeneca's or Pfizer's vaccine reduced a person's risk of developing COVID-19 symptoms caused by the Delta variant by 33%, compared to 50% for the Alpha variant. A second dose of the AstraZeneca vaccine boosted protection against Delta to 60% (compared to 66% against Alpha), while two doses of Pfizer's jab were 88% effective (compared to 93% against Alpha).<sup>21,22</sup>

## Treatment approaches & failure

### Lopinavir and Ritonavir

Lopinavir and ritonavir (Kaletra) was given to those adult patients with laboratory-confirmed SARS-CoV-2 infection with certain criteria were eligible to receive lopinavir/ritonavir for 14 days after being confirmed with (i) respiratory distress with respiratory rate  $\geq 22$ /min or SpO<sub>2</sub> of  $< 94$  per cent; (ii) lung parenchymal infiltrates on chest X-ray; (iii) hypotension defined as systolic blood pressure  $< 90$  mmHg or need for vasopressor/inotropic medication; (iv) new-onset organ dysfunction, (v) age  $> 60$  yr, diabetes mellitus, renal failure, chronic lung disease and immune-compromised patients. Patients were monitored to document clinical, laboratory and safety outcomes.<sup>23</sup>

#### Failure

In a few of the studies conducted it is concluded that in hospitalized adult patients with severe Covid-19, there was no benefit with lopinavir-ritonavir treatment beyond standard care.<sup>24</sup> Also according to the literature, it states that there was no significance in the treatment of Kaletra with COVID-19, only that there was an improvement of 1 day earlier of recovery.<sup>25</sup>

### Tocilizumab

Recommended the use of tocilizumab as a single intravenous dose of 8 mg/kg of actual body weight which can be

increased up to 800 mg given in combination with dexamethasone (6 mg daily) in certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19.

#### Failure

Tocilizumab (Actemra) did not reduce severe respiratory symptoms, intensive care visits, or death any better than standard treatments, the Italian Medicines Agency.<sup>26</sup>

### Remdesivir

recommended using remdesivir for patients who were on high-flow oxygen, mechanical ventilation, or ECMO.<sup>27</sup>

#### Failure

studies report that in patients with covid 19 who were administered with remdesivir, the patients' developed bradycardia along with signs of worsening QT interval. This reverted upon stopping remdesivir therapy. The prevalence of bradycardia with prolonged QT interval is not well-known yet with this medication.<sup>28</sup>

### Ivermectin

Studies done in vitro suggested that ivermectin acts by inhibiting the host importin alpha/beta-1 nuclear transport proteins, that is a vital intracellular transport process where viruses hijack to enhance infection thereby suppressing the host's antiviral response and also ivermectin acts by interfering with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein to the human cell membrane. Ivermectin is said to be host-directed based on its broad-spectrum activity in vitro against the viruses that cause other major viral infections. Some studies show that ivermectin has a potential anti-inflammatory property, which has been postulated to be beneficial in people with COVID-19.<sup>29</sup>

#### Failure

The small size of the study, the unclear treatment arm assignments, and the lack of accounting of disease severity at baseline make it difficult to conclude the efficacy of using IVM to treat patients with mild COVID-19.<sup>30</sup>

## Current treatment

TREATMENT	DRUGS	DOSES	SPECIAL CONSIDERATIONS/FEATURES
Tab Hydroxychloroquine	T. HCQ (In high risk patients - DM / HTN / CVA / CKD / CLD / Obesity / Age $> 60$ yrs)	Day 1 - 400 mg BD Followed by 400 mg OD x 4 Days	avoid in cardiac disease or if QTc $> 480$ ms
Antibiotics	Tab Azithromycin	500mg OD FOR 5 days	In case azithromycin is contraindicated- T. AmoxClav 625 BD
	T. Azithromycin + Inj. Piptaz OR Inj meropenem	500 mg OD x 5 Days + 4.5 mg OR 500mg IV	In case of suspected secondary bacterial infection.

Routine	T. Paracetamol Anti-tussives T. Vitamin C T. Zinc C. Omeprazole/ Inj Pantoprazole	500mg SOS 500mg OD 50mg BD 20mg BD/ 40mg OD	With adequate hydration with conservative fluids.  Oxygen maintenance: Maintain Target SpO <sub>2</sub> > 90 % NRM (10 - 15 lit / min) ↓ HFNC (10 - 60 lit / min) ↓ CPAP (TV 6ml/kg; PEEP 5-15 cm H <sub>2</sub> O; Target PP 30 cm H <sub>2</sub> O) ↓ MV (ARDS Protocol)
Anticoagulants	Inj enoxaparin	40 mg SC OD x 5 Days	can be started as prophylactic without D DIMER.  Contraindicated in ESRD, active bleeding, emergency surgery, platelets < 20,000/mm <sup>3</sup> , BP > 200/120) Inj. Dalteparin 2500 IU SC OD x5 days
Monoclonal antibodies	tolilizumab	400 mg (max 800 mg) slow IV in 100 ml NS/ 1 Hour	Contra Indications – Active Infections, TB, Hepatitis, Platelets < 1L/mm <sup>3</sup> , ANC < 2000/mm <sup>3</sup>
Steroids	Dexamethasone  inj. Methyl Prednisolone	0.1 – 0.2 mg /kg ≈ 6 mg IV OD x 5 Days  1.0 -2.0 mg/kg ≈ 80 mg x 10 Days	

Vaccinations put forward

Vaccine	Type	Manufacturer	Dose	Effectiveness	Storage
Pfizer (BNT162b2)	mRNA vaccine-	Pfizer, Inc., and BioNTech	2 shots, 21 days apart	95% against 1 <sup>st</sup> strain.  31	2-8°C
Moderna	mRNA-1273	ModernaTX, Inc.	2 shots, one month (28 days) apart	92-94.1% against 1 <sup>st</sup> strain. 3132	2-8°C for upto 30days.
Covaxin (BBV154)	Inactivated virus	Bharat Biotech's BSL-3	2 shots, one month (28 days) apart. 33	81% interim efficacy against 1 <sup>st</sup> strain	2-8°C
AstraZeneca (Covishield, Vaxzevria)	Viral vector	Oxford university	2 shots, 8-12weeks apart.	79-85% against 1 <sup>st</sup> strain	2-8°C for 6 months

\*mRNA vaccines teach our cells how to make a protein—or even just a piece of a protein—that triggers an immune response inside our bodies.<sup>31</sup>

Johnson & Johnson's Janssen COVID-19 Vaccine: CDC and FDA have recommended a pause in the use of Johnson & Johnson's J&J/Janssen COVID-19 Vaccine in the United States out of an abundance of caution as people who have received the J&J/Janssen COVID-19 Vaccine within the past three weeks developed severe headache, abdominal pain, leg pain, or shortness of breath should seek medical care right away.<sup>34</sup>

### Vaccination and Incidence of infection

During the initial implementation phases, as for every new vaccine, post-introduction evaluations will be important to address many of the remaining questions about the performance of these vaccines. When a vaccine is used outside trial populations the effects of the vaccine may differ in specific geographies or subpopulations. Vaccine effectiveness (VE) might be different against various disease outcomes, against infection and infectiousness, and newly

emerging virus variant strains. Additionally, important programmatic issues will need to be addressed, such as the effectiveness of incomplete dose schedules, variation in dose intervals, and the interchangeability of different vaccine products. Suboptimal cold chain capacity, and off-schedule and incomplete delivery of doses could lead to different vaccine performances. Vaccines might not be as effective against new variants. Finally, assessing the duration of vaccine protection requires longer-term studies.<sup>35</sup>

### Complications of Covid 19

In population about 1 in 6, have been found to show complications. Many of these complications may be caused by a condition known as cytokine release syndrome or a cytokine storm. This is when an infection triggers your immune system to flood your bloodstream with inflammatory proteins called cytokines. They can kill tissue and damage your organs, including your lungs, heart, and kidneys.<sup>36</sup>

COVID-19 complications may include Acute Respiratory Failure, Pneumonia, Acute Respiratory Distress Syndrome (ARDS), Acute

Liver Injury, Acute Cardiac Injury, Secondary Infection, Acute Kidney Injury, Septic Shock, Disseminated Intravascular Coagulation, Blood Clots, Multisystem Inflammatory Syndrome in Children, Chronic Fatigue, Rhabdomyolysis.<sup>36 37</sup>

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