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## **Analytical Review of Current Trends in Treatment and Prevention of COVID-19**

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ABSTRACT: The pandemic of coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents an unprecedented challenge to identify effective drugs for prevention and treatment. Given the rapid pace of scientific discovery and clinical data generated by the large number of people rapidly infected by SARS-CoV-2, clinicians need accurate evidence regarding effective medical treatments for this infection. he COVID-19 pandemic represents the greatest global public health crisis of this generation and, potentially, since the pandemic influenza outbreak of 1918. The speed and volume of clinical trials launched to investigate potential therapies for COVID-19 highlight both the need and capability to produce high-quality evidence even in the middle of a pandemic. Chloroquine and hydroxychloroquine appear to block viral entry into cells by inhibiting glycosylation of host receptors, proteolytic processing, and endosomal acidification. These agents also have immunomodulatory effects through attenuation of cytokine production and inhibition of autophagy and lysosomal activity in host cells. Chloroquine was successfully used to treat a series of more than 100 COVID-19 cases resulting in improved radiologic findings, enhanced viral clearance, and reduced disease progression. Remdesivir, formally known as GS-5734, is a monophosphate prodrug that undergoes metabolism to an active C-adenosine nucleoside triphosphate analogue. The agent was discovered amidst a screening process for antimicrobials with activity against RNA viruses, such as Coronaviridae and Flaviviridae. Currently, remdesivir is a promising potential therapy for COVID-19 due to its broadspectrum.

KEYWORDS: corona, covid-19, treatment, prevention, drugs, chloroquine, ramdesivir

#### I. INTRODUCTION

Coronaviruses (CoVs) are positive-stranded RNA(+ssRNA) viruses with a crown-like appearance under an electron microscope (coronam is the Latin term for crown) due to the presence of spike glycoproteins on the envelope. The subfamily Orthocoronavirinae of the Coronaviridae family (order Nidovirales) classifies into four genera of CoVs:

- Alphacoronavirus (alphaCoV)
- Betacoronavirus (betaCoV)
- Deltacoronavirus (deltaCoV)
- Gammacoronavirus (gammaCoV)[1]

BetaCoV genus is further divided into five sub-genera or lineages.[1] Genomic characterization has shown that bats and rodents are the probable gene sources of alphaCoVs and betaCoVs. On the contrary, avian species seem to represent the gene sources of deltaCoVs and gammaCoVs. CoVs have become the major pathogens of emerging respiratory disease outbreaks. Members of this large family of viruses can cause respiratory, enteric, hepatic, and neurological diseases in different animal species, including camels, cattle, cats, and bats. For reasons yet to be explained, these viruses can cross species barriers and can cause, in humans, illness ranging from the common cold to more severe diseases[2]



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Individuals of all ages are at risk of contracting this infection and severe disease. However, patients aged  $\geq 60$  years and patients with underlying medical comorbidities (obesity, cardiovascular disease, chronic kidney disease, diabetes, chronic lung disease, smoking, cancer, solid organ or hematopoietic stem cell transplant patients) have an increased risk of developing severe COVID-19 infection. The percentage of COVID-19 patients requiring hospitalization was six times higher in those with preexisting medical conditions than those without medical conditions.

In February 2020, the use of favipiravir in the experimental treatment of COVID-19 was investigated. In a prospective, randomized, multicenter study, favipiravir (1,600 mg every 12 h/first day followed by 600 mg every 12 h/day, n = 120) was compared with umifenovir (200 mg every 8 h/day, n = 120) for the treatment of moderate and severe COVID-19 infections for 10 days (Chen et al., 2020). On day 7, differences in clinical recovery were observed in patients with moderate infections (71.4% in favipiravir arm and 55.9% in umifenovir arm, p = 0.019). Favipiravir significantly improved the resolution time of pyrexia and cough.



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Many physicians hope that Convalescent Plasma CP transfusion would be effective in treating COVID-19. Seven case series reported the treatment outcomes of CP in patients with COVID-19 with disease severity ranging from mild disease to severe respiratory failure on extracorporeal membrane oxygenation (Ahn et al., 2020; Duan et al., 2020; Pei et al., 2020; Salazar et al., 2020; Shen et al., 2020; Ye et al., 2020; Zhang B. et al., 2020). In these case series, clinical improvement, radiological resolution of pneumonia, and decreased viral load were observed in most patients.[3]

#### **II. OBSERVATIONS**

Therapy/Mechanism	Authors	Country	Phase of trails	Methods	Primary outcome	Report findings	
Remdesivir (RDV)/RNA polymerase inhibitor	Wang et al	China	Ш	Double-blinded RCT; RDV (n = 158) vs. placebo (n = 79)	Clinical improvement up to 28 days	RDV was not associated with a difference in time to clinical improvement (hazard ratio 1.23 (95% CI 0.87–1.75))	
	Beigel et al	United States	Ш	Double-blinded; RDV (n = 538) vs. placebo (n = 521); hospitalized patients; favorable outcome in preliminary report	Time to recovery	Median recovery time: 11 days vs. 15 days, recovery rate ratio, 1.32; 95% Cl, 1.12-1.55; p < 0.001	
Lopinavir-ritonavir (LPV/r)/protease inhibitor	Cao et al	China	N/A	Hospitalized patients with COVID-19 and respiratory illness <sup>a</sup> ; open-label RCT; LPV/r (n = 99) vs. placebo (n = 100)	Time to clinical improvement	Modified intention-to-treat population <sup>b</sup> : Median time to clinical improvement: 15 days vs. 16 days (hazard ratio, 1.39; 95% Cl, 1.00–1.91)	
Favipiravir (FPV)/RNA polymerase inhibitor	Chen et al	China	N/A	Adults with COVID-19 pneumonia; open- label RCT; FPV (n = 120, 116 accessed) vs. UFV (n = 120)	Clinical recovery rate on day 7	Clinical recovery rate on day 7: 71,4% vs. 55.9%; rate ratio (95% Cl): 0.16 (0.03–0.28)	
Ribavirin (RBV)/Guanosine analog	Tong et al	China	N/A	Adults with severe COVID-19; retrospective study; RBV (n = 44) vs. none (n = 71)	Time to viral negative conversion	12.8 $\pm$ 4.1 vs. 14.1 $\pm$ 3.5 days (p = 0.314)	
Interferon (IFN) β-1b, RBV, LPV/r/ Combination therapy	Hung et al	Hong Kong	11	Adults with admitted COVID-19 patients; open-label RCT	Time to viral negative conversion	7 days vs. 12 days (hazard ratio,4.37; 95% Cl (1.85 ~ 10.24), <i>p</i> = 0.0010)	
Chloroquine (CQ) and hydroxychloroquine (HCQ) $% \left( \left( HCQ\right) \right) =0$	Gautret et al	France	Ш	Hospitalized patients with COVID-19 (age >12 years) regardless of their clinical status; open-label, non-RCT; HCQ ± AZI (n = 26) vs. none (n = 16)	Viral clearance at day 6	70.0% vs. 12.5%, p = 0.001	
	Mehra et al	Multinational	N/A	Hospitalized patients with COVID-19 received treatment of interest within 48 h; multinational registry analysis, CQ or HCQ ± macrolide (n = 14,888) vs. none (n = 81.144)	In-hospital mortality and <i>de novo</i> ventricular arrhythmias	Retracted owing to suspicious data sources	
Tocilizumab (TCZ)/Interleukin-6 inhibitors	Klopfenstein et al	France	II	Hospitalized adult patients with COVID-19; TCZ (n = 20) vs. control (n = 25)	Death and/or ICU admission	Patients with TCZ presented with severe form; death and/or ICU admission: TCZ 25% vs. control 72%, $\rho = 0.002$	
	Campochiaro et al	Italy	l	Severe non-ICU adult patients with COVID-19; TCZ (n = 32) vs. control (n = 33)	Survival and clinical improvement at 28 days	Clinical improvement: TCZ 69% vs. control 61%, $p = 0.61$ ; mortality rate: TCZ 15% vs. control 33%, $p = 0.15$	
	Price et al	United States	0	Hospitalized patients with COVID-19; observational study; TCZ (n = 153) vs. control (n = 86)	8	TCZ-treated patients with similar survival rates to non-severe patients (83% vs. $91\%$ , $p = 0.11$ )	
Convalescent plasma (CP)/Neutralizing antibodies	Li et al	China	11	Severe and life-threatening COVID-19; RCT; CP (n = 52) vs. standard treatment (n = 51)	Clinical improvement within 28 days	28-days clinical improvement: CP 51.9% vs. standard treatment 43.1%; hazard ratio, 1.40 (95% Cl, 0.79–2.49), $\rho = 0.26$ . Patients without life-threatening disease: 28-days clinical improvement, hazard ratio, 2.15 (95% Cl, 1.07–4.32); 72-h negative conversion rate of viral nucleic acid detection was higher in the CP group (87.2% vs. 37.5%, $\rho < 0.001$ )	
	Hegerova et al	United States	II	Adult patients with severe or critical COVID-19; case-control; CP (n = 20) vs. matched control (n = 20)	Clinical outcomes up to 14 days	Mortality rate: CP 10% vs. control 30%, $p = 0.11$ ; mechanical ventilation: CP 30% vs. control 5%, $p = 0.1$	
	Zeng et al	China	Π	Adult patients with COVID-19 and respiratory failure; case series, observational; CP ( $n = 6$ ) vs. control ( $n = 15$ )	Primary outcome: Fatality and secondary outcome: Virus shedding	Mortality rate: CP 83.3% vs. control 93.3%; duration of virus shedding: CP 23.5 days vs. control 20.0 days, $\rho = 0.38$	
<i>Qingfei paidu qecoction</i> (QPD)/Traditional Chinese medicine	Xin <i>et al</i>	China	11	COVID-19 patients admitted to the hospital (>15 years old); retrospective study; QPD + western medicines (interferon, lopinavir, or arbidol; n = 37) vs. Western medicine (n = 26)	Improvement of inflammatory markers at the end of treatment	% Of normal CRP,TLC, LDH level: Combined group > control group ( $\rho < 0.05$ )	

AZI, Azithromycin; RCT, randomized-controlled trial; UFV, umilenovir; CRP, C-reaactive protein; TLC, total lymphocyte count; LDH, lactate dehydrogenase; NA, not applicable. <sup>6</sup>Oxygen saturation <94% in room air or arterial oxygen partial pressure/fractional inspired oxygen (PaO2/FIO2) <300 mmHg.



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Safe and effective vaccines are an important tool, in combination with other measures, to protect people against COVID-19, save lives and reduce widescale social disruption.



Countries and areas in the Western Pacific Region have already completed regulatory approval and started introducing one or more COVID-19 vaccines.

Through the COVAX Global Vaccine Facility and other mechanisms, WHO and partners are working with governments to facilitate equitable access to and distribution of an initial allocation of vaccine as quickly as possible.[4]

WHO recommends that initial vaccination should prioritize groups at highest risk of exposure to infection in each country, including health workers, older persons and those with other health issues. Once COVID-19 vaccines become more available, countries can expand to vaccinate other priority groups and the general population.[5]

#### Covid vaccines in the world





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#### Which vaccine has greatest global reach? Number of locations currently administering each vaccine



#### **Covid vaccine in India**

COVAXIN<sup>®</sup>, India's indigenous COVID-19 vaccine by Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV).

The indigenous, inactivated vaccine is developed and manufactured in Bharat Biotech's BSL-3 (Bio-Safety Level 3) high containment facility.

The vaccine is developed using Whole-Virion Inactivated Vero Cell derived platform technology. Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects. They contain dead virus, incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection.[8]

Covishield Vaccine

The vaccine created by the Central Drugs Standard Control Organization (CDSCO) is named Covishield. Two doses of this vaccine are being given free by the government.

Zydus Cadila

The three-dose ZyCoV-D vaccine prevented symptomatic disease in 66% of those vaccinated, according to an interim study quoted by the vaccine maker Cadila Healthcare. This is also the first time, the firm claimed, a Covid-19 vaccine had been tested in young people in India. The jab was found to be "safe and very well-tolerated" in this age group.

Sputnik Vaccine[6]

Dr. Reddy's Laboratories has started importing it into India after research on this vaccine made in Russia. The drug is yet to be administered by the Indian drug regulator. 91.6% has been seen in the released data regarding how much Sputnik Vaccine Efficacy Rate was at the time of use of this medicine.

#### **IV. OBSERVATIONS**

#### Sputnik Vaccine Side Effects

Following the first dose of this corona vaccine created by Gamaleya National Center of Epidemiology and Microbiology in Russia, there were some common side effects. It is the first vaccine in the world, which has the



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strength to fight the SARS-CoV-2 virus. This drug has so far been used in 64 countries, including India. Common Sputnik V Vaccine Side Effects are seen after use are seen after which it has been approved.[7]



#### Common side effects were seen after vaccine: -

- 1. Fatigue (70%)
- 2. Joint pain (46.4%)
- 3. Headache (64.7%)
- 4. Muscle ache (61.5%)
- 5. Chills (45.4%)
- 6. Fever (15.5%)
- 7. Nausea and vomiting (23%)

#### **Covishield®:side effects**

Some mild symptoms may occur like injection site tenderness, injection site pain, headache, fatigue, myalgia, malaise, pyrexia, chills and arthralgia, nausea. Very rare events of demyelinating disorders have been reported following vaccination with this vaccine but without the causal relationship establishment.[9]

#### Covaxin®: side effects

Some mild symptoms AEFIs may occur like injection site pain, headache, fatigue, fever, body ache, abdominal pain, nausea and vomiting, dizziness-giddiness, tremor, sweating, cold, cough and injection site swelling. No other vaccine-related serious adverse effects have been reported.

In case of minor adverse effects such as injection site pain, tenderness, malaise, pyrexia, etc., paracetamol may be used to alleviate the symptoms.[10]

#### **V. DISCUSSION**

#### Keep yourself and others safe

#### Protect yourself and those around you:

- Get vaccinated as soon as it's your turn and follow local guidance on vaccination.
- Keep physical distance of at least 1 metre from others, even if they don't appear to be sick. Avoid crowds and close contact.
- Wear a properly fitted mask when physical distancing is not possible and in poorly ventilated settings.



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- Clean your hands frequently with alcohol-based hand rub or soap and water.
- Cover your mouth and nose with a bent elbow or tissue when you cough or sneeze. Dispose of used tissues immediately and clean hands regularly.
- If you develop symptoms or test positive for COVID-19, self-isolate until you recover.[11]



#### To properly wear your mask:

- Make sure your mask covers your nose, mouth and chin.
- Clean your hands before you put your mask on, before and after you take it off, and after you touch it at any time.
- When you take off your mask, store it in a clean plastic bag, and every day either wash it if it's a fabric mask or dispose of it in a trash bin if it's a medical mask.
- Don't use masks with valves.

#### To make your environment as safe as possible:

- Avoid the 3Cs: spaces that are closed, crowded or involve close contact.
- Meet people outside. Outdoor gatherings are safer than indoor ones, particularly if indoor spaces are small and without outdoor air coming in.
- If you can't avoid crowded or indoor settings, take these precautions:
  - Open a window to increase the amount of natural ventilation when indoors.
    - Wear a mask[12]

#### To ensure good hygiene you should:

- Regularly and thoroughly clean your hands with either an alcohol-based hand rub or soap and water. This eliminates germs that may be on your hands, including viruses.
- Cover your mouth and nose with your bent elbow or a tissue when you cough or sneeze. Dispose of the used tissue immediately into a closed bin and wash your hands.
- Clean and disinfect surfaces frequently, especially those which are regularly touched, such as door handles, faucets and phone screens.



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#### If you feel unwell, here's what to do.

- If you have a fever, cough and difficulty breathing, seek medical attention immediately. Call by telephone first and follow the directions of your local health authority.
- Know the full range of symptoms of COVID-19. The most common symptoms of COVID-19 are fever, dry cough, tiredness and loss of taste or smell. Less common symptoms include aches and pains, headache, sore throat, red or irritated eyes, diarrhoea, a skin rash or discolouration of fingers or toes.
- Stay home and self-isolate for 10 days from symptom onset, plus three days after symptoms cease. Call your health care provider or hotline for advice. Have someone bring you supplies. If you need to leave your house or have someone near you, wear a properly fitted mask to avoid infecting others.[13]
- Keep up to date on the latest information from trusted sources, such as WHO or your local and national health authorities. Local and national authorities and public health units are best placed to advise on what people in your area should be doing to protect themselves.

#### VI. CONCLUSION

#### **Prevention from corona**

#### 1. Wash your hands frequently and carefully

Use warm water and soap and rub your hands for at least 20 seconds. Work the lather to your wrists, between your fingers, and under your fingernails. You can also use an antibacterial and antiviral soap.

Use hand sanitizer when you cannot wash your hands properly. Rewash your hands several times a day, especially after touching anything, including your phone or laptop.[14]

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#### 2. Avoid touching your face

SARS-CoV-2 can live on some surfaces for up to 72 hours. You can get the virus on your hands if you touch a surface like:

- gas pump handle
- your cell phone
- a doorknob

Avoid touching any part of your face or head, including your mouth, nose, and eyes. Also avoid biting your fingernails. This can give SARS-CoV-2 a chance to go from your hands into your body.[15]



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#### 3. Stop shaking hands and hugging people — for now

Similarly, avoid touching other people. Skin-to-skin contact can transmit SARS-CoV-2 from one person to another.

#### 4. Don't share personal items

Do not share personal items like:

- phones
- makeup
- combs

It's also important not to share eating utensils and straws. Teach children to recognize their reusable cup, straw, and other dishes for their own use only.



#### **COVID 19 Prevention Practice**

#### 5. Cover your mouth and nose when you cough and sneeze

SARS-CoV-2 is found in high amounts in the nose and mouth. This means it can be carried by air droplets to other people when you cough, sneeze, or talk. It can also land on hard surfaces and stay there for up to 3 days.

Use a tissue or sneeze into your elbow to keep your hands as clean as possible. Wash your hands carefully after you sneeze or cough, regardless.[16]

#### 6. Clean and disinfect surfaces

Use alcohol-based disinfectants to clean hard surfaces in your home like:

- countertops
- door handles
- furniture

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• toys

Also, clean your phone, laptop, and anything else you use regularly several times a day.

Disinfect areas after you bring groceries or packages into your home.

Use white vinegar or hydrogen peroxide solutions for general cleaning in between disinfecting surfaces.[17]



#### 7. Take physical (social) distancing seriously

If you're carrying the SARS-CoV-2 virus, it'll be found in high amounts in your spit (sputum). This can happen even if you don't have symptoms.

Physical (social) distancing, also means staying home and working remotely when possible.

If you must go out for necessities, keep a distance of 6 feet (2 m) from other people. You can transmit the virus by speaking to someone in close contact to you.

#### 8. Do not gather in groups

Being in a group or gathering makes it more likely that you'll be in close contact with someone.

This includes avoiding all religious places of worship, as you may have to sit or stand too close to another congregant. It also includes not congregating at parks or beaches.[18]

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#### 9. Avoid eating or drinking in public places

Now is not the time to go out to eat. This means avoiding restaurants, coffee shops, bars, and other eateries.

The virus can be transmitted through food, utensils, dishes, and cups. It may also be temporarily airborne from other people in the venue.

You can still get delivery or takeaway food. Choose foods that are thoroughly cooked and can be reheated.

High heat (at least 132°F/56°C, according to one recent, not-yet-peer-reviewed lab study) helps to kill coronaviruses.

This means it may be best to avoid cold foods from restaurants and all food from buffets and open salad bars.

#### 10. Wash fresh groceries

Wash all produce under running water before eating or preparing.

The CDCTrusted Source and the FDATrusted Source do not recommend using soap, detergent, or commercial produce wash on things like fruits and vegetables. Be sure to wash hands before and after handling these items.[19]

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#### 11. Wear a (homemade) mask

The Centers for Disease Control and Prevention (CDC) recommendsTrusted Source that almost everyone wears a cloth face mask in public settings where physical distancing may be difficult, such as grocery stores.

When used correctly, these masks can help prevent people who are asymptomatic or undiagnosed from transmitting SARS-CoV-2 when they breathe, talk, sneeze, or cough. This, in turn, slows the transmission of the virus.

The CDC's website provides instructionsTrusted Source for making your own mask at home, using basic materials such as a T-shirt and scissors.

Questions	Main Reasons, Frequency (%)						
	1	2	3	4	5	6	
I. Why you are not willing to use face masks?	6 (10.5)	22 (38.6)	4 (7.0)	13 (22.8)	9 (15.8)	3 (5.3)	
<ol><li>Why you are not willing to maintain physical distan- cing and avoid overcrowding?</li></ol>	11 (13.7)	7 (8.7)	19 (23.8)	27 (33.8)	16 (20.0)	0	
3. Why you are not willing to wash your hands with soap and water?	8 (16.7)	21 (43.7)	5 (10.4)	14 (29.2)	0	0	
4. Why you are not willing to use hand sanitizers?	0	76 (67.8)	13 (11.6)	6 (5.4)	17 (15.2)	0	
5. Why you are not willing to stay home?	15 (12.4)	21 (17.4)	27 (22.3)	23 (19.0)	30 (24.8)	5 (4.1)	
6. Why you are not willing to quarantine yourself if you are suspected?	13 (33.4)	0	7 (17.9)	14 (35.8)	0	5 (12.9)	

Note: 1=COVID-19 is not serious, 2=takes too much effort (time, resource), 3=I do not think I am at risk of contracting COVID-19, 4=I doubt whether the measures help, 5=people in my environment will also not carry out the measure, 6=others.



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#### Some pointers to keep in mind:

- Wearing a mask alone will not prevent you from getting a SARS-CoV-2 infection. Careful handwashing and physical distancing must also be followed.
- Cloth masks aren't as effective as other types of masks, such as surgical masks or N95 respirators. However, these other masks should be reserved for healthcare workers and first responders.
- Wash your hands before you put on your mask.
- Wash your mask after each use.
- You can transfer the virus from your hands to the mask. If you're wearing a mask, avoid touching the front of it.
- You can also transfer the virus from the mask to your hands. Wash your hands if you touch the front of the mask.
- A mask shouldn't be worn by a child under 2 years old, a person who has trouble breathing, or a person who can't remove the mask on their own.[11]

#### **12. Self-quarantine if sick**

Call your doctor if you have any symptoms. Stay home until you recover. Avoid sitting, sleeping, or eating with your loved ones even if you live in the same home.

Wear a mask and wash your hands as much as possible. If you need urgent medical care, wear a mask and let them know you may have COVID-19.

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