A REVIEW ABOUT RISK FACTOR’S, PREVENTION AND THERAPEUTIC IMPACT OF CURRENT COVID-19 PANDEMIC

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Abstract: The novel coronavirus disease (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), remains a global challenge. COVID-19 was first reported in Wuhan, China, it is an emerging infectious disease with widespread and rapid infectiousness. World Health Organization (WHO) has declared COVID-19 as a pandemic on 11 March 2020. WHO coordinating efforts to develop vaccines and medicines to prevent and treat COVID-19, in addition to vaccine development and approaches that directly target the virus or block viral entry.

This article was aimed to review the risk factors, prevention and treatment for COVID-19. Advanced age, Smoking, Immuno compromised persons and Co-morbid illness like Diabetes, Cardiovascular disease and Respiratory Diseases were the risk factors for COVID-19.

Day by day covid-19 cases were increased only known resolution for prevention of covid-19 include frequent hand washing, wear face mask, social distancing etc. Combination of antiviral drugs with hydroxychloroquine and azithromycin may be the best option to treat the patients, depending upon patient's conditions and symptoms.

Keywords: SARS COV-2, Risk factors, Quarantine, Treatment, Remdesivir

INTRODUCTION:

The emergence of Coronavirus disease 2019 is a respiratory illness that are mainly caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and had become pandemic¹. Since the Coronavirus Disease 2019 (COVID-19) outbreak on 31 December 2019 in Wuhan, China, it’s hit 213 countries, areas or territories with 32,498,649 cases and 989,064 deaths as of 25 July 2020. World Health Organization (WHO) has declared COVID-19 as an epidemic on 11 March 2020². COVID-19 has transmitted from one person to another person through direct transmissions, like cough, sneeze, droplet inhalation, and contact transmission, such as the contact with oral, nasal, and eye mucous membranes³.

Most patients with COVID-19 exhibit mild to moderate symptoms, but approximately 15% progress to severe pneumonia and about 5% eventually develop acute respiratory distress syndrome (ARDS), septic shock and/or multiple organ failure¹. The World Health Organisation (WHO) estimates that the incubation period from infection to presentation of symptoms is 5.2 days, with a range of 1–14 days⁴.

The most important treatment of COVID-19 includes symptomatic management and oxygen therapy, with mechanical ventilation for patients with respiratory failure. There are several antiviral drugs, including the nucleotide analogue remdesivir, are being actively tested, none has been specifically approved for COVID-19. WHO coordinating efforts to develop vaccines and medicines to prevent and treat COVID-19, additionally to vaccination development and approaches that directly target the virus or block viral entry, treatments that address the immunopathology of the infection have become a serious focus.

Multiple protocols and management strategies are currently being developed worldwide to beat the issue. However, in resource-limited settings like India which cope with an enormous population base, it’s critical for the doctors to be equipped to speedily identify and treat patients who require admission and critical care. Preventive measures are the present strategy to limit the spread of cases. Now a day's drastic increases of number of cases in day by day. Early diagnosis, isolation, screening and treatment which are necessary to prevent further spread of COVID-19. Preventive strategies which are focused on the isolation of patients and careful infection control, including appropriate measures to be adopted during the diagnosis and the provision of clinical care to an infected patient.

RISK FACTORS FOR COVID-19

Current reports suggest that all demographics of the global population could be susceptible to infection of COVID-19, however there are some groups that are at higher risk of severe disease⁵. According to the CDC, older adults - further classified as over 65 years of age - are more at risk of severe disease than younger people⁶. Furthermore, patients with serious chronic underlying medical conditions, namely cardiovascular disease, diabetes, cancer (especially of the lung), chronic obstructive pulmonary disease, and hypertension are at an increased risk of severe complications⁶. A study by Michael Roth et al⁸ hypothesise that diabetes and hypertension treatment with ACE2-stimulating drugs increases the risk of developing severe and fatal COVID-19. This study suggests that patients with cardiac diseases, hypertension,
or diabetes, who are treated with ACE2-increasing drugs, are at higher risk for severe COVID-19 infection and, therefore, should be monitored for ACE2-modulating medications, such as ACE inhibitors or ARBs.

Meta-analysis of Z. Zheng, F. Peng and B. Xu et al. showed that male, aged over 65 and smoking patients might face a greater risk of developing into the critical or mortal condition and the comorbidities such as hypertension, diabetes, cardiovascular disease or respiratory diseases, the body is in a state of stress for a long time and the immunity could also greatly affect the prognosis of the COVID-19.

Dong et al. analysed 2143 pediatric COVID-19 patients across China, and found that children were susceptible to COVID-19. Bi Q, Wu Y, Mei S, et al. was reported that female contacts were more likely to be infected by SARS-CoV-2 than male contacts. T. Liu et al. found that females have more prone to occur COVID-19 than the males and their findings suggest that more preventive measures must be specifically implemented to protect females from infection during the epidemic of COVID-19.

Li Q, Guan X, Wu P, et al. found that death cases were more common in the elderly and patients with chronic underlying diseases. Approximately one-third to one-half of severe patients had underlying comorbidities, including diabetes, hypertension, and cardiovascular disease.

Jamieson DJ et al. reported that, during pregnancy, women will have some immune changes, which may lead to the sensitivity and severity of infectious diseases, the current outbreak of COVID-19, pregnant women have a high risk of developing severe infections.

Occupational risks have also been identified by various authorities. During the preliminary stages of the COVID-19 outbreak, employees of seafood and wholesale markets were most at risk of contracting the virus. There is high risk to healthcare workers who regularly came into contact with patients with suspected COVID-19. As a result, healthcare workers with pre-existing risks such as an increased age or chronic respiratory disease were more prone to develop COVID-19.

A review by Rod J E et al. found that risk factor should at a minimum include age >50 years, diabetes, smoking, respiratory disease, cancer and CVD.

COVID-19 PREVENTIONS

The strongest and most effective weapon of the COVID-19 is the limiting the spread of the virus. The WHO has stated that education, isolation, prevention, controlling the transmission, and treatment of infected persons are the critical steps in controlling contagious diseases like COVID-19. Preventive strategies that are focused on isolation of patients and careful infection control, including appropriate measures to be adopted during the diagnosis and the provision of clinical care to an infected patients.

The most important strategy for the population to undertake is frequently wash their hands and use alcohol-based hand sanitizer and avoid contact with their face and mouth after interacting with contaminated environment. To reduce the risk of transmission, individuals must be advised to wash hands diligently, practice respiratory hygiene (i.e., cover their cough), and avoid crowds and close contact with infected individuals.

Social distancing is advised in locations that have community transmission and installed quarantine helps to reduce further spread of virus.

PERSONAL PROTECTIVE EQUIPMENT

If people without respiratory symptoms, the WHO doesn’t recommend wearing a medical mask within the community. The improper use of the mask were increase chance of COVID-19 infection.

<table>
<thead>
<tr>
<th>Quarantine</th>
<th>Other measures</th>
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<tr>
<td>Voluntary quarantine</td>
<td>Hand hygiene</td>
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<td>(self-quarantine)</td>
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<tr>
<td>Mandatory quarantine</td>
<td>Isolation</td>
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<tr>
<td>o Private residence</td>
<td>Personal protective equipment</td>
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<tr>
<td>o Hospital</td>
<td>School measures/closures</td>
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<tr>
<td>o Public institution</td>
<td>Social distancing</td>
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<tr>
<td>o Others (cruise ships, etc)</td>
<td>Workplace measures/closures</td>
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</table>

In order to reduce the COVID-19 transmission from potentially asymptomatic or presymptomatic people, the ECDC recommends the use of face masks. The use of face masks in the community maybe serve as a source of control. This measure are often particularly relevant in epidemic situations when the number of asymptomatic but infectious persons within the community are often assumed to be high. Individuals who are caring for patients with suspected or documented COVID-19 at home should also wear face cover when in the same room as that patient (if the patient cannot wear a face cover).

Figure 1: Precautiona for COVID-19 Infection
SOCIAL DISTANCING

Social distancing helps to reduce interactions between people during a broader community, in which individuals could also be infectious but haven’t yet been identified hence not yet isolated. Social distancing will help to reduce the chance of COVID-19 transmission. Wei WE et al reported that the infectiousness of SARS-CoV-2 within the presymptomatic stage; social distancing is thus of critical importance in establishing control over the pandemic.

QUARANTINE

Quarantine is one of the oldest and effective tools of controlling communicable disease outbreaks. The quarantine of persons is the restriction of all activities or separation of persons who aren’t ill but who may be exposed to an infective agent or disease, with the target of monitoring their symptoms and early detection of cases. Quarantine is different from isolation, which is that the separation of infected persons from others to prevent the further spread of contamination. Pan A et al conclude that quarantine is the most effective method in reducing both the number of infected and dead. WHO recommends 14 days of room quarantine when person is contact with COVID-19 infected person. Actively monitoring the people who are quarantined, is one of the most important points for controlling the epidemic in the society.

CLEANING AND DISINFECTION

High-touch areas like bedside tables and door handles should be disinfected daily with regular household disinfectant containing a diluted bleach solution. Disposable gloves must be used when cleaning or handling surfaces, clothing, or linen soiled with body fluids. All used contaminated disposable items should be placed in a container before disposing them with other household waste.

INCREASING TESTING CAPACITY

Another important thing is preventing the spread of the disease throughout society so increase the number of tests and thus pinpoint more cases, isolate them, and trace those that are in contact. Diagnostic testing maybe a critical component of the nation’s strategy to meet the challenges of the COVID-19 pandemic. Different methods like rapid-testing kits, serologic methods and self-collected specimen tests are getting used throughout the world to determine cases.

TREATMENT FOR COVID-19

Currently, there is no medication recommended to treat COVID-19, and no cure is available. Antibiotics aren’t effective against viral infections such as COVID-19. Researchers are testing a variety of possible treatments.

NIH TREATMENT GUIDELINES FOR COVID-19

REMDESIVIR

The antiviral drug like remdesivir gained emergency use authorization (EUA) from the FDA on 1st May, 2020, based on preliminary data showing a faster time to recovery of hospitalized patients with severe disease.

Remdesivir has been shown to inhibit replication of other human coronaviruses related with high morbidity in tissue cultures, including severe SARS-CoV (acute respiratory syndrome coronavirus) in 2003 and MERS-CoV (Middle East respiratory syndrome coronavirus) in 2012. Remdesivir has been studied in several clinical trials for the treatment of COVID-19. The treatment guideline panel were supported these studies. Remdesivir should be available through the Food and Drug Administration (FDA) Emergency Use Authorization (EUA) for people with severe COVID-19. An open label trial of hospitalized patients with severe COVID-19 showed that remdesivir treatment for 5 or 10 days had similar clinical benefit.

Beigel JH et al conduct a randomized, placebo controlled, double-blind phase 3 clinical trial in hospitalized patients with COVID-19 revealed that compared to placebo, remdesivir was associated with shorter time to recovery (11 vs.15 days). Another study revealed that remdesivir and chloroquine are very effective against SARS-CoV-2 in vitro.
CHLOROQUINE OR HYDROXYCHLOROQUINE WITH OR WITHOUT AZITHROMYCIN

Chloroquine is an antimalarial drug that was developed in 1934. Hydroxychloroquine, an analogue of chloroquine, was developed in 1946. Both chloroquine and hydroxychloroquine increase the endosomal pH, inhibiting fusion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the host cell membranes. Chloroquine inhibits glycosylation of the cellular angiotensin-converting enzyme 2 receptor, which interferes with binding of SARS-CoV to the cell receptor. Both chloroquine and hydroxychloroquine also have immunomodulatory effects. It has been hypothesized that these effects are other potential mechanisms of action for the treatment of COVID-19.

High-dose chloroquine (600 mg twice daily for 10 days) has been associated with more severe toxicities than lower-dose chloroquine (450 mg twice daily for 1 day, followed by 450 mg once daily for 4 days). Hydroxychloroquine with azithromycin are approved and Chloroquine with azithromycin are not approved by the Food and Drug Administration (FDA) for the treatment of COVID-19. Gautret P et al conducted a small non-randomized study azithromycin in combination with HCQ has demonstrated substantial antiviral activity against SARS-CoV-2. Literature on azithromycin alone as a treatment option for COVID-19 is scarce, and it is not clear whether macrolides can be used alone or should be in combination with HCQ.

Masashi et al. believe that macrolides alone, or in combination with other drugs, are effective against SARS-CoV-2. Wang M et al revealed that remdesivir and chloroquine are very effective against SARS-CoV-2 in vitro.

IVERMECTIN

Ivermectin is a Food and Drug Administration (FDA)-approved antiparasitic drug that is used to treat several neglected tropical diseases, including onchocerciasis, helminthiases, and scabies. Ivermectin acts by inhibiting the host importin alpha/beta-1 nuclear transport proteins, which are part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host antiviral response. Ivermectin isn’t approved for the treatment of any viral infection, including SARS-CoV-2 infection.

L. Caly et al conducted a study on adding five μM of Ivermectin to virus-infected Vero/hSLAM cells reduced the levels of viral RNA by 5,000 times after 48-hour culture. So, it could be effective against COVID-19.

LOPINAVIR/RITONAVIR AND OTHER HIV PROTEASE INHIBITORS

Lopinavir/ritonavir and darunavir/cobicistat etc have been studied in patients with COVID-19. The replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) depends upon the cleavage of polyproteins into an RNA-dependent RNA polymerase and a helicase. Lopinavir/ritonavir or other HIV protease inhibitors are approved for the treatment of COVID-19.

A study by Kim JY et al revealed that decreased viral load next day after administration of lopinavir/ritonavir; therefore, further studies are needed to determine the direct antiviral effect of lopinavir/ritonavir.

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>DOZING REGIMENS</th>
<th>ADVERSE EFFECTS</th>
<th>PANEL’S RECOMMENDATIONS</th>
</tr>
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<tbody>
<tr>
<td>Azithromycin</td>
<td>AZM 500 mg PO once on Day 1, then AZM 250 mg PO daily on Days 2–5</td>
<td>Gastrointestinal effects (e.g., diarrhea, nausea, vomiting)</td>
<td>The Panel recommends against using HCQ plus AZM to treat COVID-19, except in a clinical trial</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>CQ 1 g PO once on Day 1, then CQ 500 mg PO once daily for 4–7 days of total treatment. Treatment duration should be based on clinical evaluation.</td>
<td>Prolonged QTc interval, torsades de pointes, AV block, ventricular arrhythmia, gastrointestinal effects (e.g., nausea, vomiting, diarrhea), Hepatitis, Hypoglycemia</td>
<td>The Panel recommends against the use of CQ for the treatment of COVID-19, in hospitalized patients. In non-hospitalized patients, the Panel recommends against the use of CQ for the treatment of COVID-19, except in a clinical trial. The Panel recommends against using high-dose CQ (600 mg twice daily for 10 days) for the treatment of COVID-19</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>HCQ 800 mg PO once on Day 1, then HCQ 400 mg PO once daily for 4–7 days of total treatment. Treatment duration should be based on clinical evaluation.</td>
<td>Prolonged QTc interval, torsades de pointes, AV block, ventricular arrhythmia, gastrointestinal effects</td>
<td>The Panel recommends against the use of HCQ for the treatment of COVID-19 in hospitalized patients. In non-hospitalized patients, the Panel recommends against the use of HCQ for the treatment of COVID-19, except in a clinical trial. The Panel recommends</td>
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CONVALESCENT PLASMA

There are insufficient data for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend for the use of COVID-19 convalescent plasma against the COVID-19. Plasma from donors who have recovered from COVID-19 may contain antibodies to SARS-CoV-2 that may help suppress the virus and modify the inflammatory response. Salazar et al. revealed that case series of 25 patients indicate that administration of convalescent plasma is a safe treatment option for those with severe COVID-19 disease. Karthick et al. concluded that in addition to antiviral/antimicrobial drugs, CPT could be an effective therapeutic option with promising evidence on safety, improvement of clinical symptoms, and reduced mortality.

IMMUNOGLOBULINS: SARS-COV-2 SPECIFIC

There are insufficient data for the COVID-19 Treatment Guidelines Panel to recommend either for or against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulins for the treatment of COVID-19. Concentrated antibody preparations which are derived from pooled plasma collected from individuals who have recovered from COVID-19 can be manufactured as SARS-CoV-2 immunoglobulin, which could potentially suppress the virus and modify the inflammatory response. The use of virus-specific immunoglobulins for other viral infections (e.g., cytomegalovirus [CMV] immunoglobulin for the prevention of post-transplant CMV infection and varicella zoster immunoglobulin for postexposure prophylaxis of varicella in individuals at high-risk) has proven to be safe and effective; however, there are currently no clinical data on the use of such products for COVID-19. Potential risks may include transfusion reactions. Roback JD et al. concluded that method of passive antibody therapy can provide an effective treatment against the rapidly rising pandemic of COVID-19.

IMMUNOGLOBULINS: NON-SARS-COV-2 SPECIFIC

The COVID-19 Treatment Guidelines Panel recommends against the use of non-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) specific intravenous immunoglobulin (IVIG) for the treatment of COVID-19, except in a clinical trial. Products which are derived from the plasma of donors without confirmed SARS-CoV-2 infection contain high titer of SARS-CoV-2 neutralizing antibodies.

MESENCHYMAL STEM CELLS

MSCs are investigational products that have been studied extensively for broad clinical applications in regenerative medicine and for their immunomodulatory properties. No MSCs are approved by the Food and Drug Administration (FDA) for the treatment of COVID-19. MSCs are multipotent adult stem cells that are present in most human tissues, including the umbilical cord. MSCs can self-renew by dividing and can differentiate into multiple types of tissues, including osteoblasts, chondroblasts, adipocytes, hepatocytes, and others, which has led to an important in clinical research agenda in regenerative medicine. It is hypothesized that MSCs could reduce the acute lung injury and inhibit the cell-mediated inflammatory response induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

CORTICOSTEROIDS

Patients with severe COVID-19 can develop a systemic inflammatory response, which can lead to lung injury and multisystem organ dysfunction. It’s been proposed that the potent anti-inflammatory effects of corticosteroids might prevent or mitigate these deleterious effects. The COVID-19 Treatment Guidelines Panel (the Panel) recommends using dexamethasone 6 mg per day for up to 10 days or until hospital discharge, whichever comes first, for the treatment of COVID-19 in hospitalized patients. If dexamethasone isn’t available, the Panel recommends using alternative glucocorticoids like prednisone, methylprednisolone, or hydrocortisone.

Zhang X et al. study was conducted study on the treatment of porcine respiratory coronavirus with dexamethasone and showed that one or two doses at earlier stages are effective in reducing pro-inflammatory responses but prolonged use may play a
role in enhancing viral replication. Cai Y, et al concluded that other studies suggest a benefit of corticosteroids in lowering overall mortality in patients with moderate disease, severe disease, and ARDS.

INTERFERONS (ALFA, BETA)

The COVID-19 Treatment Guidelines Panel recommends against the use of interferons for the treatment of patients with severe or critical COVID-19, except in a clinical trial. There are insufficient data to recommend either for or against the use of interferon beta for the treatment of early (i.e., ≤7 days from symptom onset) mild and moderate COVID-19. Shen et al. stated that interferon-2a can effectively reduce the infection rate of SARS-CoV-2, which further supports the above hypothesis.

INTERLEUKIN-1 INHIBITORS

There are insufficient data to recommend for or against the use of interleukin (IL)-1 inhibitors, such as anakinra, for the treatment of COVID-19. Anakinra is a recombinant human IL-1 receptor antagonist. It is approved by the Food and Drug Administration (FDA) to treat rheumatoid arthritis and cryopyrin-associated periodic syndromes, specifically neonatal-onset multisystem inflammatory disease. Endogenous IL-1 is elevated in patients with COVID-19 and other conditions, such as severe COVID-19.

INTERLEUKIN-6 INHIBITORS

Interleukin (IL)-6 is a pleiotropic, pro-inflammatory cytokine produced by a variety of cell types, including lymphocytes, monocytes, and fibroblasts. Infection by the severe acute respiratory syndrome associated coronavirus (SARS-CoV) induces a dose-dependent production of IL-6 from bronchial epithelial cells COVID-19-associated systemic inflammation and hypoxic respiratory failure can be associated with heightened cytokine release, as indicated by elevated blood levels of IL-6, C-reactive protein (CRP), D-dimer, and ferritin. There are two classes of Food and Drug Administration (FDA)-approved IL-6 inhibitors: anti-IL-6 receptor monoclonal antibodies (e.g., sarilumab, tocilizumab) and anti-IL-6 monoclonal antibodies (siltuximab). These classes of drugs have been evaluated for the management of patients with COVID-19 who have systemic inflammation.

ANTI-INTERLEUKIN-6 RECEPTOR MONOCLONAL ANTIBODIES

Sarilumab

Sarilumab is a recombinant humanized anti-IL-6 receptor monoclonal antibody that is approved by the FDA for use in patients with rheumatoid arthritis. It is available as a subcutaneous (SQ) formulation and is not approved for the treatment of cytokine release syndrome (CRS). A placebo-controlled clinical trial is evaluating the use of an intravenous (IV) formulation of sarilumab administered as a single dose for COVID-19.

Tocilizumab

Tocilizumab is a recombinant humanized anti-IL-6 receptor monoclonal antibody that is approved by the FDA for use in patients with rheumatologic disorders and CRS induced by chimeric antigen receptor T cell (CAR-T) therapy. Tocilizumab can be dosed for IV or SQ injection. For CRS, the IV formulation should be used. Zhang et al conducted a study of severe or critical COVID-19 patients with Tocilizumab within few days the symptoms were resolved.

ANTI-INTERLEUKIN-6 MONOCLONAL ANTIBODY

Siltuximab

Siltuximab is a recombinant human-mouse chimeric monoclonal antibody that binds IL-6 and is approved by the FDA for use in patients with Castleman’s disease. Siltuximab prevents the binding of IL-6 to both soluble and membrane-bound IL-6 receptors, inhibiting IL-6 signaling. Siltuximab is dosed as an IV infusion.

KINASE INHIBITORS: BRUTON’S TYROSINE KINASE INHIBITORS AND JANUS KINASE INHIBITORS

The COVID-19 Treatment Guidelines Panel recommends against the use of Bruton’s tyrosine kinase (BTK) inhibitors, such as Acalabrutinib, Ibrutinib, and Zanubrutinib; and Janus kinase (JAK) inhibitors, such as Baricitinib, Ruxolitinib, and Tofacitinib; for the treatment of COVID-19, except in a clinical trial. The kinase inhibitors are proposed as treatments for COVID-19 because they can prevent phosphorylation of key proteins involved in the signal transduction that leads to immune activation and inflammation (e.g., the cellular response to proinflammatory cytokines such as interleukin [IL]-6). This immunosuppression could potentially reduce the inflammation and associated immunopathologies that have been observed in patients with COVID-19.
Table: 3 FDA approved drugs for COVID-19

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>DOSING REGIMEN’S</th>
<th>ADVERSE EFFECTS</th>
<th>PANEL RECOMMENDATION</th>
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<tbody>
<tr>
<td><strong>Immunomodulators</strong></td>
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<tr>
<td>Dexamethasone</td>
<td>Dexamethasone 6 mg daily IV or PO, for up to 10 days</td>
<td>• Hyperglycemia&lt;br&gt;• Secondary infections&lt;br&gt;• Reactivation of latent infections (e.g., HBV, HSV, strongyloidiasis, TB)&lt;br&gt;• Psychiatric disturbances&lt;br&gt;• Avascular necrosis&lt;br&gt;• Adrenal insufficiency&lt;br&gt;• Increased blood pressure</td>
<td>The Panel <strong>recommends against</strong> using dexamethasone for the treatment of COVID-19 in patients who do not require supplemental oxygen</td>
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<tr>
<td><strong>Corticosteroids</strong></td>
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<tr>
<td>Dexamethasone</td>
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<tr>
<td><strong>Interleukin-1 Inhibitor</strong></td>
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<tr>
<td>Anakinra</td>
<td>• Standard adult dose is anakinra 100 mg SQ once daily&lt;br&gt;• Has also been used IV</td>
<td>• Neutropenia&lt;br&gt;• Anaphylaxis&lt;br&gt;• Headache, nausea, diarrhea, sinusitis, arthralgia, flu-like symptoms, and abdominal pain</td>
<td>There are insufficient data for the Panel to recommend either for or against the use of IL-1 inhibitors (e.g., anakinra) for the treatment of COVID-19.</td>
</tr>
<tr>
<td><strong>Interleukin-6 Inhibitors</strong></td>
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<tr>
<td>Anti-Interleukin-6 Receptor Monoclonal Antibodies</td>
<td>Sarilumab 400 mg IV (single dose)</td>
<td>Neutropenia, thrombocytopenia&lt;br&gt;• Gastrointestinal perforation&lt;br&gt;• HSR&lt;br&gt;• Increased liver enzymes</td>
<td>The Panel <strong>recommends against</strong> the use of sarilumab for the treatment of COVID-19, except in a clinical trial</td>
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<tr>
<td>Sarilumab</td>
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<tr>
<td>Tocilizumab</td>
<td>Tocilizumab 8 mg/kg IV once&lt;br&gt;• Dose should not exceed tocilizumab 800 mg.</td>
<td>• Infusion-related reactions&lt;br&gt;• HSR&lt;br&gt;• Gastrointestinal perforation&lt;br&gt;• Hepatotoxicity</td>
<td>The Panel <strong>recommends against</strong> the use of tocilizumab for the treatment of COVID-19, except in a clinical trial</td>
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<tr>
<td><strong>Anti-Interleukin-6 Monoclonal Antibody</strong></td>
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</table>
| Siltuximab | Siltuximab 11 mg/kg IV over 1 hour every 3 weeks for multicentric Castleman disease | • Infusion-related reaction  
• HSR  
• Gastrointestinal perforation  
• Neutropenia  
• Hypertension  
• Dizziness | The Panel recommends against the use of siltuximab for the treatment of COVID-19, except in a clinical trial |
| --- | --- | --- | --- |
| **Bruton’s Tyrosine Kinase Inhibitors** | Dose for FDA-Approved Indications:  
• Acalabrutinib 100 mg PO every 12 hours  
• Ibrutinib 420 mg or 560 mg PO once daily  
• Zanubrutinib 160 mg PO twice daily or 320 mg PO once daily | • Hemorrhage  
• Cytopenias (neutropenia, anemia,)  
• Atrial fibrillation and flutter  
• Infection  
• Diarrhea  
• Cytopenias  
• Atrial fibrillation and flutter  
• Infection  
• Rash | The Panel recommends against the use of BTK inhibitors for the treatment of COVID-19, except in a clinical trial |
| **Acalabrutinib** | **Doses for FDA-Approved Indications:**  
• Acalabrutinib 100 mg PO every 12 hours  
• Dose and duration for COVID-19 unknown | | |
| **Ibrutinib** | **Doses for FDA-Approved Indications:**  
• Ibrutinib 420 mg or 560 mg PO once daily  
• Dose and duration for COVID-19 unknown | | |
| **Zanubrutinib** | **Doses for FDA-Approved Indications:**  
• Zanubrutinib 160 mg PO twice daily or 320 mg PO once daily  
• Dose and duration for COVID-19 unknown | | |
| **Janus Kinase Inhibitors** | **Doses for COVID-19 in clinical trial**  
• Baricitinib 2 mg–4 mg PO once daily for 7–14 days | | The Panel recommends against the use of JAK inhibitors for the treatment of COVID-19, except in a clinical trial |
| **Baricitinib** | **Doses for COVID-19 in clinical trial**  
• Baricitinib 2 mg–4 mg PO once daily for 7–14 days | **Lymphoma and other malignancies**  
**Thrombosis**  
**Gastrointestinal perforation**  
**Treatment related changes in lymphocytes, neutrophils, haemoglobin, liver enzymes** | |
| **Ruxolitinib** | **Doses in COVID-19 clinical trials** range from ruxolitinib 5 mg PO twice daily to 20 mg PO twice daily, for 14 days. | • Anemia  
• Neutropenia  
• Liver enzyme elevations  
• Risk of infection  
• Dizziness  
• Headache | The Panel recommends against the use of JAK inhibitors for the treatment of COVID-19, except in a clinical trial |
| **Tofacitinib** | **Doses for FDA-Approved** | • Anemia  
• Risk of infection | The Panel recommends against the use of JAK inhibitors for the treatment |

The Panel recommends against the use of JAK inhibitors for the treatment of COVID-19, except in a clinical trial.
VITAMIN C

Vitamin C (ascorbic acid) is a water-soluble vitamin that thought to have beneficial effects in patients with severe and critical illnesses. Because serious COVID-19 may cause sepsis and acute respiratory distress syndrome (ARDS), the potential role of high doses of vitamin C in ameliorating inflammation and vascular injury in patients with COVID-19. There are insufficient data for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of vitamin C for the treatment of COVID-19 in noncritically ill patients and critically ill patients H. Hemila et al. suggested that Vitamin C could also be effective in preventing COVID-19 as it can reduce the severity of lower respiratory tract infections.

VITAMIN D

There are insufficient data to recommend the use of vitamin D for the prevention or treatment of COVID-19. The role of vitamin D supplementation in the prevention or treatment of COVID-19 is unknown. The rationale for using vitamin D is based largely on immunomodulatory effects that could potentially protect against COVID-19 infection or decrease the severity of illness. Wang L-s et al. suggested that the supplementation with vitamin D and vitamin E might increase resistance to SARS-CoV-2.

ZINC SUPPLEMENTATION AND COVID-19

The COVID-19 Treatment Guidelines Panel (the Panel) recommends using zinc supplementation above the recommended dietary allowance for the prevention of COVID-19, except in a clinical trial. The relationship between zinc and COVID-19, including how zinc deficiency affects the severity of COVID-19 and whether zinc supplements can improve clinical outcomes, is currently under investigation. The doses used in registered clinical trials for COVID-19 vary between studies, with a maximum dose of zinc sulfate 220 mg (50 mg of elemental zinc) twice daily.

COVID-19 TREATMENT IN INDIA

Indian government has strictly practicing of social distancing and implemented complete nation-wide lockdown to limit the spread of virus. Nation-wide complete lockdown has been executed in four phases; (1) March 25 – April 14, (2) April 14 – May 3, (3) May 4 – May 17, and May 18 – May 31, 2020. Presently, there is neither any vaccine nor any specific antiviral drug available against SARS-CoV-2. The potential vaccines as well as specific drug actions are being investigated via clinical trials. It should be taken minimum of 1 or 2 years for successful development of vaccination for COVID-19.

Anti-malarial drug like HCQ should be recommended for prophylactic use for asymptomatic healthcare personnel handling COVID-19 cases, asymptomatic frontline personnel, including para military/police staff related with COVID-19 associated activities (400 mg twice a day for 1 day subsequently 400 mg once every week for 7 weeks), and asymptomatic household contacts of the confirmed patients (400 mg twice a day for 1 day subsequently 400 mg once every week for 3 weeks). However, it is not recommended for kids with ages <15 years, pregnant and lactating women’s.

A combination of HCQ (400 mg twice a day for 1 day subsequently 200 mg twice a day for 4 days) and azithromycin antibiotic drug (500 mg once a day for 5 days) is recommended for patients with serious sickness under the appropriate medical supervision. Proper medical supervision and monitoring of any side effects including QTc interval is mandatory. India has used convalescent plasma therapy for severely-ill patients and also launched “ArogyaSetu” application an informative tool for proper awareness of COVID-19.

CONCLUSION

SARS COV- 2 is a novel and highly contagious virus. All over the world is stagnated in covid 19. Day by day number of covid cases in the world were increases. There are many risk factors for covid-19 such as age over 50years, Smoking, immunocompromised patients and co-morbid illness like diabetes, cardiovascular diseases, respiratory diseases, etc.

Proper prevention’s like wear face mask, Hand hygiene, social distancing and quarantine helps to reduce the spread of covid-19. Increasing testing capacity helps to detecting more positive patients in the community and also will enable the reduction of secondary cases with stricter quarantine rules.
There is no specific drug therapy for COVID-19 disease up to now. After reviewing number of case studies, we concluded that, Remdesivir and Hydroxychloroquine/Chloroquine with or without Azithromycin are promising treatment options for patients with mild and moderate COVID-19. However, Tocilizumab and Immunoglobulin therapy seem to be effective in treating severe disease.

Combinational therapies with some of the above-mentioned drugs or supplements, with an appropriate immunomodulatory diet, and proper mental support should be effective against COVID-19 infection.

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