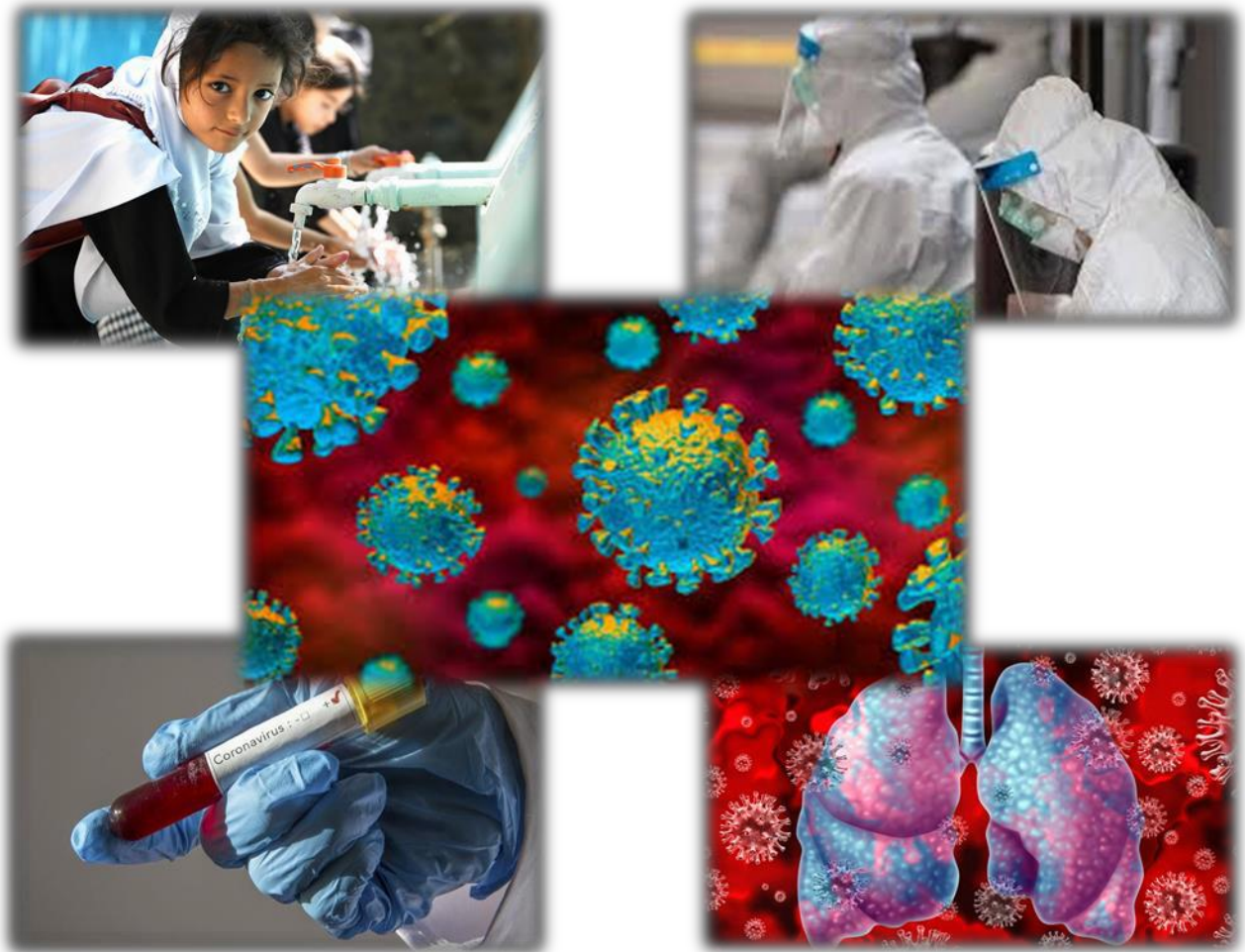




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Guidelines

Clinical Management Guidelines for COVID-19 Infections



Case Definitions and Testing Criteria

Viral Lab testing for COVID 19

Testing should be performed using PCR of a nasopharyngeal or oropharyngeal swab. Serology (IgM/IgG tests) are NOT recommended as primary means for diagnosis. Testing is based on symptoms and priority is given to certain individuals

High Priority

- Hospitalized patients with symptoms
- Healthcare workers and workers in congregate living settings with symptoms
- Residents in long-term care facilities or other congregate living settings, including prisons, shelters and hostels, with symptoms

Priority

- Outpatients with symptoms of potential COVID-19 infection, including: fever, cough, shortness of breath, chills, muscle pain, new loss of taste or smell, vomiting or diarrhea, and/or sore throat.
- Healthcare workers without symptoms, but with a history of exposure to a COVID positive patient
- Persons/TTQ identified individuals without symptoms, but with a history of close contact with a COVID positive patient/

Clinical classification of suspected or confirmed COVID-19 patients

Patients can be classified into asymptomatic, mild, moderate and severe based on their presentation.

Asymptomatic

SARS CoV2 infection but with no symptoms

Pre-symptomatic

SARS-CoV2 infection in an individual not yet symptomatic

Mild Oxygen saturation >94%

Presence of symptoms consistent with COVID such as fever, fatigue, cough, anorexia, malaise, muscle pain, sore throat, nasal congestion, or headache without any hemodynamic compromise, need for oxygen or chest x-ray findings.

Moderate

Hypoxia (Oxygen saturation \leq 94% but >90%) or chest X-ray with infiltrates involving <50% of the lung fields

Mild disease

- Upper respiratory symptoms (eg, pharyngeal congestion, sore throat, and fever) for a short duration or asymptomatic infection
- Positive RT-PCR test for SARS-CoV-2
- No abnormal radiographic and septic presentation

Moderate disease

- Mild pneumonia
- Symptoms such as fever, cough, fatigue, headache, and myalgia
- No complications and manifestations related to severe conditions

Severe disease

Mild or moderate clinical features, plus any manifestations that suggest disease progression:

- Rapid breath (\geq 70 breaths per min for infants aged <1 year; \geq 50 breaths per min for children aged >1 year)
- Hypoxia
- Lack of consciousness, depression, coma, convulsions
- Dehydration, difficulty feeding, gastrointestinal dysfunction
- Myocardial injury
- Elevated liver enzymes
- Coagulation dysfunction, rhabdomyolysis, and any other
- manifestations suggesting injuries to vital organs

Critical illness

Rapid disease progression, plus any other conditions:

- Respiratory failure with need for mechanical ventilation (eg, ARDS, persistent hypoxia that cannot be alleviated by inhalation through nasal catheters or masks)
- Septic shock
- Organ failure that needs monitoring in the ICU

COVID-19=coronavirus disease 2019. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. ARDS=acute respiratory distress syndrome. ICU=intensive care unit.

No complications and manifestations related to severe condition

Severe

Clinical signs of pneumonia (fever/ cough) plus any of the following:

- Respiratory rate > 30
- Severe respiratory distress;
- SpO₂ ≤ 90% on room air.

Critical

Any of the three manifestations

1. ARDS

- **Onset:** Within 1 week of a known clinical insult (i.e. pneumonia) or new or worsening respiratory symptoms.
- **Chest imaging:** (X-ray or CT scan): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules. Origin of pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of infiltrates/edema if no risk factor presents.
- **Oxygenation** impairment in adults
 - Mild ARDS: 200 mmHg < PaO₂/FiO₂ ≤ 300 mmHg (with PEEP or CPAP ≥ 5 cmH₂O).
 - Moderate ARDS: 100 mmHg < PaO₂/FiO₂ ≤ 200 mmHg (with PEEP ≥ 5 cmH₂O).
 - Severe ARDS: PaO₂/FiO₂ ≤ 100 mmHg (with PEEP ≥ 5 cmH₂O)

2. Sepsis

- Acute life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection.
- Signs of organ dysfunction include:
 - Altered mental status,
 - Difficult or fast breathing,
 - Low oxygen saturation,
 - Reduced urine output,
 - Fast heart rate,
 - Weak pulse,
 - Cold extremities or low blood pressure,
 - Skin mottling,
 - Laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia.

3. Septic Shock

- Persistent hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L

Hypercoagulability and COVID-19

Some patients with COVID-19 may develop signs of a hypercoagulable state and be at increased risk for venous and arterial thrombosis of large and small vessels. **Laboratory abnormalities** of COVID-19-associated coagulopathy include:

- Mild thrombocytopenia
- Increased D-dimer levels (strongly associated with greater risk of death)
- Increased fibrin degradation products



- Prolonged prothrombin time

Thrombotic complications, of hospitalized patients are most frequently deep venous thrombosis and pulmonary embolism. Other reported manifestations include:

- Microvascular thrombosis of the toes
- Clotting of catheters
- Myocardial injury with ST-segment elevation
- Large vessel strokes

Criteria for admission of suspected or confirmed COVID-19 patients

Asymptomatic and mild disease

Asymptomatic and mild cases can be managed at home with home isolation. Criteria for home isolation include:

- Those with a separate room to stay in with a separate bathroom
- Those consenting for isolation

Patients with mild or asymptomatic disease who do not have adequate home arrangements or do not consent to stay at home should be shifted to a dedicated isolation facility (as opposed to a hospital). However, the following may be considered for hospital admission for observation if resources allow.

1. Immunosuppressed (on long term steroids or other immunosuppression)
2. Age greater than or equal to 65 years
3. Co-morbid conditions: Heart Failure, Decompensated Liver Disease, Structural Lung Disease, Uncontrolled Diabetes, Chronic Kidney Disease

Moderate, severe and critical disease

Patients with the above categories should be admitted to a hospital for further management.

- Moderate disease: Admit to the general ward
- Severe disease: Admit to high dependency unit with negative pressure room
- Critical disease: Admit to ICU with negative pressure room

Management

Prophylaxis

There is no role of prophylactic chloroquine or hydroxychloroquine currently. Both these drugs are being studied for treatment of COVID. The results thus far are not robust enough that either drugs can be clearly labeled as effective in treatment of COVID. Moreover, given the side-effects associated with use of chloroquine or hydroxychloroquine (especially chronic use), the limited stocks (for moderately sick) and the lack of data showing use will prevent the infection, prophylactic use is **strongly discouraged**.

Management of mild disease

- Mild cases should be treated with supportive care only. This includes acetaminophen for fever, oral hydration in case of diarrhea and antihistamines for rhinorrhea.
- There is a theoretical risk with the use of NSAIDs or ACE-inhibitors in COVID-19. However, clinical data regarding this is lacking and at this point, a strong recommendation to avoid or to continue these medications cannot be made.
- No specific treatment (including chloroquine or hydroxychloroquine) is recommended for asymptomatic or mild disease.

Management of moderate, severe and critical disease

Patients with moderate disease should receive supportive therapy. All patients must be assessed for

the Cytokine Release Storm (CRS). For this the following investigations must be done.

Results with which may indicate CRS are in brackets

- CBC (Neutrophil to lymphocyte ratio of >5 or absolute lymphocyte count of <800 or lymphocyte percentage $<20\%$.)
- Ferritin (>1000 mcg/L and rising in last 24 hours or >2000 mcg/L with respiratory compromise)
- C-reactive protein (>70 mg/L and rising in the absence of a bacterial infection)
- Lactate dehydrogenase (>300 IU/L and rising)
- D-Dimer (>1000 ng/mL and rising)
- Chest X-ray (worsening infiltrates with increasing lung involvement)

Additional investigations indicated include

- Liver function tests
- BUN Creatinine and electrolytes
- Blood cultures
- Arterial Blood Gas (for severe and critical cases)
- Serum lactate (for severe and critical cases)
- EKG (for severe and critical cases)
- Respiratory cultures (for severe and critical cases)
- Optional investigations include
- Procalcitonin
- Troponin
- Echo
- Pro-BNP
- IL-6
- CT scan chest

Specific therapy

Supportive care

The mainstay of management for COVID-19 is oxygen therapy via nasal cannula. If available high flow oxygen can also be used. All patients with low saturations should be placed in the prone position. For those not intubated, voluntary awake proning should be encouraged for as long as the patient can manage. For patients on the ventilator, 12 to 15 hours of proning should be attempted.

Antibiotics

Antibiotics including azithromycin should only be used in cases where a bacterial infection is suspected, for example in cases with an elevated white cell count or procalcitonin. There is no role of prophylactic antibiotics to prevent a secondary infection.

Hydroxychloroquine and chloroquine

These are no longer recommended given recent studies showing potential harm and lack of clear benefit.

Therapy in Cytokine Release Storm (CSR)

Cytokine Release Storm is defined as ANY of the following

- Ferritin >1000 mcg/L and rising in last 24 hours or
- Ferritin >2000 mcg/L in patient requiring high flow oxygen or ventilation
- Lymphopenia <800 cells/ml and two of the following
- Ferritin >700 mcg/mL and rising in the last 24 hours

- LDH > 300 IU and rising in the last 24 hours
- D-Dimer >1000ng/mL and rising in the last 24 hours

- CRP >70 mg/L and rising in the last 24 hours

If any 3 presents on admission no need to document rise

- **Steroids**

Dose: 0.5 to 1 mg/kg/d of methyl prednisone or equivalent for 5 days
Avoid use if no evidence of CSR

- **Tocilizumab:**

Dose: 4 to 8 mg/kg iv. Not over 800mg (maximum). Can repeat in 12 hours once only

Contraindicated:

- Active TB
- Zoster
- Sepsis and positive blood culture
- Suspected GI perforation
- Multiple Sclerosis
- Allergy to Tocilizumab
- ALT > 5 times or Bilirubin > 2
- ANC <2000 or Thrombocytopenia <50
- Pregnancy

Anticoagulation

As patients with COVID-19 may be hypercoagulable, anticoagulation plays an important role in therapy. For all doses mentioned below, adjustment will be required in case of renal impairment

- If the patient was already on oral anticoagulation for another indication (such as atrial fibrillation):
 - In moderate disease: Continue same
 - In severe/critical: Consider switching to parenteral therapy
- If the patient was not on anticoagulation at the time of admission
 - In moderate disease: Start standard DVT prophylaxis (enoxaparin 0.5mg/kg once daily)
 - If severe disease Start aggressive prophylaxis (enoxaparin 0.5 mg/kg every 12 hourly)

Indications for therapeutic anticoagulation (any of the following):

1. Documented presence of thromboembolic disease (such as ultrasound doppler or CT for PE)
 2. Strong suspicion for thromboembolic disease when investigation cannot be done
 3. D-Dimers over 3 times upper limit normal
- Dose: Enoxaparin 1mg/kg every 12 hourly
 - Duration: 1 to 3 months (can switch to rivaroxaban on discharge).
 - If documented VTE follow standard guidelines for duration

Discontinuation of Isolation/Discharge

Isolation precautions can be discontinued in the following conditions:

In those who are symptomatic

At least 10 days from the start of symptoms AND at least 3 days after resolution of symptoms

In those who are asymptomatic:



Ten days from the date of the test. A test to document cure is **not required** in the above-mentioned patients.

However, for the following two consecutive negative PCR tests a minimum of one day apart are required to discontinue isolation

1. Immunocompromised patients
2. Those living in congregations such as jails, dorms or madrasas
3. Healthcare workers dealing with immunocompromised patients

Note: The above recommendations are being regularly reviewed by the Ministry of National Health Services, Regulations & Coordination and will be updated based on the international & national recommendations and best practices.

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