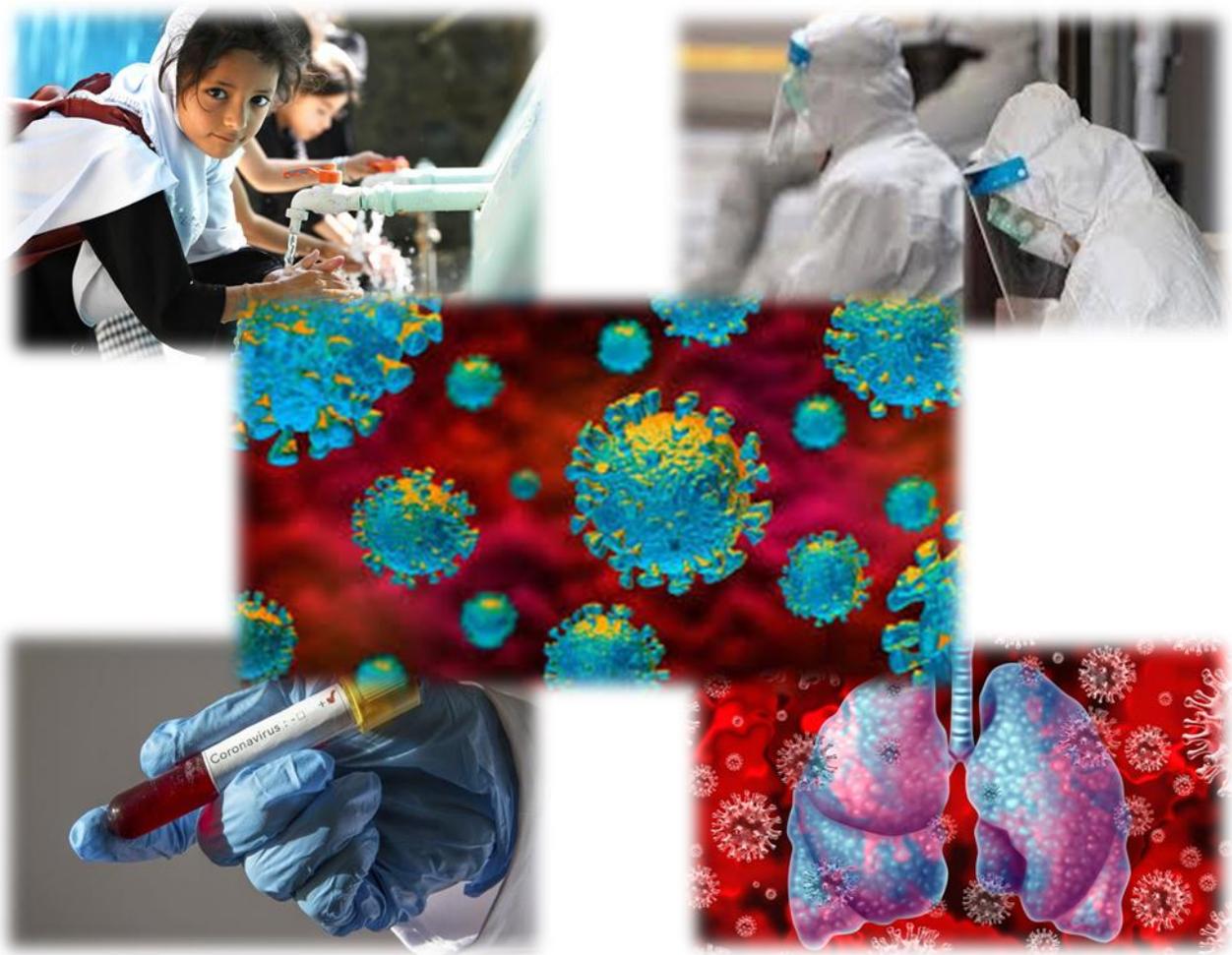




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## Guidelines

# 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.

Given the limited availability of tests, a tiered approach is recommended. Priority for testing is given to Tier-1 cases. These definitions will change as the outbreak progresses and testing capabilities are expanded.

Tier-1: High level of suspicion of COVID-19  
Always test

Tier-2: Low level of suspicion of COVID-19  
At physician discretion

If testing not performed, then home isolation until symptoms resolution is recommended.  
Reassess if symptoms worsen

### Tier-1 conditions (High suspicion, always test)

1. Presence of Fever OR Cough OR Shortness of breath and **ANY** of the following:
  - International travel in the last 14 days
  - Household contact with an asymptomatic international traveler
  - Close\* contact with a confirmed or probable COVID-19 patient
  - Caregiver of a person with pneumonia of unspecified etiology
  - Engaged in public dealing e.g. bank teller, general physician
  - Participated in large congregations
  - Healthcare worker involved in
    - i. Care of a confirmed COVID-19 patient
    - ii. Care of a patient with pneumonia of unspecified etiology
    - iii. Point of Entry like outpatient department, emergency, reception/registration counters
2. Patients admitted to the hospital with unexplained pneumonia or respiratory failure (regardless of other risk factors)
3. Household contacts of a confirmed COVID-19 patient, regardless of symptoms

### Tier 2 Conditions (Low suspicion, testing optional but isolate patient)

1. Presence of Fever OR Cough OR Shortness of breath and **ANY** of the following



- Intercity travel in the last 14 days
- Close (15 min face-to-face contact within 1 m)
- Household contact with an asymptomatic domestic traveler
- Daily or very frequent use of public transport associated with crowding e.g. crowded buses
- Patients with upper respiratory tract symptoms, body aches or other non-specific symptoms and no other risk factors

## Clinical classification of suspected or confirmed COVID-19 patients

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

### Asymptomatic

Nasopharyngeal RT-PCR positive for SARS CoV2 but having no symptoms

### Mild

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

### Moderate

Hypoxia (oxygen saturation  $\leq 94\%$ ) or mild infiltrate on chest x-ray. Persistent high-grade fever for over 3 days.

### Severe

Shortness of breath with hypoxia with moderate to severe pneumonia without meeting the criteria for critical disease.

### Critical

Presence of any of the following with COVID:

1. Respiratory rate  $> 30$  breaths/min
2. Severe respiratory distress (can't speak in sentences)
3. Central cyanosis
4. Confusion, agitation, restlessness
5. CURB 3 or 4 score
6. qSOFA score 2 or more
7. Widespread infiltrates on CXR

#### 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.



8. PaO<sub>2</sub>/FiO<sub>2</sub> ratio less than 300, or PaO<sub>2</sub> less than 65 or Rising PaCo<sub>2</sub>
9. Evidence of heart failure (Raised JVP, Gallop rhythm)
10. Signs of shock: Delayed capillary refill; Cold, clammy peripheries; Mottled skin; Systolic BP less than 90 or less than 40mm Hg of baseline in hypertensive; Urine output < 0.5 ml/kg/hr

## 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 (must fulfill all the below)

- 1- Those with a separate room to stay in with a separate bathroom
- 2- 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 should 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

If the patients cannot be admitted, then clear instructions must be given to call if any worsening occurs.

### Moderate, severe and critical disease

Admit to a hospital facility. In case of severe disease prefer a center with a high dependency unit/ICU. For patients who are critical (and if possible severe disease) preferably place in a negative pressure room (if available) especially if aerosol generating procedure(s) are anticipated.

## Management

### Prophylaxis

**There is no role of prophylactic chloroquine or hydroxychloroquine at this time.** 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 disease**

#### Investigations

The following investigations should be done in all patients

- CBC
- Electrolytes and serum creatinine
- Chest X-ray
  - Bilateral distribution of patchy shadows or ground glass opacity

Additional investigations may include the following (depending on clinical condition and availability)

- WBC count-Normal to low
- Lymphocytes count-low in moderate to severe disease
- Thrombocytopenia is common 33.7% (but platelets are rarely <100). Lower platelet count is a poor prognostic sign.
- CRP (repeated if any evidence of clinical worsening)
- C-reactive protein  $\geq 10$  mg/liter
- Procalcitonin  $\geq 0.5$  ng/ml
- Lactate dehydrogenase  $\geq 250$  U/liter
- Aspartate aminotransferase  $>40$  U/liter
- Alanine aminotransferase  $>40$  U/liter
- Total bilirubin  $>17.1$   $\mu\text{mol/liter}$
- Creatine kinase  $\geq 200$  U/liter
- Creatinine  $\geq 133$   $\mu\text{mol/liter}$
- d-dimer  $\geq 0.5$  mg/liter
- ECG (if age  $>40$  or other comorbidities or if clinically indicated)
- Cardiac enzymes if indicated
- Liver function tests

### **Treatment**

Supportive therapy with oxygen therapy via nasal cannula acetaminophen for fever control and intravenous fluids if needed should continue. In case of lobar infiltrates, antibiotics may be considered especially if associated with high white blood cell count



There is no current evidence from studies to recommend any specific anti-COVID-19 treatment for patients with suspected or confirmed COVID-19 infection. Based on the best available evidence, treatment with either of the following can be started:

1. Chloroquine 500 mg BD for 10 days
2. Hydroxychloroquine sulfate 200 mg, three times per day for ten days

On therapy, QT-interval must be monitored; especially if other medications are being administered which prolong the QT-interval.

### **Management of severe and critical disease**

Every critically ill COVID-19 patient should be managed by a group of healthcare providers which includes at least a pulmonologist, an infectious diseases expert and a critical care specialist.

### **Investigations**

Initial investigations and supportive care should proceed as in moderate disease. Additional investigations may be required according to the respiratory status of the patient, including arterial blood gases and lactate levels.

### **Treatment**

1. Empiric antibiotics may be considered if a secondary bacterial pneumonia is suspected (e.g. if raised white blood cell counts or elevated procalcitonin).
2. In patients with ARDS who are intubated, use conservative fluid management.
3. Cardiac impairment has been described and diuresis may be considered.
4. **Do not give high-dose systemic corticosteroids** or other adjunctive therapies.
5. Implement mechanical ventilation using lower tidal volumes (4–8 mL/kg predicted body weight, PBW) and lower inspiratory pressures (plateau pressure < 30 cmH<sub>2</sub>O).
6. Finally, if expertise is available, in adults with severe ARDS, **prone ventilation** for 12–16 hours per day is recommended.

### **Other Medicines Under investigations**

These medications have considerable adverse effects, have limited available and unclear efficacy. Consultation with an Infectious Diseases Specialist is mandatory prior to prescribing.

- Intravenous Remdesivir
  - Loading dose on the first day of 200 mg followed by a maintenance dose of 100 mg once daily for 5 to 10 days
- Intravenous Tocilizumab
  - 4-8 mg/kg loading Single maximum dose 800 mg.
  - Repeat once after 12 hours (same dosage) if the response to the first dose was poor, maximum two cumulative doses
- Tab Lopinavir/ritonavir
  - 400/100mg BID-14 days



## Discontinuation of isolation

Isolation precautions can be discontinued once all the following conditions have been met

1. Resolution of fever without the use of antipyretics
2. Improvement in respiratory symptoms (e.g., cough, shortness of breath)
3. Two consecutive negative PCR tests collected one day apart

Repeat PCR testing should be done 5 days after resolution of the symptoms. If the patient is still positive, a repeat sample should be obtained 5 days later.

Patients who are asymptomatic, should have repeat testing 7 days from the first test sent.

*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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### References:

1. Organization WH. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance V 1.2. 2020 [Available from: [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected)].
2. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. 2020:105949.
3. Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents*. 2020:105932.
4. Cortegiani A, Ingoglia G, Ippolito M, Giarratano A, Einav S. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *J Crit Care*. 2020.
5. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends*. 2020;14(1):72-3.
6. Al-Tawfiq JA, Al-Homoud AH, Memish ZA. Remdesivir as a possible therapeutic option for the COVID-19. *Travel Med Infect Dis*. 2020:101615.
7. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. *N Engl J Med*. 2020.
8. Liu F, Xu A, Zhang Y, Xuan W, Yan T, Pan K, et al. Patients of COVID-19 may benefit from sustained lopinavir-combined regimen and the increase of eosinophil may predict the outcome of COVID-19 progression. *Int J Infect Dis*. 2020.
9. National Action Plan for Corona virus disease (COVID-19) Pakistan. In: Ministry of National Health Services. <https://www.nih.org.pk/wp-content/uploads/2020/03/COVID-19-NAP-V2-13-March-2020.pdf>. Last accessed 28-3-20

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<http://covid.gov.pk/>

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<https://twitter.com/nhsrcoofficial>

<https://www.nih.org.pk/>

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Annex 'A'

**Summary algorithm of COVID management**

