
# COVID-19 DISASTER PREPAREDNESS COMMITTEE
# TREATMENT PROTOCOL FOR COVID-19

**Note: This document is dynamic and may be modified as per progression of the disease in India and when more data are available regarding epidemiology, transmission, and treatment.**

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*Source:*

- *World Health Organization (WHO) interim guidelines (March 2020)*
- *Surviving Sepsis Campaign COVID-19 Guidelines*
- *ICMR COVID-19 guidelines*

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# JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION AND RESEARCH - PUDUCHERRY JIPMER

## COVID-19 TASK FORCE

## TREATMENT PROTOCOL

**ABBREVIATIONS:**

AFB- Acid Fast Bacilli

ARDS- Acute Respiratory Distress Syndrome

CAP- Community Acquired Pneumonia

CBNAAT- Cartridge Based Nucleic Acid Amplification Test

CPAP- Continuous Positive Airway Pressure

CPK- Creatinine Phosphokinase

CRP- C-reactive Protein

DFA- Direct Fluorescent Antibody

DPI- Dry Powder Inhaler

FiO2- Fraction of inspired oxygen

GCS- Glasgow Coma Scale

GHCD- Government Hospital for Chest Diseases

HFNO- High Flow Nasal Oxygen

HME- Heat and Moisture Exchanger

LDH- Lactate Dehydrogenase

MAP- Mean Arterial Pressure

MDI- Metered Dose Inhaler

MERS- Middle East Respiratory Syndrome

NIV- Non-Invasive Ventilation

PaO2- Partial pressure of Oxygen in arterial blood sample

PBW- Predicted Body Weight

PEEP- Positive End Expiratory Pressure

P-Plat- Plateau pressure

RR- Respiratory Rate

SARS- Severe Acute Respiratory Distress Syndrome

Vt- Tidal Volume

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## Important notice to health care workers:

1. *Any personnel treating or entering the room of a patient with suspected or confirmed COVID-19 should wear appropriate **personal protection equipment**: gown, gloves, eye protection, and a respirator (e.g., an N95 respirator) or a 3 ply surgical mask after appropriate **training** to use the same (See JIPMER infection control SOP). As per **WHO guidelines** we are recommending **N95 mask** for wards/ICU/HDU (areas where aerosol generating procedures are carried out) and **3 ply surgical mask** for isolation rooms or wards admitting stable patients where aerosol generating procedures are less.*
2. *Asymptomatic heath care workers involved in the care of suspected or confirmed cases of COVID-19 can use **hydroxychloroquine** [dose as per box-3, page-18] for prophylaxis of SARS-COV-2 infection as per recommendation of **National task force on COVID-19 constituted by ICMR.***

## Clinical syndromes associated with COVID-19:

**1.Mild illness:**

***Without co-morbidities:***

Patients with uncomplicated upper respiratory tract viral infection, may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache. Should have stable vital signs which includes **all** the following:

- Respiratory rate <24breaths/min
- Heart rate <110 beats/min
- spO2>92 % on ambient air
- Systolic blood pressure >110 mm Hg

Rarely, patients may also present with diarrhoea, nausea and vomiting. The elderly and immunosuppressed may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, such as e.g. dyspnea, fever, gastrointestinal symptoms or fatigue, may overlap with COVID-19 symptoms.

***With co-morbidities:***

- Pre-existing pulmonary disease
- Chronic kidney disease
- Diabetes mellitus
- Systemic hypertension
- History of cardiovascular disease
- History of transplant or any immunosuppression
- HIV

**2.Pneumonia:**

Adult with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen

**3.Severe pneumonia:**

Adolescent or adult: fever or suspected respiratory infection, plus one of: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 ≤ 92% on room air.

**4.Acute respiratory distress syndrome:**

***BERLIN DEFINITION 2012***

- **Onset:** within 1 week of a known clinical insult or new or worsening respiratory symptoms.
- **Chest imaging (radiograph, CT scan, or lung ultrasound):** 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 present.

**Oxygenation impairment:**

- Mild ARDS: 200 mmHg < PaO2/FiO2 <300 mm Hg (with PEEP or CPAP ≥ 5 cmH2O, or non-ventilated)
- Moderate ARDS: 100 mmHg PaO2/FiO2 ≤ 200 mmHg (with PEEP or CPAP ≥ 5 cmH2O, or non-ventilated)
- Severe ARDS: PaO2/FiO2 ≤ 100 mmHg (with PEEP ≥ 5 cmH2O, or non-ventilated)

**5.Sepsis:**

Life-threatening organ dysfunction caused by

a.) dysregulated host response to suspected or proven infection.
b.) 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, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinemia.

**6.Septic shock:**

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

**Table No. 1. Risk factors for severe COVID-19:**

| **Epidemiological -category 1** | **Vital signs- category 2** | **Labs- category 3** |
|---|---|---|
| Age >55 | Respiratory rate >24breaths/min | D-dimer >1000ng/ml |
| Pre-existing pulmonary disease | Heart rate >110 beats/min | CPK> twice upper limit of normal |
| Chronic kidney disease | SpO2<92% on ambient air | CRP >100 |
| Diabetes with HbA1c >7.6% or random blood sugar >250mg/dl | | LDH>245U/L |
| History of uncontrolled systemic hypertension | | Elevated troponin |
| History of cardiovascular disease | | Admission absolute lymphocyte count<800/µl |
| Use of biologics | | Ferritin >300µg/L |
| History of transplant or other immunosuppression | | |
| All patients with HIV (regardless of CD4 count) | | |

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## Indications for hospital admission of suspected and confirmed COVID-19 cases:

**To admit ALL**

1. Severe pneumonia cases
2. Those having risk factors for severe COVID-19 as per table 1.

***This is general guidance regarding which patients should be admitted. However, the final decision to admit is at the treating physician discretion according to current state/institute policy.***

**Table no. 2. Baseline Investigations to be sent-**

| **Routine investigations** | **Blood investigations** | **Radiological** | **Additional investigations to be sent for risk stratification if SARS-CoV-2disease is confirmed** |
|---|---|---|---|
| • Throat swab/nasopharyngeal swab (SARS-CoV-2 and H1N1 both)<br>• Sputum gram stain and culture<br><br>*Additional investigations in immunosuppressed-*<br>• *Sputum (don't induce) for Pneumocystis DFA or serum beta D glucan,*<br>• *Sputum -AFB smear, fungal culture, CBNAAT.* | • Complete Hemogram<br>• Renal Function test<br>• Liver Function test<br>• IgM scrub typhus<br>• Malaria card test<br>• Blood culture [2 sets]<br>• Viral serology [for HIV, HCV and HBV] | Chest X-ray | • D-dimer<br>• CPK<br>• LDH<br>• Troponin<br>• Serum Ferritin<br>• CRP |

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## Management of mild illness-

Mild illness without risk factors for severe COVID-19 shall be sent to nearby Government Hospital for Chest Diseases (GHCD) for isolation purpose. There is no indication for antibiotics in mild illness. In case of onset of warning signs (shortness of breath, hemoptysis, altered mental status), patient should immediately inform the nearest health center/JIPMER.

## Management of hospitalized cases-

**General measures:**

- Oxygen supplementation to maintain SpO2 >92-94%.

  *If critically ill or those with shock or hypotension, the initial oxygen therapy is a **reservoir mask at 15 L/min** pending the availability of reliable oximetry readings.*
  *For patients with spontaneous circulation and a reliable oximetry reading, it may quickly become possible to reduce the oxygen dose while maintaining a target saturation range of **92–94%.***
  *If oximetry is unavailable, continue to use a reservoir mask until definitive treatment is available.*
  ***When a patient is hypoxaemic, the initial oxygen therapy is nasal cannula at 2–6 L/min or simple face mask at 5–10 L/min unless saturation is below 85% (use reservoir mask) or if at risk from hypercapnia** (see below). The recommended initial target saturation range, unless stated otherwise, is 92–94%. If oximetry is not available, give oxygen as above until oximetry or blood gas results are available.*
  *If patients have **COPD or other risk factors for hypercapnic respiratory failure**, aim at a saturation of 88–92% pending blood gas results but adjust to 92–94% if the PCO2 is normal (unless there is a history of respiratory failure requiring NIV or IMV) and recheck blood gases after 30–60 min.*
- In the absence of shock, conservative fluid management should be done. Symptomatic treatment for cough with anti-tussive. Blood culture should be sent at time of admission before starting anti-microbials

Box no.1 Empirical antimicrobials:

*Empirical antibiotics (to be initiated within 1 hour)*

*Inj. Ceftriaxone 1-2gm i.v OD 5-7days + Inj. Azithromycin 500mg i.v OD or Inj. Doxycycline 100mg i.v BD 5 days + Tab Oseltamivir 75mg po BD for 5 days**

**In severe cases, Oseltamivir to be given 150mg BD for 10 days.*

*Antibiotics choice and duration shall depend on patient clinical status and physician assessment. Shall be started initially to cover for CAP; they should be discontinued once the diagnosis of COVID-19 is confirmed. However, if concurrent secondary bacterial infection is suspected either at admission or during the hospital course, appropriate antibiotics should be given. Oseltamavir started initially may be discontinued if SARS COV-2 RT-PCR is positive and H1N1 influenza PCR is negative.*

- Systemic corticosteroids are not recommended, unless indicated for any other reason.
- MDI/DPI [with or without spacer] preferred over nebulization to reduce risk of aerosolization.
- Avoid NSAIDS.

**Specific therapy:**

- *No specific ANTIVIRALS have been proven to be effective as per currently available data. Clinical data with strong evidence is yet to be published.*
- *Most of the evidence for these drugs are extrapolated from in vitro studies and from SARS, MERS cases.*
- *Treating physician shall make the decision on case to case basis after taking informed consent.*

**Indications:**

1. Any COVID-19 pneumonia case with ARDS features.

Box no. 2. Specific therapy

*Hydroxychloroquine* 400mg BD for one day, followed by 400mg OD per day while hospitalized, up to 5 days.*

**Check ECG both before and after initiation because of risk of QTc prolongation.*



## Criteria for intubation-

- PaO2/FiO2 < 200, or
- PaO2/FiO2 < 300 with hypotension requiring vasopressor support, or
- GCS < 8 with threatened airway.

## How to intubate-

***Place of intubation**: at a pre-planned designated area by a trained physician/doctor after taking proper precautions to prevent cross contamination and environmental contamination.*

- Pre-oxygenation with 100% FiO2

- Try to **avoid bag and mask ventilation** (due to aerosol generation) but can be used if required by connecting an HME
- The **most skilled** member of the team should be identified at the beginning of each shift for performing intubation
- If difficult airway is anticipated (past history of difficult airway, mouth opening < 3cm, thyromental distance < 6cm, restricted head and neck mobility), critical care physician/anesthesiologist to attempt intubation using video-laryngoscope
- In unanticipated difficult airway, use laryngeal mask airway and simultaneously call ICU critical care team
- Rapid sequence intubation to be done using induction agents (propofol or etomidate) and muscle relaxant (Succinyl choline or Rocuronium)
- During induction, monitor for hemodynamic instability and use fluids and vasopressors if required
- Use end-tidal CO2 or X-ray chest to confirm correct position of tube
- **After intubation, appropriate cleaning/disinfection of equipment and environment should be done**

## Care of ventilated patient:

- Fresh ventilator circuit to be used for every new patient
- HME to be changed every 24-48 hours
- Ventilator tubing to be changed when visibly soiled or when clinically indicated.
- Used closed suctioning technique and avoid routine suctioning
- Sedation and muscle relaxants may be used in difficult to ventilation patients
- ARDS management as per Table no.3

## Criteria for ICU/HDU admission:

- Requiring mechanical ventilation
- Hypotension requiring vasopressor support
- Worsening mental status
- Requiring close monitoring.

*Final decision to shift to an ICU/HDU should be made by treating physician/doctor based on his clinical judgement and patient condition.*



***The following recommendations pertain to adult patients with ARDS that are treated with non-invasive or high-flow oxygen systems-***

- High-flow nasal oxygen (HFNO) should only be used in selected patients with hypoxemic respiratory failure if there is no urgent indication for intubation with close monitoring and short interval assessment for worsening of respiratory failure.
- Non-invasive ventilation (NIV) should only be used in selected patients with hypoxemic respiratory failure (humidifier should be avoided in view of aerosol generation) if there's no urgent indication for intubation with close monitoring and short interval assessment for worsening of respiratory failure.

*These are to be used under supervision of a trained critical care physician preferably in a ICU/HDU.*

**Table no. 3. ARDS ventilation strategy**

*To be followed under a supervision of a trained critical care physician.*

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| Part I: Ventilator Set Up and Adjustment<br>1. Calculate predicted body weight(PBW)<br>Males = 50+2.3[Height in inches-60]<br>Females = 45.5=2.3[Height in inches -60]<br>2. Use assist/control mode and set initial tidal volume (Vt) to 8ml/kg PBW<br>3. Reduce Vt by 1ml/kg at intervals ≤ 2h until Vt =6ml/kg PBW<br>4. Set initial rate to approximate baseline minute ventilation (but not >35bpm)<br>5. Adjust Vt and RR to achieve pH and plateau pressure goals | Part II : Oxygenation Goal<br>PaO2 =55-80mm Hg or SpO2 = 88-95%<br>Fio2 –PEEP combinations to achieve oxygenation goal: as per ARDS net protocol. |
| Part III : Plateau Pressure(Pplat) Goal :<30cm H2O<br>1. Check Pplat (use 0.5 sec inspiratory pause),SpO2, total RR, Vt and ABG (if available) at least every 4 h and after each change in PEEP or Vt.<br>2. If Pplat>30cm H2O, decrease Vt by 1ml/kg steps (minimum 4ml/kg)<br>3. If Pplat<25cm H2O and Vt <6ml/kg, increase Vt by 1ml/kg until Pplat>25cm H2O or Vt =6ml/kg.<br>4. If Pplat<20cm H2O and breath stacking or dys-synchrony occurs, Vt may be increased in 1ml/kg increments (to a maximum of 8ml/kg) | Part IV: pH Goal: 7.30-7.45 (pH as low as 7.15 is acceptable if there is no other organ dysfunction)<br>Acidosis management: as per ARDS net protocol |

## Indications for prone ventilation for ARDS:

*To be followed under a supervision of a trained critical care physician after standard precautions.*

- PaO2:FiO2<150 mm Hg with FiO2>0.6, PEEP>5cm H2O

  OR

- $PaO_2$:$FiO_2$ of ≤100 mmHg with a $PaO_2$ ≤60 mmHg despite optimization of the ventilator settings on $FiO_2$ of 1.0

**Supportive treatment in critically ill patients:**

- Head end elevation
- Oral hygiene with mouthwash [chlorhexidine]
- Glycemic control to maintain blood sugar below 180 mg/dl
- Ulcer prophylaxis with proton pump inhibitors
- Thromboprophylaxis with subcutaneous low molecular weight heparin or unfractionated heparin.
- Foley's catheter and Ryle's tube
- Central venous catheter under strict aseptic precautions
- Bedsore prevention by position change every 2 hours

**Pregnant patients**:

1. Testing to be prioritized

2. Steroids may be given for fetal indications as per obstetrician's advice

3.Obstetrician to monitor fetal well-being daily

**Breastfeeding patients**: Currently there is no data suggestive of viral transmission via breast milk. However, due to close contact and risk of droplet transmission, breastfeeding should be avoided in COVID-19 confirmed mothers.

## Discharge Criteria:

- Suspected case – if the laboratory results for COVID-19 are negative, discharge is to be decided as per discretion of the treating physician based on his provisional/confirmed diagnosis.
- Confirmed case – resolution of symptoms, radiological improvement with a documented virologic clearance in 2 samples at least 24 hours apart



## Recommendation for empiric use of hydroxy-chloroquine for prophylaxis of SARS-C0V-2 infection:

The National Taskforce for COVID-19 recommends the use of hydroxy-chloroquine for prophylaxis of SARS-CoV-2 infection for selected individuals as follows:

Eligible individuals:

Asymptomatic healthcare workers involved in the care of suspected or confirmed cases of COVID-19

Box no. 3. Dose of Hydroxychloroquine

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| *Day 1: 400 mg twice a day*<br>*followed by*<br>*400 mg once weekly for next 7 weeks (to be taken with meals).* |

Exclusion/contraindications:

- The drug is not recommended for prophylaxis in children under 15 years of age.
- The drug is contraindicated in persons with known case of retinopathy, known hypersensitivity to hydroxychloroquine, 4-aminoquinoline compounds.

*Refer to National COVID-19 Task Force document for full details.*

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## TREATMENT PROTOCOL

### COVID-19 Treatment protocol flow chart: