

STANDARD TREATMENT PROTOCOL FOR COVID 19

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1. Protocol For Treatment of Confirmed COVID-19 Hospitalized Patients

Proposed Clinical Staging System

Stage 1: Mild (Early Infection) - Groups A B & C

Stage IIa: Moderate (Pulmonary Involvement Without Hypoxia) - Group D

Stage IIb: Moderate (Pulmonary Involvement With Hypoxia) - Group E

Stage III: Severe (Systemic Hyperinflammation with Cytokine Storm)- Group F

State & Group		Criteria	Investigations	Site of Admission	Treatment	Remarks
Stage –I	Group A	Asymptomatic but positive for COVID-19	CBC, RFT, RBS, LFT, ECG	Isolation ward	T. HCQ 400mg BD on Day 1 followed by 200 mg BD for 4 days	Baseline ECG for QTc
	Group B	Symptomatic/URTI without comorbidity 3 out of 4 <ul style="list-style-type: none"> • Fever • Dry cough • Shortness of breath • Myalgia RED FLAG SIGNS <ol style="list-style-type: none"> 1. Neutrophil Lymphocyte ratio > 3.5 2. Resting tachycardia 	CBC, RFT, RBS, LFT, CXR, ECG, ABG	Isolation ward	T. Cefixime 200 mg BD OR T. Augmentin 625 TDS OR T. Azithromycin 500mg OD for 5 days + Tab. HCQ 400mg BD on day 1 then 200 mg BD for 4 days	Baseline ECG for QTc If patient is symptomatic at day 5 also continue therapy for additional 5 days
	Group-C	Symptomatic/URTI with comorbidity <ul style="list-style-type: none"> • Obesity • >60 Yrs • DM • HTN/IHD • COPD/Chronic lung disease • Immunocompromised state • Immunosuppressive drugs • CKD RED FLAG SIGNS <ol style="list-style-type: none"> 1. Neutrophil Lymphocyte ratio > 3.5 2. P:F ratio less than 300 3. 3-4 min exercise induced deoxygenation 4. Resting tachycardia 5. Raised CRP/ S.Ferritin D-dimer/LDH/ Triglycerides 	CBC, LFT RFT, RBS CXR, ABG ECG ESR, CRP LDH S.Ferritin D-dimer If QTc prolongation in ECG then daily S.electrolytes ionic calcium & Magnesium	Isolation ward	T. Cefixime 200 mg BD OR T. Augmentin 625 TDS OR Tab. Azithromycin 500mg OD for 5 days + Tab. HCQ 400mg BD on day 1 then 200 mg BD for 4 days If SpO2 <88% 1) Consider CARP protocol 2) Inj. MPS 40 mg IV BD	ECG - Baseline & daily to look for QTc prolongation If patient is symptomatic at day 5 also, continue therapy for additional 5 days

Stage-IIa	Group D	Pneumonia (LRTI) without respiratory failure RED FLAG SIGNS 1. Neutrophil Lymphocyte ratio > 3.5 2. P:F ratio less than 300 3. Raised CRP/ S.Ferritin D-dimer/LDH/ Triglycerides	CBC, LFT RFT, RBS CXR, ECG, ABG ESR, CRP S.Ferritin D-dimer/LDH If QTc prolongation in ECG then daily S.electrolytes ionic calcium & Magnesium	Isolation Ward/SO S ICU	Inj. Ceftriaxone 1 g IV OD for 5-10 days + Tab. HCQ 400 mg BD on day 1 then 200 mg BD for 9 days + If SpO2 < 88% - 1) Consider CARP protocol 2) Inj. MPS 40mg IV BD If CAT C patient progresses to ARDS/MODS and if HCQs cannot be given for any contraindication like prolong QTc or G6 PD deficiency Lopinavir/Ritonavir may be considered in dose of 200/50mg twice daily for 14 days or 7 days after asymptomatic	ECG - Baseline & daily to look for QTcprolongation
Stage-IIB	Group E	Pneumonia (LRTI) with respiratory failure RED FLAG SIGNS 1. Neutrophil Lymphocyte ratio > 3.5 2. Raised CRP/Ferritin/D-dimer/LDH/Triglycerides/ Troponin I/CPK-MB	CBC, LFT RFT, RBS CXR, ECG, ABG, ESR, CRP S.Ferritin D-dimer LDH S. Triglycerides Troponin I CPK-MB If QTc prolongation in ECG then daily S.electrolytes ionic calcium & Magnesium	ICU	Inj. Piperacilin-tazobactam 4.5g, IV TDS extended infusion over 4 hours + Tab. HCQ 400 mg BD on day 1 then 200 mg BD for 9 days Inj. LMWH 40mg SC OD +/- When SpO2 88% consider	ECG - Baseline & daily to look for QTc prolongation Can consider 1. CARP protocol (see below) 2. Mechanical ventilation if not a candidate for CARP protocol

					1. CARP protocol 2. Inj. MPS 40 mg IV BD 5 days & review	
Stage III	Group-F	Pneumonia (LRTI) with respiratory failure multi organ dysfunction syndrome RED FLAG SIGNS 1. Neutrophil Lymphocyte ratio > 3.5 2. Raised CRP/Ferritin/D-dimer/LDH/Triglycerides/Troponin I /CPK-MB	CBC, LFT RFT, RBS CXR, ECG, ABG ESR, CRP S.Ferritin D-dimer LDH, S. Triglycerides Troponin I CPK-MB Blood culture & sensitivity If QTc prolongation in ECG, then daily S.electrolytes ionic calcium &S.Magnesium	Isolation-ICU	Inj. Meropenem 1 g IV TDS extended infusion over 3 hours + Tab. HCQ 400 mg BD on day 1 then 200 mg BD for 9 days Inj. LMWH 40 mg SC BD	ECG - Baseline & daily to look for QTc prolongation 1. Mechanical ventilation as per CARDSnet protocol 2. Can consider use of convalescent plasma 3. If evidence of cytokine storm then administer Inj.MPS 500 mg IV OD for 5 days and review.

* If any investigation is not available at treating hospital, it may be outsourced.

Note:

1. All suspected symptomatic patients to be given T.Oseltamivir 75 mg BD (for URTI) and 150 mg BD (for LRTI)for 5 days irrespective of status.
2. In addition drugs may be given to improve immunity and possibly reduce viral replication.
 - Zinc Supplementation 50 mg BD, Vitamin C 100 mg BD, Vitamin A 25000 IU single dose, Vitamin D 4000 IU Daily, Magnesium Sulphate 2 gm IV
3. Use of Tocilizumab, Colchicine, Ivermectin and Convalescent Serum is not part of this protocol and the decision on the use of these therapeutic options are left to treating physicians.

2. Important Considerations

A) Indications for Intubation

Intubation has to be planned and conducted with adequate sedation and neuromuscular paralysis with minimum personnel.

1. Persistent hypoxia SpO₂ below 88% on 60% venturi mask.
2. Respiratory Rate (RR) > 30/ min
3. Systolic BP below 90 mmHg despite IV fluids and vasopressors
4. GCS less than 8

Trial of Oxygen therapy with High Flow Nasal Cannula / Venturi mask. If signs of respiratory distress persist then consider immediate intubation.

B) Cytokine Storm (on Day 7/8 of disease)

To be ruled out from Group C onwards

Cardinal features:

- Unremitting fever
- Cytopenias
- Hyperferritinemia
- Pulmonary involvement (including ARDS)

Screening for Hyperinflammation:

- Elevated ferritin (Predictor of mortality)
- Elevated ESR & CRP
- Elevated liver transaminases
- Bicytopenia/ pancytopenia
- Elevated Triglycerides
- Hepatosplenomegaly

Management of Cytokine Storm

- Inj Methyl Prednisolone (MPS) 500 mg IV OD x 3-5 days

C) COVID Awake Repositioning/Proning Protocol (CARP)

Prone positioning improves oxygenation in spontaneously breathing non-intubated patients with hypoxemic acute respiratory failure

Indications for Awake Proning:

(1) Isolated hypoxemic respiratory failure without substantial dyspnea (**the "paradoxically well appearing" hypoxemic patient**). A reasonable candidate might meet the following criteria:

- not in multi-organ failure
- expectation that patient has a fairly *reversible* lung injury and may avoid intubation
- no hypercapnia or substantial dyspnea
- normal mental status, able to communicate distress
- no anticipation of difficult airway

(2) Patients who do not wish to be intubated. The main risk of awake proning is that it could cause excessive delays in intubation. In the patient who do not give consent for intubation, there is little to be lost by trial of awake proning.

Patients with a PF Ratio (po_2/Fio_2) of < 100 on Non Invasive Ventilation (NIV) are not suitable candidates and this may delay an unavoidable intubation. Patients should prone, as tolerated for 2-4 hours/session for 2-4/days. Patients may receive light sedation in order to tolerate pronation. While the evidence is far from robust, this technique is currently being used and has both physiological and laboratory basis. More importantly, it has a demonstrated anecdotal benefit to avoid intubation.

CARP Protocol

Timed Position Changes

Every 2 hrs, ask patient to switch between the following positions. Bed adjustments will be required between positions

1. Left Lateral Recumbent
2. Right Lateral Recumbent
3. Sitting Upright 60-90 degrees
4. Lying Prone in bed

If these 4 positions are not raising the Oxygen Saturation, a 5th position can be tried:

5. Trendelenburg position (Supine, Bed 30 degrees Head Down)

10-15 Minutes after each position change, check to make sure that Oxygen Saturation has not decreased. If it has, try another position.

- **Position Changes to Counter Hypoxemia**

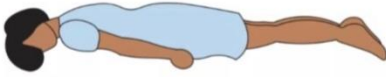
If patient has a significant drop in Oxygen saturation, follow these steps:

1. Ensure that the source of the patient's Oxygen is still hooked up to the wall and is properly placed on the patient (this is a common cause of desaturation)
2. Ask patient to move to a different position as above

PHOTOS BELOW TO DEMONSTRATE THIS:

LAS FOTOS DEBAJO DEMUESTRAN ESTO:

1. 30 minutes – 2 hours: laying on your belly



2. 30 minutes – 2 hours: laying on your right side



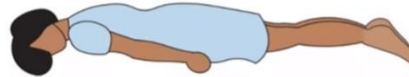
3. 30 minutes – 2 hours: sitting up



4. 30 minutes – 2 hours: lying on your left side



Then back to Position 1. Lying on your belly!



Self Positioning Guide_Elmhurst Hospital_SB

3. ICU Admissions and Ventilation Strategies

A. Criteria For ICU Admissions

• Need for mechanical ventilation.
• Need for vasopressors.
• Respiratory rate >25 breaths per minute.
• PaO ₂ <60 mm Hg on room air or SpO ₂ <85% on supplemental oxygen of 6 L/M.
• Confusion.
• N/L ratio > 3.5
• Thrombocytopenia.
• Uremia
• Multilobar infiltrates.
• Hypotension requiring fluid resuscitation.
• Hypothermia.

3 B. Ventilation Strategies (ARDS with Low Compliance)

Before Mechanical Ventilation – Try Awake ,Prone, High Flow Nasal O2 – It May Avoid Invasive Ventilation
<i>Ventilation Protocol for Patients with Acute Respiratory Distress Syndrome</i>
All patients who present with acute breathlessness (less than 7 to 10 days) and having all of the following:
<ul style="list-style-type: none"> • PaO₂/FiO₂ ≤ 300 • Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema • No clinical evidence of left atrial hypertension
are diagnosed with acute respiratory distress syndrome (ARDS)/ SARI (severe acute respiratory illness)
<ul style="list-style-type: none"> • Ventilation strategies will primarily depend upon the severity of SARI/ARDS
<u>Ventilator Setup and Adjustment</u>
<ul style="list-style-type: none"> • Calculate PBW. • Males = 50 + 2.3 [height (inches)—60]. • Females = 45.5 + 2.3 [height (inches)—60]. • Select volume A/C mode on the ventilator. • Set ventilator settings to achieve initial VT = 6 mL/kg PBW. • Set initial rate to approximate baseline minute ventilation (not >35 bpm). Aim for a pH over 7.2, do not worry about the PaCO₂. If the PaCO₂ keeps going up too much in spite of a respiratory rate (RR) of 35, reduce the dead space in the circuit. If the pH drops below 7.2, consider adding sodium bicarbonate infusion. • Adjust VT and RR to achieve pH and plateau pressure goals as mentioned below.
<u>Oxygenation Goal: PaO₂ 55–80 mm Hg or Oxygen Saturation (SpO₂) 88–95%</u>
<ul style="list-style-type: none"> • Use a minimum positive end expiratory pressure (PEEP) of 5 cm H₂O. Consider the use of incremental FiO₂/PEEP combinations as shown below to achieve the goal. • Plateau pressure goal: ≤30 cm H₂O • Check P_{plat} (0.5 second inspiratory pause) at least every 4 hours and after each change in PEEP or VT. • If the P_{plat} remains above 30 cm H₂O, decrease VT by 1 mL/kg steps (minimum = 4 mL/kg).
Noninvasive ventilators (NIVs) can be used for patients not requiring high FiO ₂ and for recovering patients, so that the high performance ICU ventilators can be preserved for sicker patients.

<p>Transport ventilators can also be included in the inventory. Home NIVs and high-flow nasal cannula (HFNC) devices can play an important role in cases with mild severity of disease.</p>
<p>Both these modes (NIV, HFNC) are likely to produce aerosol transmission of COVID-19 disease. Hence to be tried under full PPE coverage. Early elective intubation is preferred for these patients.</p>
<p>Proning</p>
<p>If patient does not show improvement in oxygenation, then proning should be tried, preferably early in the course of the disease.</p>
<p>It is usually associated with significant improvement in oxygenation status. On an average 16 to 18 hours of pruning should be done.</p>
<p>Follow thorough aerosol precautions while pruning and take utmost precaution to avoid disconnection of the ventilator circuit.</p>
<p>Although Outcome data on Prone positioning in COVID-19 (used in 12% of patients in one ICU study from Wuhan 15) are currently lacking, the tendency for SARS-Cov-2 to affect the peripheral and dorsal areas of the lungs provides the ideal conditions for a positive oxygenation response to prone positioning.</p>

3 C. Ventilation Strategies (ARDS with Near Normal Lung Compliance)

<ul style="list-style-type: none">• After intubation check lung compliance on ventilator
<ul style="list-style-type: none">• If near normal - ventilation settings as follows.
<ul style="list-style-type: none">• PEEP <10 cms of water with BP monitoring
<ul style="list-style-type: none">• FIO₂ < 60 - 70% to keep SaO₂ > 85, PaO₂ < 60 mmhg
<ul style="list-style-type: none">• Tidal volume - 8-10 ml/kg
<ul style="list-style-type: none">• IV fluids to maintain VT<10-12 cms of water
<ul style="list-style-type: none">• Prone ventilation not indicated
<ul style="list-style-type: none">• Try semi recumbent position
<ul style="list-style-type: none">• Try weaning slowly, watch for mucosal oedema, Hydrocortisone 200mg, IV 30 minutes before extubation.

4. Supportive Care For ICU/Non ICU Patients

• Semi-recumbent position if not contraindicated.
• Avoid Nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen other than paracetamol unless absolutely necessary
• All inhaled medicines (bronchodilators) should preferably be given by metered dose inhalers (MDIs) to reduce the chances of aerosolization. Avoid nebulised drugs
• Use of histamine-2 receptor blockers or proton-pump inhibitors to prevent gastrointestinal bleeding. Sucralfate can be added
• Consider discontinuation of inhaled steroids as they may reduce local immunity and promote viral replication . But if discontinuation of inhaled steroids is likely to worsen the preexisting lung disease , decision on the same can be taken by the treating doctor
• A conservative or de-resuscitative fluid strategy after initial resuscitation with early detection of myocardial involvement through the measurement of troponin
• Pharmacologic thromboprophylaxis, if not contraindicated, should be given. Mechanical thromboprophylaxis using intermittent pneumatic compression stockings can be used in cases where pharmacologic thromboprophylaxis is contraindicated.
• Judicious use of sedation
• Daily sedation-free intervals, and assessment for weaning readiness.
• Use of disposable ventilator circuits for each patient.
• Appropriate use of heat moisture exchanger or humidifier.
• Standardized slower weaning protocols.
• Closed suction and HME filters should be preferred to prevent aerosol spread.
• Optimal care to reduce the incidence of catheter-related blood stream infections.
• Early enteral nutrition (within 24 to 48 hours of admission) if not contraindicated.
• Frequent position change to prevent pressure sores.
• Early mobilization including passive and active rehabilitation exercises to prevent critical illness-related neuromuscular weakness.
• Tracheostomy in patients with prolonged mechanical ventilation.

5. DISCHARGE CRITERIA

Discharge Criteria to Step-down Unit or Ward
• When patient's physiological status has stabilized and the need for ICU monitoring and care is no longer necessary
• Heart rate <90/minutes
• SBP >120 mm Hg off vasopressors
• RR <20/minutes
• Conscious, oriented
• Tolerating feeding
• Not needing any organ support treatment [continuous renal replacement therapy (CRRT), liver support, etc.]

Criteria To Discharge From The Hospital
Clinical recovery and two negative RT-PCR assays performed 24 hr apart on admission day 14 & 15.
If day 14 & 15 swab sample remains positive -- patient remains admitted – Swab needs to be taken again on day 20 & 21 --- If these two consecutive samples are negative then patient becomes eligible for discharge However
Patient remains under observation for two more days after two samples taken 24 hr apart are negative as sudden deaths have been reported
At the time of discharge Pt needs to be advised about remaining home quarantine , hand hygiene , social distancing , use of masks