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Clinical Guidelines for the Management of Moderate to Severe COVID-19 Disease – Bangladesh Model

Joint Collaboration of Australian and Bangladeshi COVID-19 Frontline Physicians

Version 1

16th April,2020

Dedicated to the Memory of Late Dr Moyeen Uddin – The 1st COVID-19 Martyr Physician of Bangladesh
A great clinician and benevolent human being

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Disclaimer

The COVID-19 Management Guidelines-Bangladesh Model has been developed to assist clinicians (Internal Medicine, Pulmonologist and Critical Care Medicine) to prepare and plan clinical care services in the event of a pandemic, to provide a safe working environment for staff and patients and to give guidance on the identification and treatment of patients with COVID-19 infection. The recommendations have been put together by a team of specialists- Respiratory, Internal medicine, Infectious disease, Immunology and Intensive Care doctors from Australia and Bangladesh who are directly involved in COVID-19 management. The authors have made considerable effort to ensure the information contained within the recommendations is correct at the time of publication. Information provided has been sourced from the best available evidence and expert opinions. This recommendation entails changes from international recommendations due to extremely limited resources in Bangladesh. Further iterations of these guidelines will be published as new information comes to hand. The Society accepts no responsibility for any inaccuracies, information perceived as misleading, or the success or failure of any of the recommendations detailed in the document. The information in this document cannot replace professional advice.

Acknowledgements

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- This guideline is applied for patients with moderate to Severe COVID cases – Oxygen saturation <92% in RA, RR >30/min, evident lung infiltrate or on invasive ventilatory support and/or High-risk group- Age >55 Y, comorbidities e.g. HTN, Type 2 DM, CKD, Chronic heart and lung disease etc.

- The regimen is applicable in acute medical ward, HDU or ICU setting.

- This document covers potential off-label and/or experimental/compassionate use of medications. There is no good evidenced based effective medications proven against SARS COV-2 at this stage. Any medications used must be at the discretion of the clinician treating the patient preferably as part of a clinical trial.

- Consensus is required between Internal Medicine, Respiratory and ICU team.

<table>
<tr><th colspan="2">Laboratories for diagnosis, prognosis / risk stratification, and/or safety of agents Suggested for <u>all hospitalized</u> patients with confirmed or suspected COVID-19</th></tr>
<tr><td><u>Recommended daily labs</u>:
CBC with diff (trend total lymphocyte count)
Liver and renal function.</td><td><u>Viral serologies (if deranged LFT / anti-viral considered)</u>:
HBV serologies (sAb, cAb, and sAg)
HCV antibody, unless positive in past
HIV 1/2 Ab/Ag</td></tr>
<tr><td><u>For risk stratification (may be repeated q2-3 days if abnormal or with clinical deterioration)</u>:
D-dimer
Ferritin / CRP / ESR
LDH
Troponin/ CPK
Baseline ECG (Monitor QTc)</td><td><u>If clinically indicated</u>:
• Routine blood cultures (2 sets)
• For acute kidney injury- send urinalysis and spot urine protein: creatinine
• Procalcitonin (if available)</td></tr>
<tr><td><u>Radiology</u>:
• Portable CXR at admission
• High threshold for PA/lateral in ambulatory patients, consider only if low suspicion for COVID-19 and result would change management.
Non-contrast CT is of limited utility in definitively diagnosing COVID-19 and should only be considered if it is likely to change management.</td><td><u>Respiratory workup with appropriate PPE</u>:
• Nasal SARS-CoV-2 PCR (Nose and throat), if not already performed. Tracheal aspirate if already intubated.
• Nasal viral PCR for influenza A, B and RSV test if available.
• As indicated, routine sputum for bacterial gram stain and culture, Legionella, Strep pneumonia urinary antigen.</td></tr>
</table>

COVID-19 Treatment Protocol

1.Supportive therapy – Hydration, antipyretics (Paracetamol), close monitoring of vitals including Oxygen saturation. For respiratory failure please follow **COVID-19 Acute Respiratory Care Pathway** as attached here**.**

2. Broad spectrum antibiotics should be considered for all cases with Lung infiltrates

- IV Ceftriaxone 2 gm daily or IV Meropenem 1 gm TDS plus IV Azithromycin.
- Plus, IV Vancomycin for patients on invasive ventilation.

3. If Anti-viral drug NOT available: Oral Azithromycin 500 mg daily plus Hydroxychloroquine 200 mg PO bd (400 mg bd on day 1) for 5-7 days. Monitor QTc when these drugs are combined.

Hydroxychloroquine:

- No dose reduction in renal or hepatic impairment. Consider drug-drug interactions with QTc prolonging agents such macrolides.
- Adverse effects – headache, blurred vision, nausea, vomiting, alopecia, rash, Class D drug in pregnancy, hypoglycaemia in patients with DM, myelosuppression, retinopathy, corneal deposits.

4. If Anti-viral drug is available: Hydroxychloroquine 200 mg PO bd (400 mg bd on day 1) plus either Lopinavir/Ritonavir or Favipiravir for 5-7 days can be considered**.**

A. Lopinavir/Ritonavir: Lopinavir/Ritonavir (200/50) mg (Anti-HIV drug) two tablets PO bd for 5-7 days

- No dose reduction in renal impairment. Caution in end stage liver disease.
- Perform baseline ECG.
- Avoid drugs -Rifampicin, amiodarone, flecainide, fluticasone, macrolides, statins, azoles.
- *Adverse effects* – pancreatitis, hepatitis, headache, nausea, vomiting, diarrhoea, hyperlipidaemia, hyperglycaemia, weight gain, rash, taste disturbance.

B. Favipiravir 1600 mg PO BD on Day 1 then 600 mg BD for total 10 days.

C. Remdesivir 100 mg IV daily (200 mg on first day) for 5-7 days.

- ***Inclusion criteria*: Patient on mechanical ventilation**
- *Exclusion criteria*: Evidence of multi-organ failure, Pressor requirement to maintain blood pressure, ALT > 5xULN, creatinine clearance < 30 ml/min or dialysis or renal replacement therapy.
- *Adverse effects*: No available data.

5. Biological Therapy: This is to be considered at any treatment stage if there is evidence of cytokine storm.
Preferred option: **Tocilizumab (Anti-IL-6) 400 mg IV or 8mg/kg** (infusion over an hour) and repeated the same dose after 12 hours if there is clinical deterioration.

CytoSorb Device (FDA approved) could be considered as an alternative but would be a weak recommendation. It can absorb good cytokines as well leading to immune paresis.

Indication:

- Bilateral lung infiltrates
- Needs supplemental oxygen to maintain saturation above 92% or PaO2 /FiO2 <300 mmHg, RR > 30/min
- Features suggestive of cytokine storm(hyperinflammation) including ferritin ≥ 500, CRP>50, LDH>250, Lymphocyte count <0.6, D-dimer >1000 ng/ml (at least 2 criteria fulfilled)
- Patient requires baseline QuantiFERON gold, Hepatitis B serology (including cAb), Hepatitis C serology, baseline D-dimer, Troponin, CK

Adverse effects: Mild neutropenia, deranged LFTs.

Exclusion:
Active diverticulitis or oesophageal perforation
LFT 5x times of the reference range
Current TB, bacterial or fungal infection not being treated

6. We recommend each individual should be on DVT Prophylaxis (LMWH 40 mg SC daily or Heparin 5000 units SC BD) until there is any contraindication. COVID-19 probably is a prothrombic state and there is raising concern of pulmonary micro-vascular thrombosis formation. D-dimers and DIC screening (INR, APTT, Fibrinogen) should be routinely done. We suggest to be vigilant for venous thromboembolism (DVT/PE) and consider for therapeutic anticoagulation with caution if indicated.

7. Systemic steroids: Systemic steroids should in general be AVOIDED for these patients given potential harm. Steroids may be considered if indicated for another reason e.g. refractory septic shock, severe ARDS, evident cytokine storm etc. Methyprednisolone IV 1mg/kg body weight for 3 days can be used.

8. Convalescence Plasma (Hyperimmune immunoglobulins) therapy has shown some efficacy in COVID cases on mechanical ventilation or ECMO in observational data. There is increased prothrombotic risk with this therapy. (Weak recommendation at this stage if locally available).

9. A single dose of Ivermectin (ant-parasitic drug) showed viral clearance in 48 hours in laboratory setting. There is nil human study available at this stage (No recommendation).

10. Currently there are no data to support either starting or stopping ACEi/ARBs on any patients with COVID-19.

11. There are reports of NSAID use preceding clinical deterioration in some patients with severe COVID-19 disease. We recommend to avoid prescribing NSAIDs while patients are admitted.

COVID-19 Acute Respiratory Care Pathway

1. **Supplemental oxygen** (Nasal prongs/ Face Mask/ Face mask with reservoir bag) therapy to maintain oxygen saturation at 92%-96% *(Figure 1,2)*.

2. **High flow nasal oxygen (HFNO) therapy:** HFNO therapy can be used for hypoxia associated with COVID-19 disease, provide good nasal progs fitting and staff wearing optimal airborne PPE and preferably should be done in a single / negative pressure room.

3. **Non-invasive ventilation (NIV):** Routine use of non-invasive ventilation (BiPAP/CPAP) is not recommended. Current experience suggests that NIV for COVID-19 hypoxic respiratory failure is associated with a high failure rate, delayed intubation, and possibly increased risk of aerosolization with poor mask fit. This can be only considered where there is no ventilation facility or skilled manpower available or as a bridging therapy to emergent intubation or in cases of COPD and Cardiac failure.

4. **Non-invasive ventilation** (single limb) (*Figure 3*) machine should be converted to a NIV with **Non-vented mask** plus exhalation port plus antimicrobial filter *(Figure 3,4*) to mitigate the aerosolization risk and should be preferably delivered in a single / negative pressure room strictly with full PPE. The other option would be to use the standard dual limb invasive ventilatory machine with Non-vented mask as a NIV therapy if endotracheal intubation is not an option for the given case or cannot be offered due to staffing / local expertise issue.

5. **Helmet Mask** (*Figure 5*): We are not able to make a recommendation regarding the use of Helmet NIV Mask compared to full face mask NIV. This is an option, but we are not certain about its safety or efficacy for COVID-19 patients.

6. **We suggest NIV to be delivered at lower pressure settings – BiPAP max 12/6 cm or CPAP max 10 cm CPAP** with entrained oxygen via side port (*Figure 3*) with close monitoring (if intubation deemed to be inappropriate or not available at the center).

Oxygen Delivery Algorithm

(WHO IMAI Clinician Manual, Volume 1 WHO 2011)

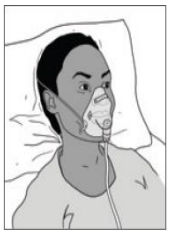
Place prongs inside the nostril. Hook tubing behind ears. Flow rates higher than 5-6 L will dry mucous membranes.

- Start oxygen at 2-6 L/min
- Use nasal prongs
- Assess response

If increasing respiratory distress or SpO_2 < 90% (88% in COPD)

Estimated FiO2 on different oxygen device

- 2-6 L/min - FiO2 28-40%
- 6-10 L/min - FiO2 40-60%
- 10-15 L/min-FiO2 60-95%



Secure mask firmly on face over nose and mouth. Pull strap over head.

- Use face mask
- **Increase oxygen to 6-10 L/min**
- Assess response

If increasing respiratory distress or SpO_2 <90% (<88% in COPD)

Make sure bag is full to deliver highest oxygen concentration. An empty bag is dangerous.

- Use face mask with reservoir
- **Increase oxygen to 10-15 L/min**
- Make sure bag inflates
- Call for help
- Assess response

If increasing respiratory distress or SpO2 <90% (<88% in COPD)

Transfer to a hospital with available invasive mechanical ventilator possible

- Call for help for possible endo-tracheal intubation
- Start manual ventilation (Bag and mask with good fit) with high-oxygen flow
- Alternatively, HFNO if available and intubation not appropriate or not available.

Figure 1: Step wise escalation of supplemental oxygen delivery algorithm

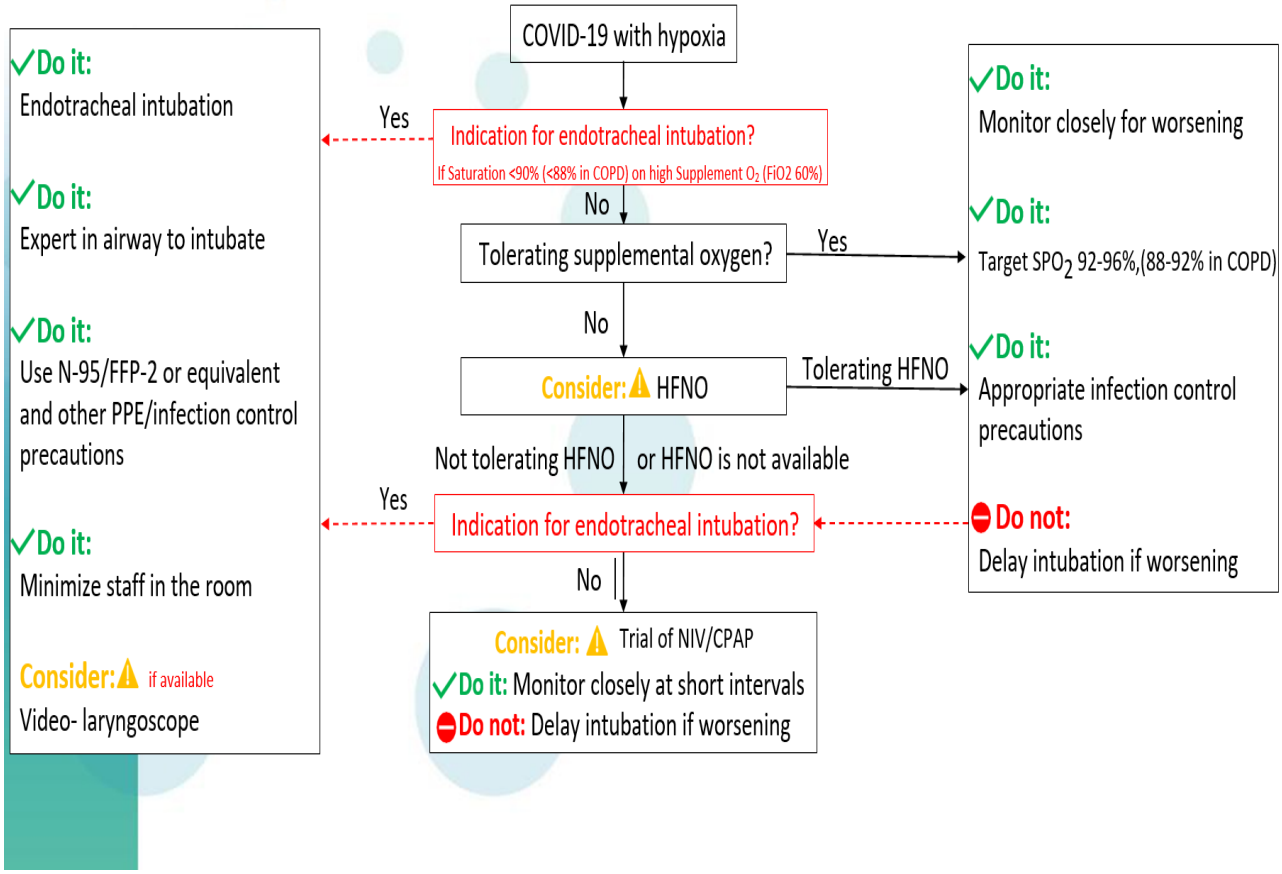


Figure 2: Algorithm of Acute respiratory failure management

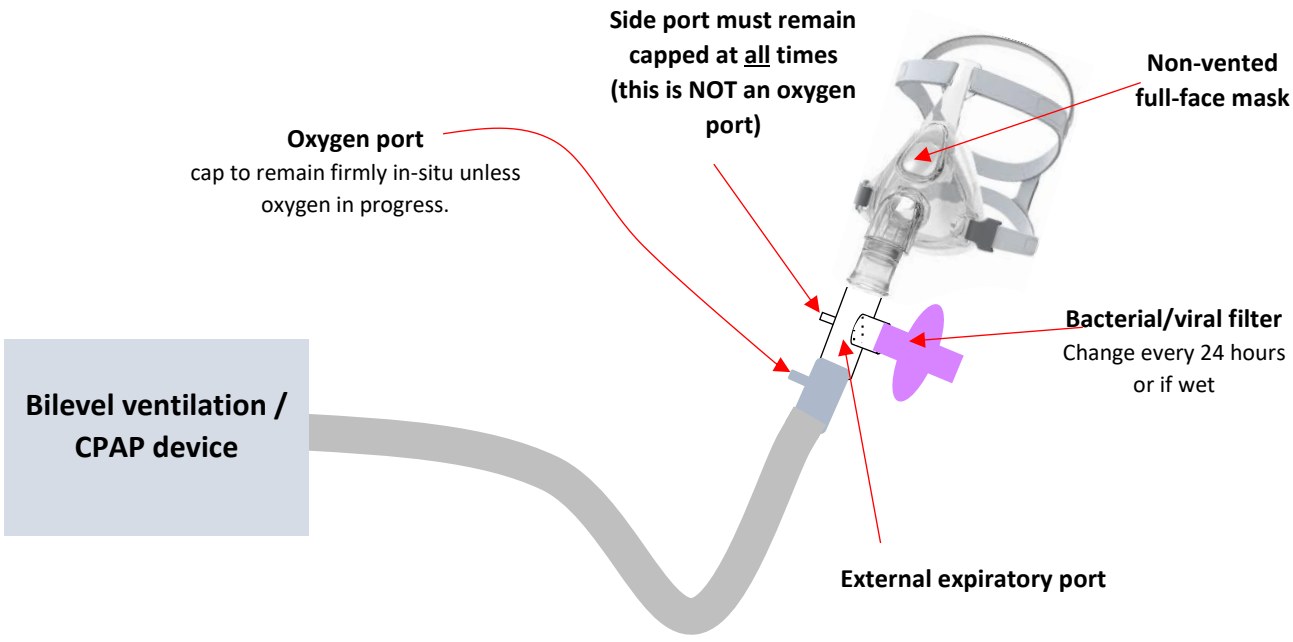


Figure 3: Single Limb NIV with non-vented mask, expiratory and oxygen port and filter

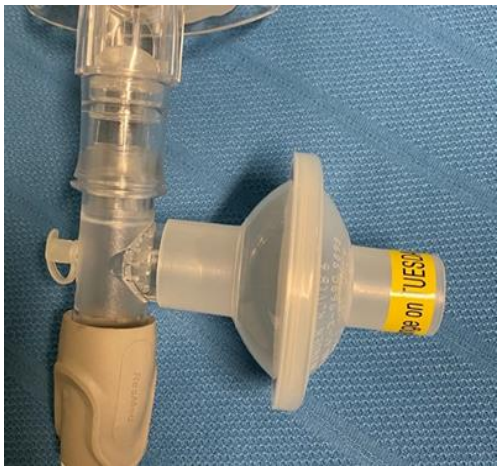


Figure 4: Antimicrobial Filter

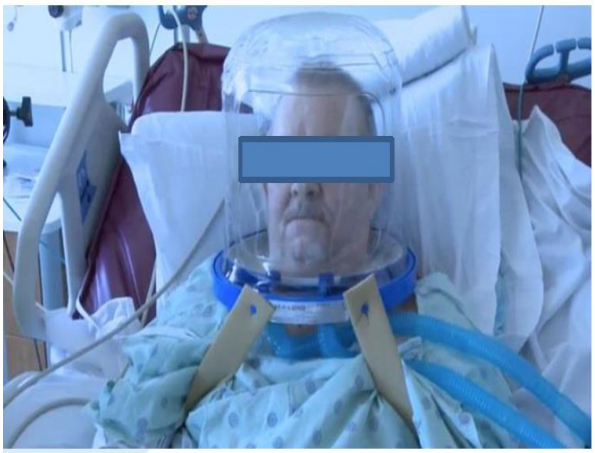


Figure 5: Helmet Mask

7. **Mechanical ventilation:**
   Indication: Clinical judgment on the basis of the following parameters:

- Signs of respiratory distress (e.g., accessory muscle use; paradoxical abdominal breathing)
- Rapid progression of disease.
- SpO2 sat <90% despite maximal supplemental oxygen.
- Arterial pH <7.3 with PaCO2 >50.
- Patient requiring >40 L/minute HFNO and FiO2 >0.6.
- Hemodynamic instability; multiorgan failure.

Lung protective mechanical ventilation (MV) is recommended for management for acute respiratory failure - Low tidal volume strategy (4-8ml/kg predicted body weight) and limiting plateau pressures < 30 cmH2O. Permissive hypercapnia is usually well tolerated and may reduce volutrauma.

8. **Prone positioning:** Suggest prone ventilation if the low tidal volume ventilation fails e.g. PaO2/FiO2 [P/F] ratio <150 mmHg or worsening oxygenation after intubation. This should be done in the context of a hospital guideline (Preferably 12-16 hrs/day) that includes suitable PPE for staff, and that minimises the risk of adverse events, e.g. accidental extubation.

9. **For patients who fail prone ventilation** (e.g. P/F ratio <150 mmHg while prone), may consider the following interventions:

- Lung recruitment maneuvers and high positive end expiratory pressure (PEEP) strategies as follows:

Principle for FiO2 and PEEP adjustment

FiO2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
PEEP	**5**	**5-10**	**10-18**	**18**	**18**	**18**	**18**	**18-24**

- Neuromuscular blockade for patients with refractory hypoxemia (eg, P/F <100 mmHg) or ventilator dys-synchrony.

- Trial of inhaled pulmonary vasodilators such as Nitric Oxide or Prostacyclin e.g. epoprostenol/Iloprost (data lacking, increased risk of aerosolization, should not be administered unless a specific protocol and experienced staff are in place).

- ECMO as a last resort; however, ECMO is not universally available.

10. **Fluid management:** A conservative fluid management strategy is recommended until evident tissue hypoperfusion. Where possible avoid 'maintenance' intravenous fluids, high volume enteral nutrition, and fluid bolus for hypotension.

11. **Suctioning:** Closed inline suction catheters are recommended. Any disconnection of the patient from the ventilator should be avoided to prevent lung decruitment and aerosolization. If necessary, the endotracheal tube should be clamped and the ventilator disabled (to prevent aerosolization).

12. **Nebulisation:** Use of nebulisers is not recommended and use of metered dose inhalers are preferred where possible.

13. **Bronchoscopy:** Diagnostic bronchoscopy is not recommended. It is not necessary for the diagnosis of viral pneumonia and should be avoided to minimise risk of aerosolization. Tracheal aspirate samples for diagnosis of COVD-19 are sufficient and Bronchio-alveolar lavage (BAL) is not usually necessary.

14. **Extubation from mechanical ventilation:** Standard weaning protocols should be followed. HFNO and/or NIV (well fitted facemask with separate inspiratory and expiratory limbs) can be considered as bridging therapy post-extubation but must be provided with strict airborne PPE.

15. **Tracheostomy:** This represents an aerosolizing procedure and must be considered in clinical decision making. Optimal PPE should be utilized at all times.

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