



National Guidelines on Clinical Management of COVID-19

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Directorate General of Health Services
Ministry of Health & Family Welfare
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World Health
Organization

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Preface

Coronavirus Disease-2019 (COVID-19) outbreak, which started in Wuhan, China, in December 2019, have turned into a pandemic. Bangladesh have started the preparation to control and contain the pandemic in the country since January 2020 based on the National Preparation and Response Plan. As a part of the preparation process, a guideline on COVID-19 clinical management was developed by Bangladesh Society of Medicine late January, 2020. To further update the document with the latest evidences and the WHO guidelines, we have prepared this 'Guidelines on Clinical Management of COVID-19'. Many esteemed clinicians and public health specialists have contributed to the development of the guidelines. We are grateful for their contribution. We request every clinician/hospital, who will treat COVID-19 'confirmed', 'probable', or 'suspect' cases, to follow the guidelines.

This is a living document. We will update the guidelines from time to time to incorporate latest evidences and recommendations of WHO. We welcome every suggestion and feedback on this document.



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Abbreviation:

AGP	Aerosol Generating Procedure
AST/ALT	Aspartate Aminotransferase/Alanine Amino Transferase
BMP	Basic Metabolic Panel
CAP	Community Acquired Pneumonia
CBC	Complete Blood Count
COVID-19	Coronavirus Disease 2019
CRRT	Continuous Renal Replacement Therapy
GGO	Ground-glass Opacity
CRP	C-Reactive Protein
ECMO	Extracorporeal Membrane Oxygenation
HCP	Health Care Provider
HCW	Health Care Worker
HDU	High Dependency Unit
ICU	Intensive Care Unit
ILI	Influenza like illness
IVIG	Intravenous Immunoglobulins
LAN	Lymphadenopathy
LDH	Lactate Dehydrogenase
LFT	Liver Function Tests
MAP	Mean Arterial Pressure
MERS-CoV	Middle eastern respiratory syndrome
NIPPV	Non-Invasive Positive Pressure Ventilation
PNA	Pulmonary Nodular Amyloidosis
PPE	Personal Protective Equipment
RSV	Respiratory Syncytial Virus
RT-PCR	Real time- Polymerase Chain Reaction
RVP	Respiratory Virus Panel
SARS	Severe acute Respiratory Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
VV	Venovenous

Executive Summary

Coronavirus disease-2019 (COVID- 19) caused by SARS-CoV-2 virus is declared as a pandemic by the World Health Organization (WHO) on 11th March 2020. It is at exponentially rising state across the globe appearing as second wave in many countries. Bangladesh is also facing the toll of this highly transmissible zoonotic disease with community transmission (at different rate) across the country. This is a new coronavirus, still evolving, and has put the scientific authority in a puzzle. The epidemic curve of this pandemic, which started in Wuhan of China and had spread to rest of the world, showed a typical pattern of being slow to start with steep rise in few days and then leading to a quick upsurge and thus collapsing the health system of affected country very quickly. The number of affected cases and deaths both have become exponential during this pandemic. WHO considers the agent as highly infectious and urges every nation to take it most seriously. To handle the pandemic, the main strategy is containment. The peak can be delayed or more precisely be flattened by isolation of cases, quarantine of contacts and physical distancing of people. Early diagnosis can help identifying cases and areas for individual and group isolation. From 'draconian' process of complete lockdown to confirmatory diagnosis and isolation is being practiced by almost every nation. Bangladesh has already started different mitigation processes to gain some control over this epidemic situation. This guideline is a part of the strategy addressing the case management of COVID-19 cases in Bangladesh with specific recommendations:

1. Case definition of suspect, probable, confirmed COVID-19 and death will be followed by every physicians of Bangladesh which will be updated regularly. All cases have to be reported to the health authority (civil surgeon, DGHS).
2. The concept of testing and isolation of cases, tracking, tracing, and quarantine of close contacts will be followed.
3. The clinical syndrome ranges from mild illness, pneumonia, severe pneumonia, ARDS, sepsis, septic shock and multiorgan failure. Post-COVID syndromes are also a big concern.
4. Specific test for confirmation will be done by RT-PCR taking samples from upper and lower respiratory tract until and unless serological tests and other WHO recommended tests are available. In case of initial negative test, if suspicion remains high, the patient should be treated as COVID-19 based on clinical judgement and others tests. Rt-PCR test should be repeated.
5. The mild cases of influenza like illness (ILI) will be managed by telemedicine service.
6. **Every hospital (public and private) shall provide treatment to COVID and non-COVID patients. These hospitals shall create separate zone for COVID and NON COVID patients in the hospital premises (subject to Government policy) and a triage system will be applied to classify and differentiate the patients. COVID zone will have two separate areas; one for confirmed COVID and another for suspected or probable COVID patients.**

7. The mild cases with major risk factor, moderate, severe and critical cases will be treated in all public and private hospital in Bangladesh (Severe and Critical cases preferably in tertiary care).
8. The principles of management will be appropriate supportive therapy in pneumonia cases ranging from low to high flow oxygen therapy, proning, antibiotic (in suspected bacterial infections), antiviral, anticoagulant for all hospitalized patients, steroids in severe to critical illness and mechanical ventilation for ARDS cases.
9. Every admitted patient with COVID-19 will receive thromboprophylaxis.
10. COVID-19 patients have increased cardiovascular complications. Observe for features of cardiovascular disease and other comorbidities during the acute COVID illness and also as 'long haulers' case.
11. For critically ill patients, careful fluid (avoid excessive fluid) balance and oxygen administration is the mainstay of therapy. SaO₂ target of 88-96% should be the aim.
12. Consider HFNC, NIV (CPAP and BIPAP) where facilities are available, awake proning before mechanical ventilation.
13. A comprehensive system of infection prevention and control (IPC) is important in every aspects of case management from community to hospital ICU. A separate national guideline is available in this aspect.
14. Healthcare personnel do not need to go for self-isolation if they have been termed as contact with a patient of COVID-19. They can carry on their duty on patient care with proper PPE unless symptomatic or tested positive for COVID-19. (Follow the standard protocol of quarantine & isolation during and after duty in COVID-19 ward)

Introduction

COVID-19 is the pandemic disease declared by World Health Organization (WHO) on 11th March 2020 which is a potentially severe acute respiratory infection caused by a novel evolving severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus was identified as the cause of an outbreak of 'pneumonia of unknown cause' in Wuhan City, Hubei Province, China, in December 2019. In most cases the clinical presentation is that of a respiratory infection with a symptom severity ranging from a mild influenza like illness, to a severe viral pneumonia leading to acute respiratory distress syndrome that is potentially fatal. But in some cases, presentation may be varied and may involve multiple organs leading to multi organ dysfunction or failure.

Globally 214 countries are reported to have the pandemic going on and the situation is evolving rapidly with global case counts and deaths increasing every day. The World Health Organization rates the global risk assessment as very high and community transmission is occurring in many countries, but it is uncertain how easily the virus spreads between people.

According to the 2020 World Health Statistics published by WHO, the COVID-19 pandemic is causing significant loss of life, disrupting livelihoods, and threatening the recent advances in health and progress towards global sustainable development goals.

In Bangladesh, COVID-19 infections are being reported from Directorate General of Health Service on daily basis. So far, we have around 410988 cases with 5966 deaths (2 November, 2020).

Early diagnosis, recognition, rapid isolation and quarantine are essential to prevent transmission and provide appropriate care in time frame. High index of clinical suspicion is needed for diagnosing COVID-19 patients and evaluation should be performed according to pneumonia severity indexes and sepsis guidelines (if sepsis is suspected) in all patients with severe illness.

There is no specific treatment found to be unequivocally effective (regarding mortality) for COVID-19 yet other than steroid; therefore, the mainstay of management is early diagnosis and optimum supportive care to relieve symptoms and to support organ function in more severe illness. Patients should be managed in a hospital setting when possible; however, home care may be suitable for selected patients; asymptomatic and cases with mild illness (without comorbidity) unless there is concern about rapid deterioration or an inability to prompt transfer to hospital if necessary. Even for those suitable for home care, if self-isolation at home is not possible because of lack of care giver, overcrowding at home or for any other cause, patient should be brought to the hospital for institutional isolation in a designated area. Designated isolation centers with necessary facilities should be developed across the country.

Rationing of medical resources may be required during the pandemic if healthcare infrastructures are overwhelmed. This raises many ethical questions on how to best triage patients to save the most lives. Recommendations have been suggested, but there is no international guidance on this issue yet.

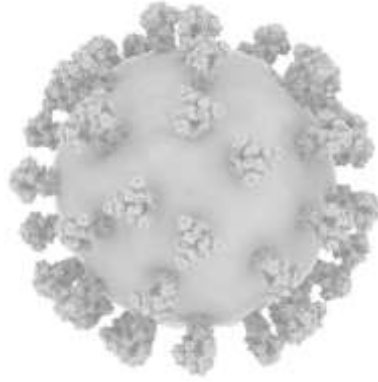
A surveillance-based case definition and approach to diagnosis and management principles are highlighted in this guideline. This version will be updated from time to time in response to the evolving situation of the epidemic in the country, availability of new scientific knowledge, better understanding of disease pathology and results of different clinical trials ongoing across the world and in accordance with the guidance provided by different organizations like WHO, CDC, ECDC and others.

Virology

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a previously unknown beta coronavirus that was discovered in bronchoalveolar lavage samples taken from clusters of patients who presented with pneumonia of unknown cause in Wuhan City, Hubei Province, China, in December 2019. Coronaviruses are a large family of enveloped RNA viruses, some of which causes illness in human (e.g., common cold), and others that circulate among mammals (e.g., bats, camels) and birds. Rarely, animal coronaviruses can spread to humans and subsequently spread between people, as was the case with severe acute respiratory syndrome (SARS-CoV) and Middle eastern respiratory syndrome (MERS-CoV).

SARS-CoV-2 belongs to the *Sarbecovirus* subgenus of the *Coronaviridae* family, and is the seventh coronavirus known to infect humans. The virus has been found to be similar to SARS-like coronaviruses from bats, but it is distinct from SARS-CoV and MERS-CoV. The full genome has been determined and published in GenBank.

The clade and lineage nomenclature is rapidly changing. Specific combinations of 9 genetic markers shows 95% of the hCoV-19 data in GISAID can be further classified in major 6 clades named S, L, V, G, GH, GR (Khailany RA, 2020). Initially the virus was classified into 2, then further into 3 super clades (Forster et al., 2020, Pachetti et al., 2020). The initial assessment of 3 clades indicates distinct geographic distribution (China, USA and Europe). In Bangladesh, a study found more than 96% of the isolates belonged to the G clade and its two major branches GH and GR clade. The common distinctive feature of these three clades is D614G mutation (Bangladesh Study). Though, this mutation took place in spike protein, there is no association found with severity, fatality or receptor binding domain property (Grubaugh et al., 2020, Hu et al., 2020, Ozono et al., 2020).



Picture showing ultrastructural morphology of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) when viewed with electron microscopically (*Centers for Disease Control and Prevention*)

N.B: Origin, transmission dynamics, viral load, shedding, genetics, pathophysiology of the novel virus (SARS-CoV2) are beyond the scope of this guideline. Interested readers are being encouraged to acquire further knowledge in this regard from peer reviewed sources from biomedical journals and open access sources like WHO, CDC and ECDC.

Case Definition

Suspected COVID-19 case (two suspected case definitions, A or B):

A. A person who meets the clinical AND epidemiological criteria:

Clinical criteria:

1. Acute onset of fever & cough OR
2. Acute onset of ANY THREE OR MORE of the following signs or symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhoea, altered mental status.

Epidemiological criteria:

1. Residing or working in an area with high risk of transmission of the virus: for example, closed residential settings and humanitarian settings, such as camp and camp-like settings for displaced persons, any time within the 14 days prior to symptom onset;

OR

2. Bangladeshi residence or traveling to an area/country reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset.

OR

3. Health care worker, working in health setting, including within health facilities anytime within the 14 days prior to symptom onset.

B. A patient with severe acute respiratory illness (SARI: acute respiratory infection with history of fever or measured fever of $\geq 38\text{ C}^\circ$; and cough; with onset within the last 10 days; and who requires hospitalization).

Probable COVID-19 case:

- A. A patient who meets clinical criteria above AND is a contact of a probable or confirmed case, or epidemiologically linked to a cluster of cases which has had at least one confirmed case identified within that cluster.
- B. A suspected case (described above) with chest imaging showing findings suggestive of COVID-19 disease

(* Typical chest imaging findings suggestive of COVID-19 include the following (Manna 2020):

- chest radiography: hazy opacities, often rounded in morphology, with peripheral and lower lung distribution
- chest CT: multiple bilateral ground glass opacities, often rounded in morphology, with peripheral and lower lung distribution
- lung ultrasound: thickened pleural lines, B lines (multifocal, discrete, or confluent), consolidative patterns with or without air bronchograms.)

C. A person with recent onset of anosmia (loss of smell) or ageusia (loss of taste) in the absence of any other identified cause.

D. Death, not otherwise explained, in an adult with respiratory distress preceding death AND who was a contact of a probable or confirmed case or epidemiologically linked to a cluster which has had at least one confirmed case identified within that cluster.

Confirmed case:

A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.

Definition of contact:

A contact is a person who has experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:

1. face-to-face contact with a probable or confirmed case within 1 metre and for at least 15 minutes
2. direct physical contact with a probable or confirmed case
3. direct care for a patient with probable or confirmed COVID-19 disease without using recommended personal protective equipment

N.B. for confirmed asymptomatic cases, the period of contact is measured as the 2 days before through the 14 days after the date on which the sample that led to confirmation was taken.

COVID-19 is a notifiable disease. Please report all cases to health authority (civil surgeon, DGHS) as surveillance. The clinical data will be reported as Mild (ILI)/ Moderate (Pneumonia), Severe (Severe pneumonia) and Critical (ARDS and Sepsis and Septic shock)

Definition of COVID-19 death:

COVID-19 death is defined (for surveillance purposes) as a death resulting from a clinically compatible illness in a probable or confirmed COVID-19 case, unless there is a clear alternative cause of death that cannot be related to COVID-19 disease (e.g. trauma). There should be no period of complete recovery between the illness and death.

All deaths should be documented and reported.

Clinical syndromes associated with COVID-19

- Mild illness (Influenza like illness-ILI)
- Pneumonia
- Severe pneumonia
- Acute respiratory distress syndrome
- Sepsis
- Septic shock

<p>Mild illness (ILI)</p>	<p>Patients with uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), sore throat, nasal congestion, anorexia, anosmia, ageusia, malaise, or headache. Rarely, patients may also present with diarrhoea, nausea, and vomiting.</p> <p>The elderly and immunosuppressed may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, such as dyspnoea, fever, GI-symptoms or fatigue, may overlap with COVID-19 symptoms</p>
<p>Pneumonia</p>	<p>Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia.</p> <p>Child with clinical signs of non-severe pneumonia (cough or difficulty breathing + fast breathing and/or chest indrawing) and no signs of severe pneumonia.</p> <p>Fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 (55). While the diagnosis can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications</p>
<p>Severe pneumonia</p>	<p>Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO₂ < 90% on room air .</p> <p>Child with clinical signs of pneumonia (cough or difficulty in breathing) + at least one of the following:</p> <ul style="list-style-type: none"> • Central cyanosis or SpO₂ < 90%; severe respiratory distress (e.g. fast breathing, grunting, very severe chest indrawing); general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions • Fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40.

	<p>While the diagnosis can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications.</p>						
<p>Acute respiratory distress syndrome (ARDS)</p>	<ul style="list-style-type: none"> > Onset: within 1 week of a known clinical insult (i.e. pneumonia) 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/oedema if no risk factor present. > Oxygenation impairment in adults: <ul style="list-style-type: none"> a • Mild ARDS: $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$ (with PEEP or CPAP $\geq 5 \text{ cmH}_2\text{O}$). b • Moderate ARDS: $100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}$ (with PEEP $\geq 5 \text{ cmH}_2\text{O}$). c • Severe ARDS: $\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mmHg}$ (with PEEP $\geq 5 \text{ cmH}_2\text{O}$). > Oxygenation impairment in children: note OI and OSI. Use OI when available. If PaO_2 not available, wean FiO_2 to maintain $\text{SpO}_2 \leq 97\%$ to calculate OSI or $\text{SpO}_2/\text{FiO}_2$ ratio: <ul style="list-style-type: none"> • Bilevel (NIV or CPAP) $\geq 5 \text{ cmH}_2\text{O}$ via full face mask: $\text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$ or $\text{SpO}_2/\text{FiO}_2 \leq 264$. • Mild ARDS (invasively ventilated): $4 \leq \text{OI} < 8$ or $5 \leq \text{OSI} < 7.5$. • Moderate ARDS (invasively ventilated): $8 \leq \text{OI} < 16$ or $7.5 \leq \text{OSI} < 12.3$. • Severe ARDS (invasively ventilated): $\text{OI} \geq 16$ or $\text{OSI} \geq 12.3$. > In resource limited settings, 'Kigali-modification of Berlin criteria' can be followed- <ul style="list-style-type: none"> > No arterial blood gas analyser to assess degree of hypoxaemia= $\text{SpO}_2/\text{FiO}_2 \leq 315$ is ARDS > No mechanical ventilation= Remove PEEP and CPAP from definition > No chest radiograph or CT scan= Use ultrasound to document bilateral chest opacities 						
<p>Sepsis</p>	<p>Sepsis: adults</p> <p>Life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection.</p> <table border="0" style="width: 100%;"> <tr> <td style="width: 50%;">Signs of organ dysfunction</td> <td style="width: 50%;">Laboratory evidence of:</td> </tr> <tr> <td>Altered mental status</td> <td>Coagulopathy</td> </tr> <tr> <td>Difficult or fast breathing</td> <td>Thrombocytopenia $< 50,000/\text{cmm}$</td> </tr> </table>	Signs of organ dysfunction	Laboratory evidence of:	Altered mental status	Coagulopathy	Difficult or fast breathing	Thrombocytopenia $< 50,000/\text{cmm}$
Signs of organ dysfunction	Laboratory evidence of:						
Altered mental status	Coagulopathy						
Difficult or fast breathing	Thrombocytopenia $< 50,000/\text{cmm}$						

	<p>Low oxygen saturation</p> <p>Reduced urine output</p> <p>Fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling</p> <p>Children: suspected or proven infection and ≥ 2 age- based systemic inflammatory response syndrome criteria, of which one must be abnormal temperature or white blood cell count.</p>	<p>Raised lactate</p> <p>Hyperbilirubiemia</p>
Septic shock	<p>Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L.</p> <p>Children: any hypotension (SBP < 5th centile or > 2 SD below normal for age) or two or three of the following: altered mental state; tachycardia or bradycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or feeble pulse; tachypnoea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia (21).</p>	

**Sepsis and septic shock from other causes should be excluded and referred to a non-COVID zone/facility/hospital after proper evaluation.

N.B: When PaO₂ is not available, SpO₂/FiO₂ ≤ 315 suggests ARDS (including in non-ventilated patients). Oxygenation Index (OI) is an invasive measurement of the severity of hypoxaemic respiratory failure and may be used to predict outcomes in paediatric patients. It is calculated as follows: percentage of fraction of inhaled oxygen multiplied by the mean airway pressure (in mmHg), divided by the partial pressure of arterial oxygen (in mmHg).

Oxygen saturation index (OSI) is a non-invasive measurement and has been shown to be a reliable surrogate marker of OI in children and adults with respiratory failure. OSI replaces PaO₂ with oxygen saturation as measured by pulse oximetry (SpO₂) in the OI equation. The SOFA score ranges from 0 to 24 and includes points related to six organ systems: respiratory (hypoxaemia defined by low PaO₂/FiO₂); coagulation (low platelets); liver (high bilirubin); cardiovascular (hypotension); central nervous system (low level of consciousness defined by Glasgow Coma Scale); and renal (low urine output or high creatinine).

Sepsis is defined by an increase in the sepsis-related SOFA score of ≥ 2 points. Assume the baseline score is 0 if data are not available.

SIRS criteria: abnormal temperature (> 38.5 °C or < 36 °C); tachycardia for age or bradycardia for age if < 1 year; tachypnoea for age or need for mechanical ventilation; abnormal white blood cell count for age or $> 10\%$ bands.

Testing for COVID-19

Whom to test: All Suspected cases (according to the case definition)

Detection of virus

➤ Specimen- Specimen type include

- Upper airway specimens: Oropharyngeal swabs, nasal swabs, nasopharyngeal secretions.
- Lower airway specimens: sputum, bronchoalveolar lavage fluid, airway secretions

Note: Sputum and other lower respiratory tract specimens have a high positive rate of nucleic acids and should be collected preferentially. SARS-CoV-2 preferentially proliferates in type II alveolar cells (AT2) and peak of viral shedding appears 3 to 5 days after the onset of disease. Therefore, if the nucleic acid test is negative at the beginning, samples should continue to be collected and tested on subsequent days.

➤ Detection of viral nucleic acid

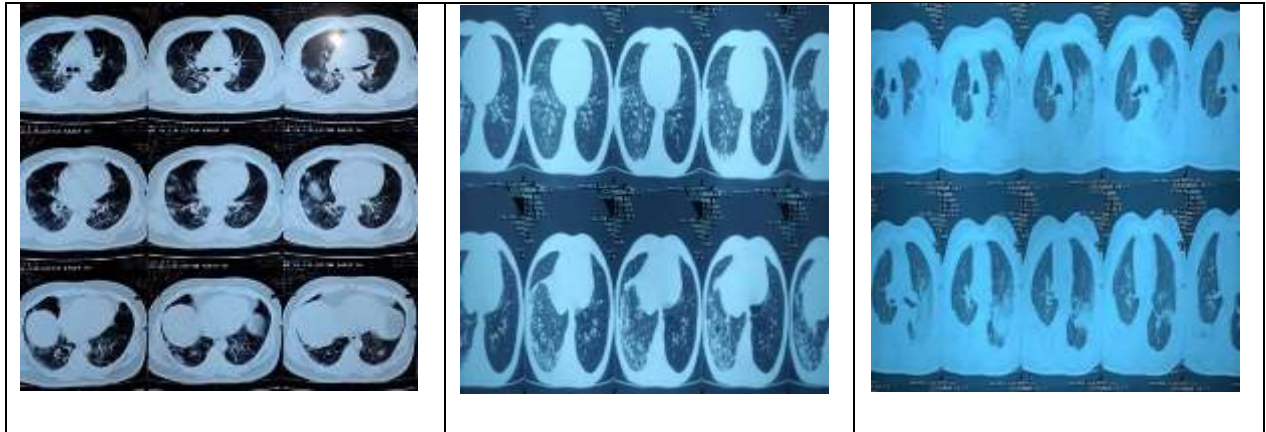
Nucleic acid testing is the preferred method for diagnosing COVID-19. In our country viral nucleic acid is detected by RT-PCR. The sensitivity of detection depends upon following factors, 1. Specimen site 2. Quality of specimen 3. Temperature of storage 4. Faulty collection techniques 5. Faulty transport.

Serological test: (See in Annex 4)

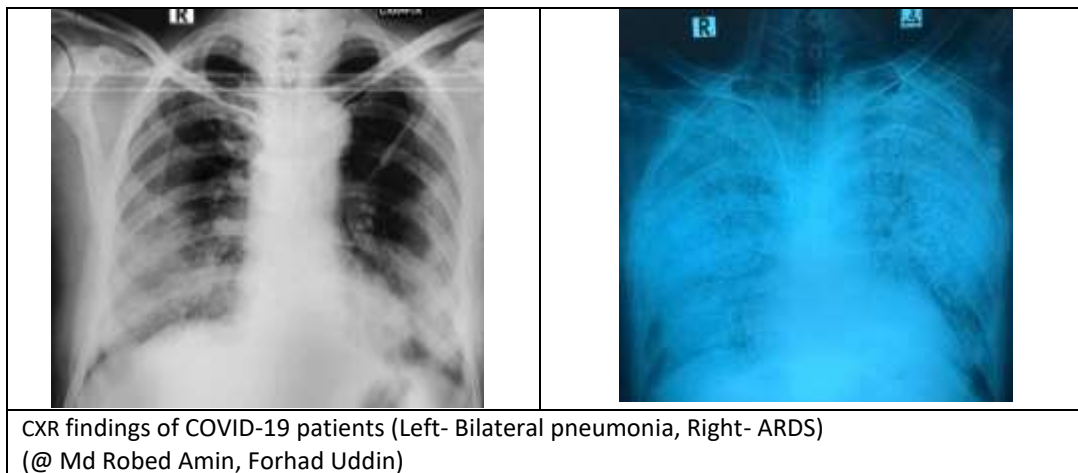
Radiology and imaging.

- CT Chest- a high-resolution CT is highly preferable. Following are the classical CT findings
 - Bilateral involvement in most patients
 - Multiple areas of consolidation
 - Ground-glass opacities (GGO): bilateral, subpleural, peripheral
 - Crazy paving appearance (GGOs and inter-/intra-lobular septal thickening)
 - Bronchovascular thickening in the lesion
 - Traction bronchiectasis
- Chest Xray- Is not as sensitive as HRCT. CT is better than Chest Xray for diagnosis early. Bilateral pneumonia is a common finding of COVID-19 pneumonia
- USG of chest- there are specific sonographic findings however it requires a skilled operator who has training on Pulmonary Ultrasonography

All of the above techniques (CXR, CT, sonography) are nonspecific. Patchy ground-glass opacities may be caused by a broad range of disease processes (e.g. viral and bacterial pneumonias). Ultimately, the imaging is only one bit of information which must be integrated into clinical and epidemiological context.



CT findings of a COVID-19 patient (Ground glass opacities, Bilateral pneumonia) (© Md Robed Amin, A Ghose)



CXR findings of COVID-19 patients (Left- Bilateral pneumonia, Right- ARDS)
(@ Md Robed Amin, Forhad Uddin)

Supportive investigations

- CBC: lymphopenia (83%), leukopenia (9–25%), leucocytosis (24–30%), thrombocytopenia.
- Patients with a low total number of lymphocytes at the beginning of the disease generally have a poor prognosis. Severe patients have a progressively decreased number of peripheral blood lymphocytes. A ratio of Neutrophil to lymphocyte more than 3.5 is a prognostically poor sign.
- CRP and Procalcitonin: Most patients with COVID-19 have a normal level of procalcitonin with significantly increased levels of C-reactive protein. A rapidly and significantly elevated C-reactive protein level indicates a possibility of secondary infection.
- Blood culture: to detect secondary bacterial infection.
- Liver and Renal function test, Arterial blood gas analysis.
- Serum Ferritin, S.LDH, D-dimer (D-dimer levels and Ferritin are significantly elevated in severe cases, which is a potential risk factor for poor prognosis).

- Considering endemicity of other febrile illness malaria, dengue and tuberculosis test can be done to exclude other diseases
- Treating clinician may order other relevant investigations if required.

N.B: The combination of Normal or low WBC, Elevated C-Reactive Protein, and associated Bilateral pneumonia in Chest Xray or Ground Glass Opacities (GGO) in HRCT of chest suggests a diagnosis of COVID-19 during this pandemic, irrespective of the RT-PCR result.

Clinical Classification

For the practical purpose of patient management, the six syndromes of COVID-19 have been categorized into mild, moderate, severe and critical cases.

Clinical classification for case management		
01	Mild	Influenza like illness (ILI)
02	Moderate	Pneumonia (CRB 65 score 0)
03	Severe	Severe Pneumonia, Sepsis
04	Critical	ARDS, Septic shock

N.B. Some patients of COVID-19 may have hypoxia without clinically evident dyspnoea and cyanosis. Thus, wherever available, pulse oximetry should be used to rule out hypoxia and respiratory failure.

N.B. After evaluation and testing for respiratory distress, cases due to cardiac causes/ non COVID-19 causes will be sent to NON COVID zone.

Clinical Case definition

1. Mild cases

- The clinical symptoms are mild, and there is no sign of pneumonia on imaging.
- Symptoms may be: fever, cough, sore throat, malaise, headache, muscle pain without shortness of breath or abnormal imaging

2. Moderate cases

- Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia.
- Respiratory distress with < 30 breaths /min
- Pulse oxymetry showing saturation > 90% at ambient air

3. Severe cases

Cases meeting any of the following criteria:

- Respiratory distress (≥ 30 breaths/ min);
- Finger oxygen saturation $\leq 90\%$ at rest;
- Arterial partial pressure of oxygen (PaO₂)/fraction of inspired oxygen (FiO₂) ≤ 300 mmHg (1mmHg=0.133kPa)

4. Critical cases

Cases meeting any of the following criteria:

- Respiratory failure and requiring mechanical ventilation.
- Shock.
- With other organ failure that requires ICU care.

Treatment Protocol for COVID-19 cases

Mild cases can be managed at home through telephone/telemedicine service (Annex 2) while mild case with risk factor, moderate, severe and critical patients should receive hospital care after appropriate triage.

Laboratory investigations

To be chosen based on availability. The most important investigations are initial CBC and Chest X-ray (may require to be repeated). CT scans have high sensitivity for diagnosis even in PCR negatives. Not advised routinely, but if available, will be better than Chest Xray. Any clinically defined case should be tested with RT-PCR.

Mild cases: CBC with CRP, Chest X-ray, ECG (>50 yr age),

Moderate cases: CBC with CRP, D-dimer, Chest Xray (P-A view) (preferably portable), LFT, RFT, , ECG (>50 yr age). CT chest is more sensitive than chest Xray for early diagnosis And also for follow up

Severe cases: CBC with CRP, S electrolytes, ABG, Coagulation profile (D-dimer especially), LDH, Ferritin, LFT, RFT, Blood culture, Procalcitonin, Lactate, Echocardiogram, Troponin I & Pro-BNP, ECG. CT chest is more sensitive than chest X ray for early diagnosis and also for follow up.

Critical Cases: All investigations for severe cases with additional ICU investigations as deemed necessary.

Case record Form (CRF): All the clinically defined cases (Mild, Moderate, Severe and Critical) in hospital setting need to be documented in a CRF where the demographic, clinical presentation, investigations and treatment will be included. (Annex 8 is the prototype of the CRF)

General Management

- Bed rest and strengthening support therapy.
- Ensuring sufficient calorie intake.
- Monitoring vital signs and oxygen saturation.
- Timely initiation of effective oxygen therapy.
- Treatment venue will be determined according to severity of the disease:
 - Suspected and confirmed cases should be isolated and preferably treated at designated hospitals with effective isolation, protection and infection prevention conditions in place.
 - A mild case may be treated in isolation in a single room at home. (Home isolation protocol should be followed).
 - Mild cases with comorbidity/risk factor, Moderate & Severe cases should be treated in hospital
 - Critical cases should be admitted to ICU as soon as possible.

Pharmacological and supportive Treatment

A. Asymptomatic patients

Supportive care + Isolation protocol (either home or institutional depending on national strategy).

Advice for cases in home isolation:

- Rest at home in self-isolation (If self-isolation at home is not possible because of lack of care giver, overcrowding at home or for any other cause, patient should be brought to the hospital for institutional isolation in a designated area.)
- Physical distancing with family members (If possible, remain in a separate single room)
- No visitor
- Hand wash (20 seconds each time) (Repeated hand wash is beneficial)
- Cough etiquette (use tissue paper or elbow followed by hand wash)
- Medical mask (both patient and caregiver)

B. Mild cases

A mild case may be treated in isolation in a single room at home. (above mentioned home isolation protocol should be strictly followed).

Symptomatic patients in risk group (like DM, HTN, IHD, Prior Asthma/COPD/ILD patients, Known CKD, CLD, Known Malignancy, High risk pregnancy, Obesity (BMI>25)) should be admitted in the isolation ward.

- Tab Paracetamol (500mg) 1 tab if temp is more than 101°F
- Antihistamine if there is rhinorrhoea
- Antitussive if there is dry cough
- Thromboprophylaxis: For Mild COVID 19 cases with risk factors: Enoxaparin 40 mg, SC, once daily (for obese patients, 40 mg BID). Adjust dose when CrCl < 30ml/min or start Unfractionated heparin 5000 unit SC /day. (follow flow chart page 36)
- Monitor closely.

N.B:

- Follow up
 - Self-home isolation for 14 days after clinical recovery
 - Ask about: dyspnoea, chest pain, persistent or worsening dry or productive cough, haemoptysis
 - SPO₂ measurement through pulse oximeter if possible

- When patient should immediately seek and get hospital care?
 - Respiratory distress (Respiratory Rate >24 or SPO₂ < 94%)
 - Worsening cough and fever
 - Altered mental status
 - Extreme lethargy or unable to proper talk

Admission criteria

1. All suspected/ confirmed cases of COVID-19 presenting with
 - Mild case with major risk factor [DM, HTN, IHD, Prior Asthma/COPD/ILD patients, Known CKD, CLD, Known Malignancy, High risk pregnancy, Obesity (BMI>25)] and deteriorating mild cases in home/institutional isolation
 - Moderate case- clinical or radiological evidence of pneumonia
 - Severe Pneumonia
 - ARDS, Sepsis, Septic shock
 - Hypoxia (SpO₂ <94%) in the absence of any clinical signs
2. All cases with respiratory distress must be admitted for further evaluation and testing

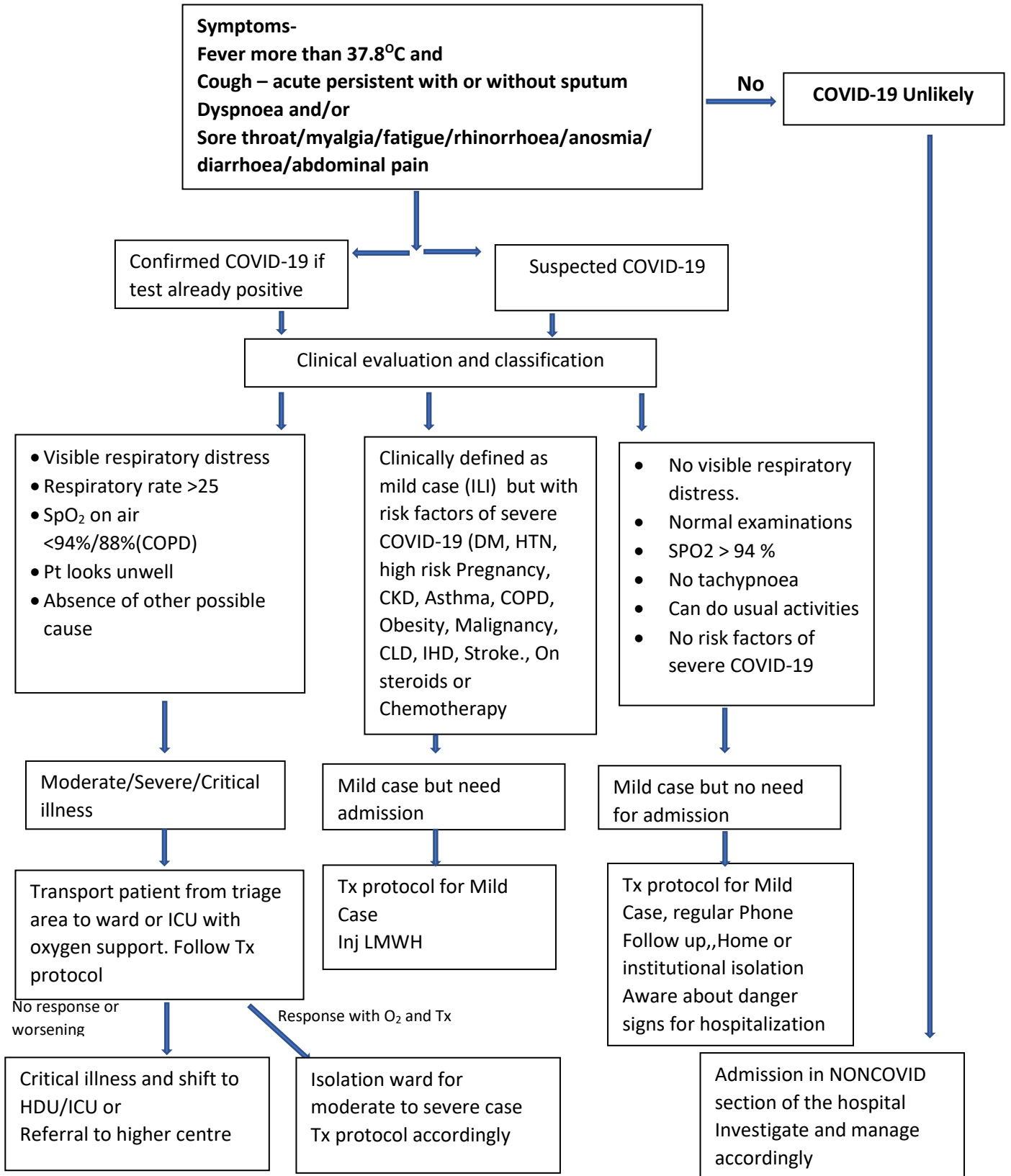
Hospital Management and Triage

All hospitals of Bangladesh should have a triage system in their emergency and out-patient department (OPD) or makeshift emergency (like tent). COVID -19 is not only a respiratory disease but a multisystem disorder and hence every hospital should have a plan to categorize, deal with and admit patients of COVID-19 as well as Non COVID cases (subject to national strategy). This can be achieved through an appropriate triage system and proper use of infection prevention and control system in hospital with proper use of Personal Protective Equipment. The hospital administration should arrange separate zone/compartment/section/building in the same/separate premise for COVID-19 or suspected COVID cases and Non COVID cases.

The triage at the emergency/OPD will prepare a flow by which the patients coming to hospital can be separated quickly as confirmed COVID-19 cases, suspected cases (which can be COVID or non COVID) and confirmed non COVID cases. The initial triage must also ensure quick admission and treatment initiation for the patients who require immediate management in hospital. After initial triage and appropriate separation protocol, when test results become available for suspected cases, the new confirmed cases of COVID -19 cases can be sent to isolation zone/ward/room/cabin and confirmed non-COVID cases will be shifted to their designated section of the hospital. [Every hospital should be prepared from now on to serve both COVID and Non-COVID cases whenever warranted].

At entry point of triage, the rapid point of care test (serological antigen-based paper test) would make confirmation quickly for zone based admission of patients. (Annex-4)

Until the RT-PCR test result for SARS-CoV-2 is available in suspected case, the patient should remain in isolation ward (suspected patient zone) with every bed at 6 feet distance with proper IPC. When result is negative and clinical course (with lab reports) is no more consistent with COVID -19, patient may be shifted to Non COVID section of the hospital. When result is negative but clinical course (with supporting lab reports) is consistent with COVID-19, patient will remain in 'suspected patient zone'. If result comes as positive, patient will remain in isolation ward (positive patient zone).



This is a simplified triage for every hospital in Bangladesh (Public or private).

C. Moderate case: (Clinical or radiological pneumonia case)

Mild symptomatic Treatment Protocol

Plus

- Oxygen through nasal canula (Maximum 5 L/min) if required.
- Proning- Prone position at least 4-6 hrs/day
- LMW heparin (Inj enoxaparin) Enoxaparin 1mg/kg SC twice daily/ day (dose adjust with CrCl< 30ml/min) (Follow flow chart page 36)
Or if LMWH cant be given or contraindicated
- Inj Unfractionated heparin (UFH): 60U/kg bolus+12units/kg/hr infusion-for ACS
80U/Kg bolus +18units/kg/hr infusion-for VTE and AF
- Thromboprophylaxis should be given until symptom resolves or improves and followed by Tab rivaroxaban 10 mg once daily for 1 month
- Antiviral: For moderate to severe cases who need oxygen therapy and/or are hospitalisation Inj Remdesivir has been advocated. Dosage of Remdesivir: 200 mg IV infusion (within 30 min-2 hours) on Day 1 followed by 100 mg infusion (within 30 min to 2 hours) from Day 2 to Day 5 . If Remdesivir is started, then other antiviral (e.g. favipiravir) should be stopped.
Remdesivir should be used at the discretion of consultant working in the hospital and can be used in the treatment of all hospitalized adult and pediatric patients (>12 years old) with suspected or laboratory-confirmed COVID-19, irrespective of their severity of disease.
- Any Moderate case on treatment – if no response or deterioration at 24 hours in hospital:
 - Oral Dexamethasone 6 mg/day in single or two divided dose for 10 days (market formulation is 0.5 mg and so for adult 12 tab is needed) or Oral Methylprednisolone (60-80 daily) in single or two divided doses for 7 days with antiulcerant coverage and antihelminthic coverage.

N.B: Antiviral drugs are expensive, have side effects and should be used judiciously under the discretion of consultant/Expert in a hospital. As per physician discretion, favipiravir may be used in non-hospitalized moderate cases. Dosage: 800 mg BID on day 1 followed by 600 mg BID from day 2 to day 10.

Antibiotics should not be used as routine drug in COVID-19 case. However, they should be considered in a older people and children < 5 years of age, to provide empirical treatment for possible bacterial pneumonia.

Simple antibiotic (e.g amoxycillin and clavulanic acid) should only be prescribed at the discretion of consultant and if there is strong suspicion of secondary bacterial infection (Commonly procalcitonin is high in bacterial infection).

During management of hospitalized patient in ward or isolation room-

- Avoid Nebulization and advanced respiratory treatments as far possible. Use MDI with volume spacers if required.
- Avoid non-invasive ventilation
- **Early referral to the HDU/ ICU** for a patient with increasing respiratory signs/symptoms.

Referral of patients with Severe and Critical COVID-19 (From upazilla health complex /district hospital to tertiary care hospital)

It is extremely difficult to frame rigid guidelines for referral because of non-uniformity in availability of facilities in small hospitals and financial constraints of the patients. However, following are few guidelines to help the treating doctors in taking a decision.

Indications for referral

1. Severe and Critical COVID-19
2. Respiratory distress (not due to over hydration) [ARDS].
3. Persisting oliguria even after correction of dehydration.
4. Multi organ failure.
5. Active bleeding.
6. Any serious Cardiovascular or Cerebrovascular disease (MI, ACS, stroke etc).

The following measures should be taken while referring a patient to referral hospital

Pre-referral:

- Information to family, guardian and patient about diagnosis and treatment plan
- Explain where to refer and how to transfer
- Make sure referral facility has ventilatory or renal replacement support
- Communicate if possible, with the referring hospital.
- If possible send the patient in a designated ambulance with oxygen and proning with an accompanying medical personnel who can manage the above scenario.

During transfer:

- Give oxygen
- Maintain airway
- Have suction available
- Maintain IV access and infusion IV fluids to correct dehydration
- Provide life support system and guidance to the person accompanying the patient
- Insert a urethral catheter in patient with reduced urine output
- Provide a referral note

D. Severe cases with respiratory symptoms

Management of Moderate case protocol (Except oral steroid)

Plus

- Steroids- **Inj Dexamethasone 6 mg daily for 10 days**
or
Inj Methylpredniolone-250 mg daily for 5 days (switch to IV from oral if already started)
- Maintain euvolaemia (Avoid fluid load)
- Early Norepinephrine for hypotension
- **Broad spectrum antibiotics— IV drug at the discretion of consultant**
- Consider for cytokine storm/ HLH (Hemophagocytic lymphohistiocytosis) picture:
 1. Tocilizumab*
 2. Convalescent Plasma therapy**

***Tocilizumab:** Adult Dosing (≥ 18 years): 8 mg/kg (max: 800 mg/dose) • Pediatric Dosing (< 18 years): Wt < 30 kg—12 mg/kg; Wt > 30 kg—8 mg/kg (Max: 800 mg/dose) Duration: 1 dose; Can be repeated after 12 hours if no clinical improvement. Max 2 doses

Indication of Tocilizumab:

1. COVID-19 positive and All of the following respiratory findings:
 - a. Abnormal chest imaging consistent with COVID-19
 - b. Rapidly worsening gas exchange/respiratory status over 24-48 hours and requiring > 6 L/min O₂ or on mechanical ventilation
2. Absence of systemic bacterial, fungal or parasitic co-infection
3. High clinical suspicion for cytokine release syndrome and clinically deterioration of the patient

Convalescent Plasma therapy: Donor should be healthy subject recovered from COVID-19 and preferably after 28 days with neutralizing titre more than 1:160 and binding titre more than 1:1000

Indication of convalescent plasma:

1. Age > 18 years old
2. Positive SARS-CoV-2 and symptoms more than 8-10 days
3. Informed consent
4. Severe or life-threatening disease defined by at least one of the following:
 - Increasing dyspnea
 - Respiratory rate > 30
 - SpO₂ $< 88\%$
 - P/F ratio < 300
 - Lung infiltrate $> 50\%$ within 24-48 hours
 - Septic shock
 - Multi organ failure

N.B:

1. In severe case, broad spectrum antibiotic can be prescribed if secondary bacterial infection is suspected and the choice of drug should be under the discretion of consultant working in hospital.
2. In severe case, If Antiviral drug (IV Remdesivir) is prescribed, it is better to prescribe it as early as possible.
3. In severe cases, after appropriate therapy with Oxygen, antiviral and steroids, if there is clinical deterioration and there is indication of IL-6 inhibitor and or convalescent plasma present, then these modalities of treatment should be provided with frequent monitoring of disease and drug related phenomena.
4. Prior to administration of convalescent plasma, the binding titer and or neutralizing titer should be measured in donor from appropriate centre and expert opinion should be sought.
6. Immunomodulator, Monoclonal antibody or JAK inhibitor should not be used without evidence of clinical trial

Thromboprophylaxis in severe case:

- LMW heparin (Inj enoxaparin) enoxaparin 1mg/kg/day SC twice daily (dose adjust with CrCl< 30ml/min)
Or if LMWH cant be given or contraindicated
Inj unfractionated heparin (UFH): 60U/kg bolus+12units/kg/hr infusion-for ACS
80U/Kg bolus +18units/kg/hr infusion-for VTE and AF
- Thromboprophylaxis should be given until symptom resolves or improves and followed by tab rivaroxaban 10 mg once daily for 2 months
- Appropriate dose (upper limit) of anticoagulant should be practised in severe to critical illness of COVID-19

E. Critical cases with respiratory symptoms (SOB; hypoxia: admit to ICU)

In addition to the treatment protocol stated above, following measures are part of critical case management.

Escalation of respiratory support: Following are important for severe to critical patients who need intensive monitoring:

- **Prone positioning (more than 12 hrs/day) for improvement of Oxygenation.**
- **Low flow O2 delivery devices:**
Nasal cannula (up to 4-6LPM and provide up to 50% FiO₂; Simple mask (up to 10 LPM and provide up to 60% FiO₂); Venturi mask (up to 15 LPM and provide 24 -60% FiO₂); Partial rebreather mask (15 LPM and provide 70% FiO₂); Non rebreather mask (15 LPM and provide 100% FiO₂)
- **High flow delivery device:**
High Flow Nasal cannula (HFNC): up to 60-70 LPM and provide 100% FiO₂
Advantages: Well tolerated, generate PEEP in closing mouth.
- **Non-invasive positive pressure ventilation:**
CPAP: (Setting 5-20 cmH₂O) and used for type I respiratory failure;
BiPAP (Setting EPAP 4-16 cm H₂O, IPAP 10-20 cmH₂O and minimum pressure support 4 cmH₂O) and used for both type I and type II respiratory failure.
 Increase CPAP or EPAP for hypoxia
 Increase pressure support (IPAP-EPAP) for hypercapnia
- **Mechanical ventilation.** (When all the above measures fail or indicated.)

Monitoring for severe to critical patients (if facility is available)

Depends on the severity of the patients and discretion of the consultant. To close monitor of the vital organs following investigations can be recommended

- Daily: CBC, CRP, RBS, ECG, Ferritin, , D-dimer, Electrolyte. Blood urea , Serum Creatinine, LFT , ABG(if possible) CRP and Ferritin are good biomarkers and track disease severity.
- Follow CXR, CT scan of Chest or Bed side USG
- Follow Troponin and ECHO closely; patient sometime develops severe cardiomyopathy/myocarditis.

Hospital care Principles

- Mild cases with risk factors, severe and critical cases of suspected (or probable) or confirmed COVID-19 require hospital care.
- Management of such patients warrant immediate implementation of appropriate infection prevention and control measures.
- Patients with severe disease often need oxygenation support.

- Aerosol generating procedures such as endotracheal intubation, bronchoscopy, nebulization, cardiopulmonary resuscitation, open suctioning of respiratory tract, tracheostomy etc. demand specific protection of healthcare workers with appropriate personal protective equipment (PPE).
- The safety of high-flow oxygen and non-invasive positive pressure ventilation in these measures is uncertain, and they should be considered aerosol-generating procedures that warrant specific isolation precautions.
- Patient with sepsis with or without shock may require treatment in high dependency unit (HDU) or ICU depending on disease severity and clinical judgement of treating physicians.
- If patients develop acute respiratory distress syndrome, intubation with mechanical ventilation will be needed.
- Aerosol generating procedures such as endotracheal intubation, bronchoscopy, nebulization, cardiopulmonary resuscitation, open suctioning of respiratory tract, tracheostomy etc. demand specific protection of healthcare workers with appropriate personal protective equipment (PPE).
- The safety of high-flow oxygen and non-invasive positive pressure ventilation in these measures is uncertain, and they should be considered aerosol-generating procedures that warrant specific isolation precautions.
- Patient with sepsis with or without shock may require treatment in high dependency unit (HDU) or ICU depending on disease severity and clinical judgement of treating physicians.
- If patients develop acute respiratory distress syndrome, intubation with mechanical ventilation will be needed.

COVID-19 ICU Management Strategies

Respiratory failure:

- It is conventionally defined by an arterial oxygen tension (PaO_2) of <8.0 kPa (60 mmHg), an arterial carbon dioxide tension (PaCO_2) of >6.0 kPa (45 mmHg) or both. (**Silent Hypoxia- Hypoxia without clinical symptoms, common in COVID-19**)
- Hypoxemic respiratory failure (type I) is characterized by an arterial oxygen tension (PaO_2) lower than 60 mm Hg (<8 kPa) with a normal or low arterial carbon dioxide tension (PaCO_2).
- Hypercapnic respiratory failure (type II) is characterized by a PaCO_2 higher than 45 mm Hg (>6 kPa). Hypoxemia is common in patients with hypercapnic respiratory failure.

ARDS (Berlin definition): (See page- 14)

- Acute onset <7 days
- Bilateral pulmonary infiltrate
- $\text{PaO}_2:\text{FiO}_2$ ratio <300 on PEEP 5

ARDS severity	$\text{PaO}_2/\text{FiO}_2$	Mortality
Mild	$>200, <300$	27%
Moderate	$>100, <200$	32%
Severe	<100	45%

ARDSnet FiO_2 /PEEP table:

Lower PEEP/Higher FiO_2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24

Higher PEEP/Lower FiO_2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	24

In **Covid-19 patients** the pulmonary injury pattern is not entirely similar to ARDS, as hypoxia is prevalent and pulmonary compliance is generally high. In general, two categories of patients may be identified:

2. High-pulmonary compliance patients with isolated viral pneumonia.

- A) The main finding is hypoxic vasoconstriction, explaining the observed severe hypoxemia. In those patients, the major issue is related to perfusion, as lungs are inflated and increasing PEEP may not help.
- B) High PEEP and prone positioning do not lead to recruitment of collapsed areas, but they only adjust pulmonary perfusion.

3. Low-pulmonary compliance patients with lung injury pattern similar to traditional ARDS.

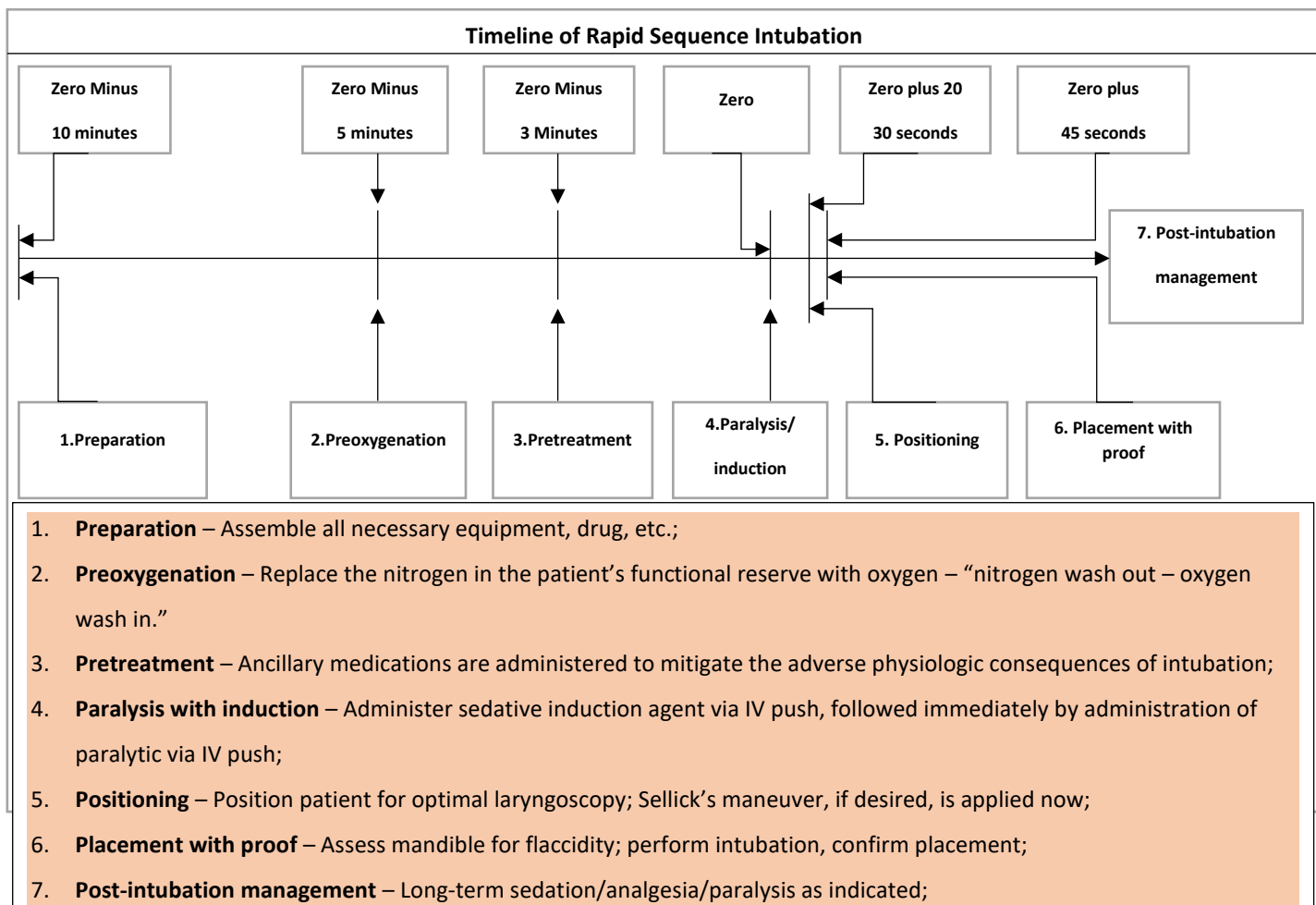
- A) These may have concomitant bacterial or other co-infections or interstitial lung injury
- B) Standard ARDSnet strategy should be used for tidal volume, plateau pressure and PEEP goals

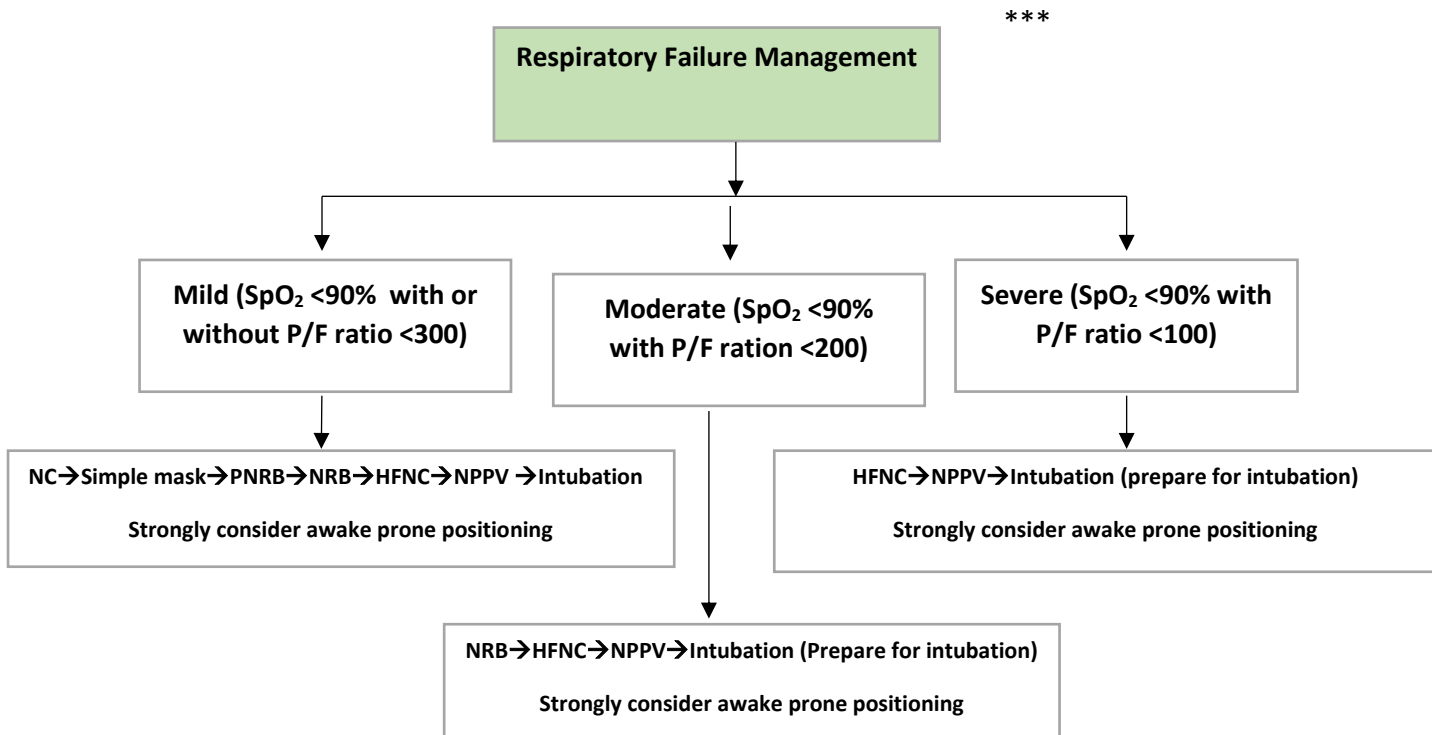
Approach considerations:

- 1- **Low flow O_2 delivery devices:** Nasal cannula
- 2- **High flow delivery device:** High Flow Nasal cannula (HFNC)

- 3- **Non-invasive positive pressure ventilation:** CPAP, BiPAP . Increase CPAP or EPAP for hypoxia. Increase pressure support (IPAP-EPAP) for hypercapnia
- 4- **Mechanical ventilation.**
- 5- **ECMO**

Intubation Protocol	Extubation Protocol
<ul style="list-style-type: none"> • It's an aerosol generating procedure • Use proper PPE including face shield/goggles, N95 or KN95 • Bed-up-head -elevated position • • Use exhalation HME filter if bagging required • Adequate preoxygenation with NRB or HFNC • Have vasopressors prepared prior to induction Rapid sequence intubation (RSI) using adequate sedation and neuromuscular blockade. • Video laryngoscopy over direct laryngoscopy if possible • Post-intubation and ventilation should only be initiated once ETT cuff is inflated. 	<ul style="list-style-type: none"> • After decision is made to extubate, huddle with nurses to have game plan and back up options • It is aerosol generating procedure • Nurse turns off tube feeding. • All should wear PPE including N95, + face shield /goggles • Airway management equipment for reintubation • Place surgical mask on patient's face above ETT. • Feeding tube is removed first, mouth and ETT suctioned • Nasal cannula with O₂ placed before extubation • Ventilator shut off first • ETT removed and at same time mask pulled down over patient's mouth



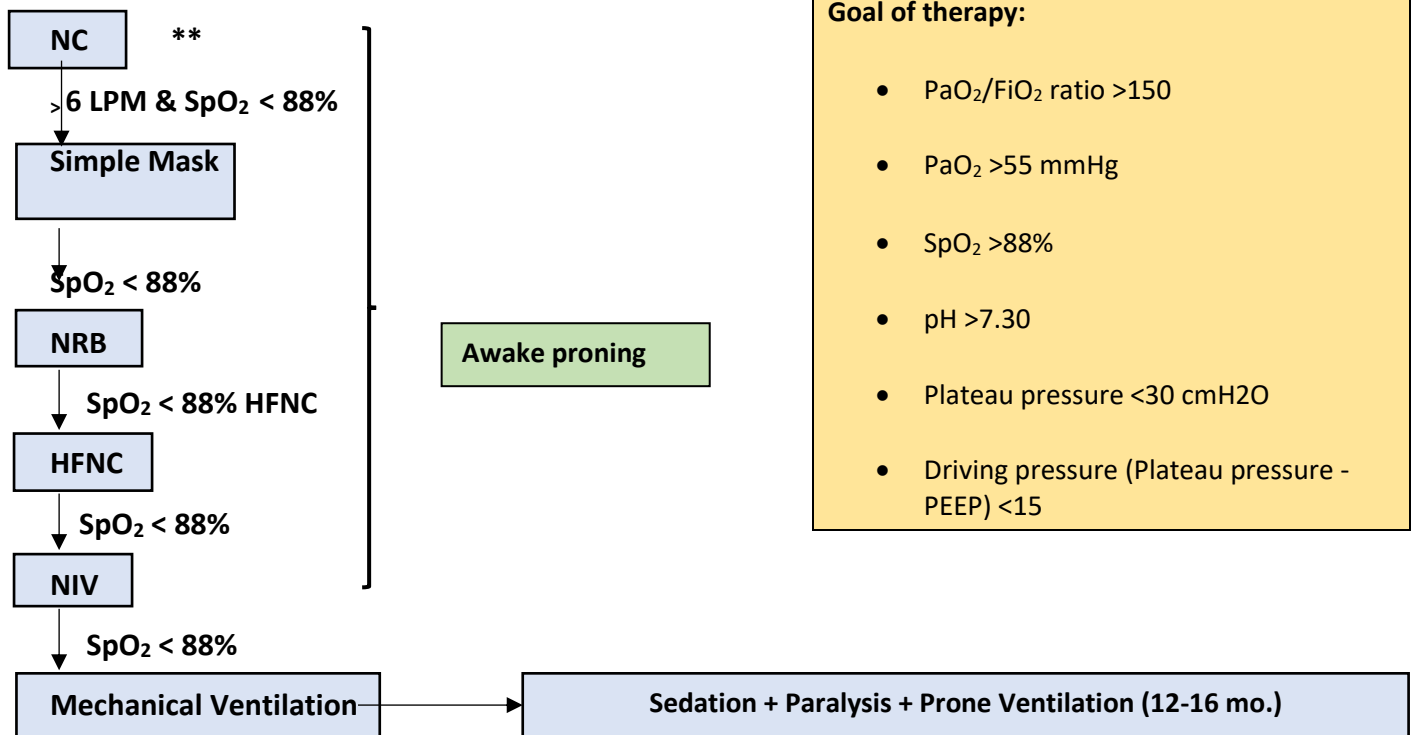


Awake Proning:

While proning has been used with good result in patient with ARDS but recent anecdotal reports showed benefit in non-intubated patient. A CARP (COVID Awake Repositioning/Proning Protocol) has been suggested.

Aerosol Generating Procedures (AGPs)

- Intubation
- Extubation
- Bronchoscopy
- Nebulizer
- NIV
- Open Suction
- Tracheostomy
- CPR
- AMBU/manual bagging



- Initial Mechanical Ventilation Setting:**
- **Pressure Controlled Ventilation for high lung compliance patients**
 - PC 15 to 25cmH₂O range (above PEEP)
 - Plateau pressure <30cmH₂O
 - Respiratory Rate <20/min
 - Inverse Ratio Ventilation may be used
 - **ARDSnet Strategy for low lung compliance patients**
 - TV 4-8 ml/kg IBW based
 - PEEP Strategy as per ARDSnet PEEP/FiO₂Table
 - Optimize sedation & analgesia
 - Consider Recruitment Maneuver
 - Diuresis if clinically indicated
 - UOP ≥ 0.5ml/kg/hr. with MAP ≥ 60mmHg

- PLATEAU PRESSURE GOAL: ≤ 30 cm H₂O:**
- Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or VT.
 - If Pplat > 30 cm H₂O: decrease VT by 1m/kg steps (minimum= 4 ml/kg)
 - If Pplat < 25 cm H₂O and VT < 6 ml/kg, increase VT by 1 ml/kg until Pplat > 25 cm H₂O or VT= 6 ml/kg.
 - If Pplat <30 and breath stacking, or dys-synchrony occurs: may increase VT in 1 ml/kg increments to 7 or 8 ml/kg if Pplat remains <30 cm H₂O;

HFNC is preferred if patient require Oxygen >15 LPM.

Recommended Induction Agents and Dosing:

MED	DOSE	RANGE
Propofol	1.5 mg/kg	1-2 mg/kg
Ketamine	2 mg/kg	1-2 mg/kg
Midazolam	0.3 mg/kg	0.2-0.3 mg/kg
Fentanyl	4 mcg/kg	2-5 mcg/kg

Etomidate	0.3 mg/kg	0.2-0.6 mg/kg
Succinylcholine	1 mg/kg	1-2 mg/kg
Rocuronium	1 mg/kg	1-2 mg/kg

Caution: Prolong use of Propofol may increase triglyceride

Recommended Lab tests:

On admission: COVID-19 testing; CBC with differential; LFT; Urea; Creatinine; CRP; D-dimer; Ferritin; LDH; S electrolyte, ABG, Troponin and BNP.

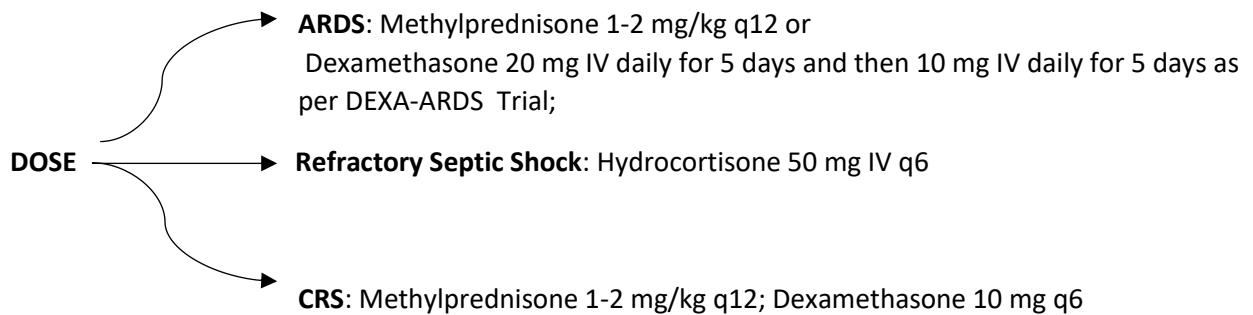
Every 72 hours: CBC with differentials, CRP, D-dimer, Urea, Creatinine and Troponin

Others: Blood and Urine culture etc

MEDICATION THERAPIES and SUPPORTIVE CARE IN ICU:

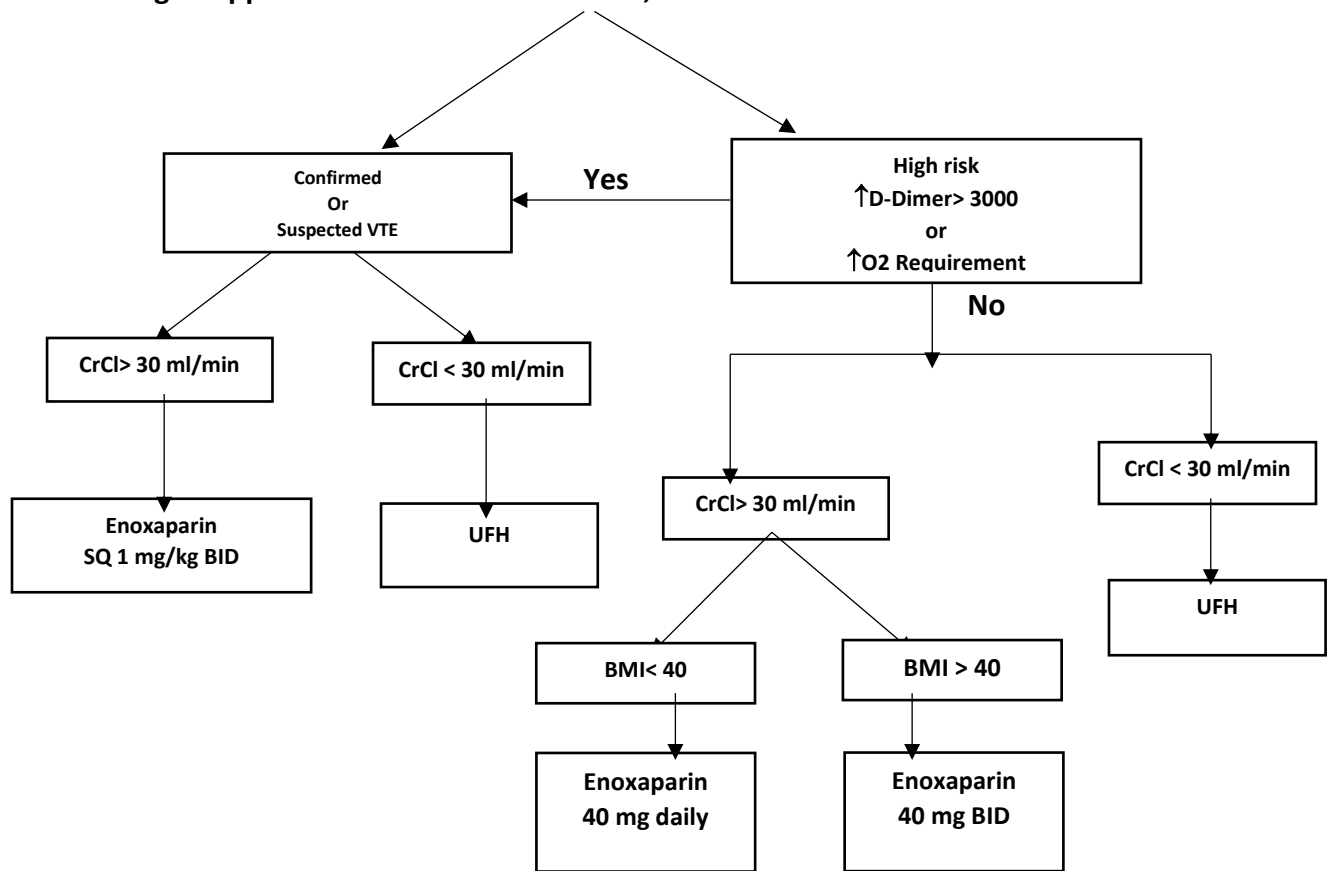
Steroid:

1. Dose for ARDS:



Haematological Issues:

Haematologic support: Mild with comorbidities, Moderate or Severe COVID



***UFH:** Unfractionated Heparin

<p>Inclusion: All admitted patients with moderate to severe COVID-19</p> <p>Exclusion: High risk of bleeding as judged by treating physician, older age, advanced liver or renal disease, previous h/o bleeding;</p>
<p>Baseline and daily: CBC, PT/PTT, D-dimer</p>

Empiric antibiotics: Consider strongly as per local antibiogram.

In patients with COVID-19 and hypoxic respiratory failure requiring mechanical ventilation, superinfection is reasonably common in this population. About 3% patients had bacterial coinfection and 15% of hospitalized COVID-19 patients developed a secondary bacterial infection and the median time to secondary bacterial infection was 17 days (13 to 19 days).

Sedation:

1. Target RASS 0 to -2
2. Target RASS -3 or -4 if continuous NMBA is needed.
3. Fentanyl is the first choice (address pain and sedation).
4. Not routinely utilizing ketamine infusions over other agents such as propofol or midazolam.
5. Dexmedetomidine shouldn't be used as first agent.
6. Propofol and hypertriglyceridemia: Increased risk due to probable HLH-type syndrome monitor CK, acidosis, and early checking of triglycerides.

Neuromuscular blockade:

1. Considerations for NMBA
2. Consider intermittent boluses first and assess for efficacy
3. If continuous infusion is needed due to persistent Dyssynchrony or profound hypoxia
4. Monitor train of four (TOF) to assist in titrating to lowest effective dose
5. Complications of NMBA:
 - a) Corneal abrasion and the need of lubricating eye ointment
 - b) Prolonged weakness
 - c) Higher incidence thrombosis and the need for DVT prophylaxis

Hemodynamic support:

1. Target MAP>60, instead of >65.
2. Consider balanced crystalloid fluid (Ringer lactate, Hartmann's) over normal saline (higher incidence of AKI) and colloid.
3. Fluid sparing strategies and dynamic measures like PLR, Lactate, capillary refilling time to assess fluid status/responsiveness.
4. Conservative over liberal fluid strategy.
5. Norepinephrine as the first-line vasoactive agent, over other agents.
6. If norepinephrine is not available, either vasopressin or epinephrine as the first-line vasoactive agent, over other vasoactive agents.
7. Vasopressin as a second-line agent over increasing norepinephrine.
8. If there is evidence of cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation and norepinephrine, add dobutamine, over increasing norepinephrine dose.
9. Refractory shock add low-dose corticosteroid therapy ("shock-reversal"), over no corticosteroid therapy (IV Hydrocortisone 50 mg q6).

Feeding strategies (Nutrition):

1. Early enteral feeding within 24-48 hours is helpful.
2. Starting feeds at 25-50% caloric goal and increasing to 100% over 3-7 days is reasonable.
3. Use trophic or trickle diet (10-20 cc/hour) in hemodynamically or respiratory unstable patient
4. Don't check gastric residual volumes (GRVs) routinely.
6. Consider prokinetics in a patient with high GRVs or vomiting.
7. Avoid post pyloric feeding in unstable patient (higher incidence of non-occlusive bowel necrosis)

Blood glucose (BG):

1. Target BG 140-180 mg/dl.

DGHS website have a guideline named 'CARING FOR CRITICALLY ILL COVID- 19 PATIENT: QUICK GUIDE FOR ICU CARE' which can be followed for detailed management strategies.

Special situation

Caring for infants and mothers with COVID-19: IPC and breastfeeding (Check out paediatrics and OGSB guideline)

- Infants born to mothers with suspected, probable or confirmed COVID-19 infection, should be fed according to standard infant feeding guidelines, while applying necessary precautions for IPC.
- As with all confirmed or suspected COVID-19 cases, symptomatic mothers who are breastfeeding or practising skin-to-skin contact or kangaroo mother care should practise respiratory hygiene, including during feeding (for example, use of a medical mask when near a child if with respiratory symptoms), perform hand hygiene before and after contact with the child, and routinely clean and disinfect surfaces which the symptomatic mother has been in contact with.
- Breastfeeding counselling, basic psychosocial support and practical feeding support should be provided to all pregnant women and mothers with infants and young children, whether they or their infants and young children have suspected or confirmed COVID-19.
- In situations when severe illness in a mother due to COVID-19 or other complications prevent her from caring for her infant or prevent her from continuing direct breastfeeding, mothers should be encouraged and supported to express milk, and safely provide breastmilk to the infant, while applying appropriate IPC measures.
- Mothers and infants should be enabled to remain together and practise skin-to-skin contact, kangaroo mother care and to remain together and to practise rooming-in throughout the day and night, especially immediately after birth during establishment of breastfeeding, whether they or their infants have suspected, probable or confirmed COVID-19 virus infection
- Parents and caregivers who may need to be separated from their children, and children who may need to be separated from their primary caregivers, should have access to appropriately trained health or non-health workers for mental health and psychosocial support.

Special Considerations in Pregnancy

SARS-CoV-2 infection in pregnant patients can present as asymptomatic/presymptomatic disease or with a wide range of clinical manifestations, from mild symptoms that can be managed with supportive care at home to severe disease and respiratory failure requiring ICU admission. As with other patients, in the pregnant patient with symptoms compatible with COVID-19, the illness severity, underlying comorbidities, and clinical status should all be assessed to determine whether in-person evaluation for potential hospitalization is needed.

The key considerations regarding the management of COVID-19 in pregnancy.

- Pregnant women should be counseled about the potential for severe disease from SARS-CoV-2 infection and the recommended measures to take to protect themselves and their families from infection.
- If hospitalization for COVID-19 is indicated in a pregnant woman, care should be provided in a facility that can conduct maternal and fetal monitoring, when appropriate
- Management of COVID-19 in the pregnant patient should include: Individualized delivery planning, multispecialty team-based approach as appropriate
- The potentially effective treatment for COVID-19 should not be withheld from pregnant women because of theoretical concerns related to the safety of therapeutic agents in pregnancy
- Decisions regarding the use of drugs approved for other indications or investigational drugs for the treatment of COVID-19 in pregnant patients must be made with shared decision-making between the patient and the clinical team.

Special Considerations in Children

Data on disease severity and pathogenesis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children are limited. SARS-CoV-2 has been associated with a potentially severe inflammatory syndrome in children (multisystem inflammatory syndrome in children [MIS-C]).

The key considerations regarding the management of COVID-19 in children.

- Children with risk factors recognized in adults, including obesity, diabetes, and hypertension, may also be at risk.
- There are insufficient data to recommend for or against the use of specific antivirals or immunomodulatory agents for the treatment of COVID-19 in pediatric patients.
- MIS-C present with persistent fever, evidence of systemic inflammation, and a variety of signs and symptoms of multiorgan system involvement, including cardiac, gastrointestinal, renal, hematologic, dermatologic, and neurologic involvement. Many centers consider the use of intravenous immune globulin, steroids, and other immunomodulators and antiplatelet and anticoagulant therapy. MIS-C management decisions should involve a multidisciplinary team of pediatric specialists.

Caring for older persons with COVID-19

- For older people with probable or suspected COVID-19, provide person-centred assessment, including not only conventional history taking, but a thorough understanding of the person's life, values, priorities and preferences for health management.

- Ensure multidisciplinary collaboration among physicians, collaboration with nurses, pharmacists, other health care professionals in the decision making process to address multimorbidity and functional decline.
- Early detection of inappropriate medication prescriptions is recommended to prevent adverse drug events and drug interactions for those being treated with COVID-19.
- Older people are at greater risk of polypharmacy, due to newly prescribed medications, inadequate medication reconciliation and a lack of care coordination which increases the risk of negative health consequences

Special Considerations in cardiovascular diseases

If cardiology assessment or intervention is considered urgent care should not be delayed. The patient should be considered positive for covid-19 until proven otherwise and appropriate personal protective equipment measures taken. Patients with suspected or confirmed covid-19, who are also at risk of cardiogenic shock (eg, large acute myocardial infarction or acute decompensated heart failure) should be identified early, and sepsis and myocarditis should be considered.

The key considerations regarding the management of COVID-19.

- Patients with chronic coronary syndromes should continue to take aspirin for secondary prevention. Treatment for acute heart failure should be the same for all patients, regardless of infection status.
- No changes are recommended to the treatment of hypertension, unless a patient becomes acutely unwell. If a patient with hypertension is hospitalised and tests positive for covid-19, plasma potassium should be monitored. This is because of the increased risk of arrhythmias from hypokalaemia.

Special Considerations in Immune deficiency Condition

Recommendations for the triage, management, and treatment of COVID-19 in people with immune deficiency are the same as those for the general population.

The key considerations regarding the management of COVID-19 in immune deficiency status

- In people with advanced immune deficiency and suspected or documented COVID-19, opportunistic infections (OIs) should also be considered in the differential diagnosis of febrile illness
- Starting treatment for COVID-19 in a patient, clinicians should pay careful attention to potential drug-drug interactions and overlapping toxicities among COVID-19 treatments, antimicrobial therapies, and other medications

Avoiding medical damage in special populations

Special populations include pregnant women, patients with hepatic and renal insufficiency, patients supported by mechanical ventilation, patients under continuous renal replacement therapy (CRRT) or, extracorporeal membrane oxygenation (ECMO), etc. The following aspects need to be noted during drug administration.

1. Pregnant women: Inj Remdesavir as antiviral can be provided after strict risk benefit ratio observed. Favipiravir and chloroquine phosphate are prohibited. (check out OGSB guideline at DGHS website)
2. Patients with hepatic insufficiency Drugs that are excreted unchanged through the kidney are preferred, such as penicillin and cephalosporins, etc.
3. Patients with renal insufficiency (including those on haemodialysis).
Drugs that are metabolized through the liver or excreted through the liver-kidney double channels are preferred, such as linezolid, moxifloxacin, ceftriaxone, etc.
4. Patients under CRRT for 24h For vancomycin, the recommended regimen is loading of 1g and maintenance dose 0.5 g, q12h. For imipenem, the maximum daily dosage should not exceed 2 g.

Discontinuing of transmission-based precaution including isolation and return to workplace criteria

Limited published and pre-published information on viral shedding estimates up to 9 days for mild patients and up to 20 days in hospitalized patients. Additionally, there are reports that patients can remain consistently PCR positive for many weeks, or even test PCR positive after days/weeks of a negative test.

Recommendation for release from isolation:

- For asymptomatic patients: 10 days after sample collection
- For symptomatic Mild patients: 10 days after symptom onset, plus at least 3 days without symptoms (without fever and significant improvement of the respiratory symptoms).
- For hospitalized patients: 21 days after symptom onset plus at least 3 days without symptoms (without fever and significant improvement of the respiratory symptoms).

Exception: Severe or critical patients may still require ongoing rehabilitation, or other aspects of care, based on clinical needs in the COVID-19 pathway. For these patients several clinical considerations such as medication reconciliation, plan for follow up with clinical provider in place, review of routine immunization status, among others, should be taken into account by treating physicians

Discharge criteria

1. Resolution of fever without the use of fever-reducing medications e.g paracetamol for at least 3 (three) days and
2. Significant improvement in the respiratory symptoms (e.g., cough, shortness of breath) for 3 days, and
3. After discharge, continue home or facility isolation for the duration which extends from the day of symptom onset to 21st day for hospitalized patients
4. For severe or critical patients – physician’s discretion

Medication after discharge

Generally, antiviral drugs are not necessary after discharge. Treatments for symptoms can be applied if patients have mild cough, poor appetite, thick tongue coating, etc.

Home isolation

Recommended home isolation conditions are:

- Independent living area with frequent ventilation and disinfection.
- Avoid contacting with infants, the elderly and people with weak immune functions at home.
- Patients and their family members must wear masks and wash hands frequently.

- Body temperature are taken twice a day (in the morning and evening) and pay close attention to any changes in the patient's condition.

Follow-up

A specialized doctor should be arranged for each discharged patient's follow-ups. The first follow-up call should be made within 48 hours after discharge. The outpatient follow-up will be carried out 1 month, 3 months and 6 months.

Examinations include liver and kidney functions, blood test, nucleic acid test of sputum and stool samples, and pulmonary function test or lung CT scan should be reviewed according to the patient's condition. Follow-up phone calls should be made 3 and 6 months after discharge.

Management of patients tested positive again after discharge

Strict discharge standards should be implemented in hospital. However, there are some reported cases that patients are tested positive again, after being discharged based on the standards of their national guidelines (negative results from at least 2 consecutive throat swabs collected at an interval of 24 hours; body temperature remaining normal for 3 days, symptoms significantly improved; obvious absorption of inflammation on lung images). It is mainly due to sample collection errors and false negative testing results. However, few true reinfections are also reported in different countries. For these patients, the following strategies are recommended:

- Isolation according to the standards for COVID-19 patients.
- Continuing to provide antiviral treatment which has been proved to be effective during prior hospitalization.
- Discharge only when improvement is observed on lung imaging and the sputum and
- Stool samples are tested negative for 3 consecutive times (with an interval of 24 hours).
- Home isolation and follow-up visits after discharge in accordance with the requirements mentioned above.

Long haulers/ Longings in COVID-19

COVID-19 infection looks different for different people, and it's been reported to have prolonged effect or long haulers/longings. Based on available data, few important health issues are observed

Respiratory Effects: COVID-19 is thought of primarily as a respiratory disease, characterized by cough and shortness of breath. So, it's no surprise that some patients are experiencing prolonged lung damage as a result of their initial infection. Lung fibrosis, poor lung function and thrombotic lung damage has been reported. Even people with asymptomatic COVID-19 infection may show signs of lung inflammation. In post-COVID-19 pulmonary fibrosis. the patients could have had underlying lung disease without realizing it

and that could create symptoms [like] shortness of breath and cough as lungs heal. This process could take weeks or months, depending on your specific severity of illness.

Cardiovascular Effects: There is increasing evidence to show that the disease also takes a toll on your heart, with up to one in five COVID-19 patients showing signs of cardiac dysfunction. An MRI based papers revealed about 78% longings can develop in heart. The common of the clinical findings are perimyocarditis, rhythm disturbance, RV and LV dysfunction, cardiomyopathy (ischaemic and non-ischaemic) Research has increasingly shown that blood clotting associated with COVID-19 can lead to heart attacks or put stress on your heart due to lack of adequate blood flow.

Neurological Effects: Perhaps the scariest emerging long-term effect of COVID-19 is its potential impact on the brain. Severe COVID-19 illness exhibit signs of brain damage or brain injury (though this is uncommon). It could be that the virus targets the brain, or that the inflammation caused by the immune reaction is affecting blood flow to the area. In rare cases, serious blood clotting can lead to strokes in COVID-19 patients who are otherwise young and healthy. Brain damage could occur as a result of hypoxia—low oxygen caused by the respiratory effects of the virus.

Psychological Trauma: If a patient experiences severe illness from COVID-19, they are likely to feel some lasting psychological effects from their ordeal. Common of them are as post-traumatic stress disorder, depression, and anxiety. Patients who have spent weeks in the ICU could experience lingering mental and physical health effects from that experience. “They may also suffer from post-intensive care syndrome (PICS). “Physical impairment due to malnutrition, cognitive impairment which can result in decreased memory, decreased attention, and decreased mental sharpness or ability to solve problems, and psychiatric impairment can be observed in long term.

Chronic Fatigue: Survivors sometimes showed signs of fatigue and muscle weakness for years afterward. Patient had poorer exercise capacity and health status and had chronic fatigue symptoms persist for long. The specific cause of chronic fatigue syndrome is unknown, but one notable trigger is viral infections, which can cause significant stress to your internal organs.

Unfortunately, it won't be clear for a while which effects of COVID-19 are long-lasting or permanent. The longings need to observe at least a year before understanding which of the organs involved in infection could show some damage that become long haulers. The key will be identifying survivors at different intervals for doctors to assess. “We need to follow up survivors at one-month intervals, three-month intervals, one-year intervals, and ten-year intervals

Management: Multidisciplinary team should be involved in managing the long haulers of COVID-19 with different specialist.

Vaccines

Currently more than 150 vaccines are in preclinical and clinical trials for COVID-19. Among them, three reported vaccine has completed phase 1, 2 or ½ trial as of today. These 3 vaccines were found safe, tolerated, and immunogenic, while reactogenicity was reduced with paracetamol. A single dose elicited both humoral and cellular responses against SARS-CoV-2, with a booster immunisation augmenting neutralising antibody titres. The preliminary results of these first-in-human clinical trial supported clinical development progression into ongoing phase 2 and 3 trials. Older age groups with comorbidities, health-care workers, and those with higher risk for SARS-CoV-2 exposure are being recruited and assessed for efficacy, safety, and immunogenicity of these 3 vaccines given as a single-dose or two-dose administration regimen in further trials conducted in world. Vaccine will also be evaluated in children, once sufficient safety data have been accumulated in adult studies.

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- Obstetrics and Gynaecological Society of Bangladesh (OGSB)
- Bangladesh Society of Infectious and Tropical Diseases (BSITD)
- Bangladesh Society of Anaesthesiologists (BSA)

Further Reading:

1. Ren LL, Wang YM, Wu ZQ, et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. *Chin Med J (Engl)*. 2020 Jan 30 [Epub ahead of print]
2. World Health Organization. Infection prevention and control during health care when COVID-19 is suspected [https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-\(ncov\)-infection-is-suspected-20200125](https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125)
3. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. 18 March 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-18-march-2020> [Google Scholar](#)
4. World Health Organization. Thailand joins the WHO "Solidarity Trial": global testing of effective treatments of COVID-19 across 8 countries – an aggressive effort to save lives from the pandemic (press release), 20 March 2020. <https://www.who.int/thailand/news/detail/20-03-2020-thailand-joins-the-who-solidarity-trial-global-testing-of-effective-treatments-of-covid-19-across-8-countries-an-aggressive-effort-to-save-lives-from-the-pandemic>. [Google Scholar](#)
5. World Health Organization. R&D Blueprint COVID-19 Informal consultation on the potential role of chloroquine in the clinical management of COVID 19 infection. 13 March 2020. <https://www.who.int/blueprint/priority-diseases/key-action/RD-Blueprint-expert-group-on-CQ-call-Mar-13-2020.pdf?ua=1>. [Google Scholar](#)
6. https://apps.who.int/iris/bitstream/handle/10665/77751/9789241548290_Vol2_eng.pdf?sequence=3
7. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. *J Am Med Assoc* 2020 (in press) <https://doi.org/10.1001/jama.2020.2648>
8. McIntosh Uptodate 2020
9. 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;14:72–3
10. Gautret P *et al*. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents* (in press)
11. <https://doi.org/10.1016/j.ijantimicag.2020.105949>
12. Cao B *et al*. A trial of lopinavir–ritonavir in adults hospitalized with severe COVID-19. *N Engl J Med* 2020 (in press) <https://doi.org/10.1056/NEJMoa2001282>
13. Holshue ML *et al*. First case of 2019 novel coronavirus in the United States. *N Engl J Med* 2020;382:929–36.
14. Reuters. China approves use of Roche drug in battle against coronavirus complications. www.reuters.com/article/us-health-coronavirus-china-roche-hldg/china-approves-use-of-roche-arthritis-drug-for-coronavirus-patients-idUSKBN20R0LF [Accessed on 21 March 2020].
15. Intensive Care Medicine GUIDELINES Un-edited accepted proof* © European Society of Intensive Care Medicine and the Society of Critical Care Medicine 2020 Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19
16. An Aid to the Management of COVID-19 in Bangladesh: "Lessons from the Western Experience" Fighting on the Front Line First Edition is published on May 2, 2020 .This guidebook is available free for download and distributing from the following website (also future updates) shakilfarid.com/covid19

Annex1: হাসপাতালে কোভিড-১৯ রোগের ব্যবস্থাপনা

হাসপাতালের প্রবেশ মুখে স্বাস্থ্য কর্মী দ্বারা সম্ভাব্য শ্বাসতন্ত্রের সংক্রমণজনিত রোগের লক্ষণসহ (জ্বর, কাশি, শ্বাস কষ্ট) রোগী সনাক্ত। রোগীসহ সকলে মাস্ক পরিধান করবেন এবং সাবান পানি দিয়ে হাত ধুবেন।

- শনাক্তকৃত রোগীকে আলাদা বিশেষ বহির্বিভাগ / জরুরী বিভাগ রুমে স্থানান্তর।
- রোগীর তাপমাত্রা পরিমাপ করা হবে

চিকিৎসক রোগীর ভ্রমণ ইতিহাস বা সংস্পর্শে আসার ইতিহাস লিপিবদ্ধ করবেন এবং স্বাস্থ্য পরীক্ষা করবেন। কোভিড-১৯ রোগের লক্ষণসমূহ থাকলে (জ্বর, কাশি, শ্বাস কষ্ট, গলা ব্যথা, নাক দিয়ে পানি পড়া, ডায়রিয়া, বমি) সেই সাথে ভ্রমণ ইতিহাস বা সংস্পর্শে আসার ইতিহাস থাকলে রোগের আদর্শ সংজ্ঞা অনুসারে সন্দেহজনক কোভিড-১৯ রোগ সনাক্ত করবেন।

সন্দেহজনক কোভিড-১৯ রোগীকে আইসোলেশন ওয়ার্ড বা কেবিনে পাঠান এবং রোগীকে চিকিৎসা প্রটোকল অনুযায়ী চিকিৎসা প্রদান শুরু করুন

সন্দেহজনক কোভিড-১৯ রোগ না হলে রোগ অনুযায়ী চিকিৎসা প্রদান। ভ্রমণ ইতিহাস বা অন্য দেশ থেকে আসা মানুষের/ কোভিড-১৯ রোগীর সংস্পর্শে আসার ইতিহাস থাকলে ১৪ দিনের হোম কোয়ারেন্টাইনে রাখা হবে

রোগীর কাছ হতে কোভিড-১৯ এর RT-PCR পরীক্ষার জন্য নমুনা সংগ্রহ করুন

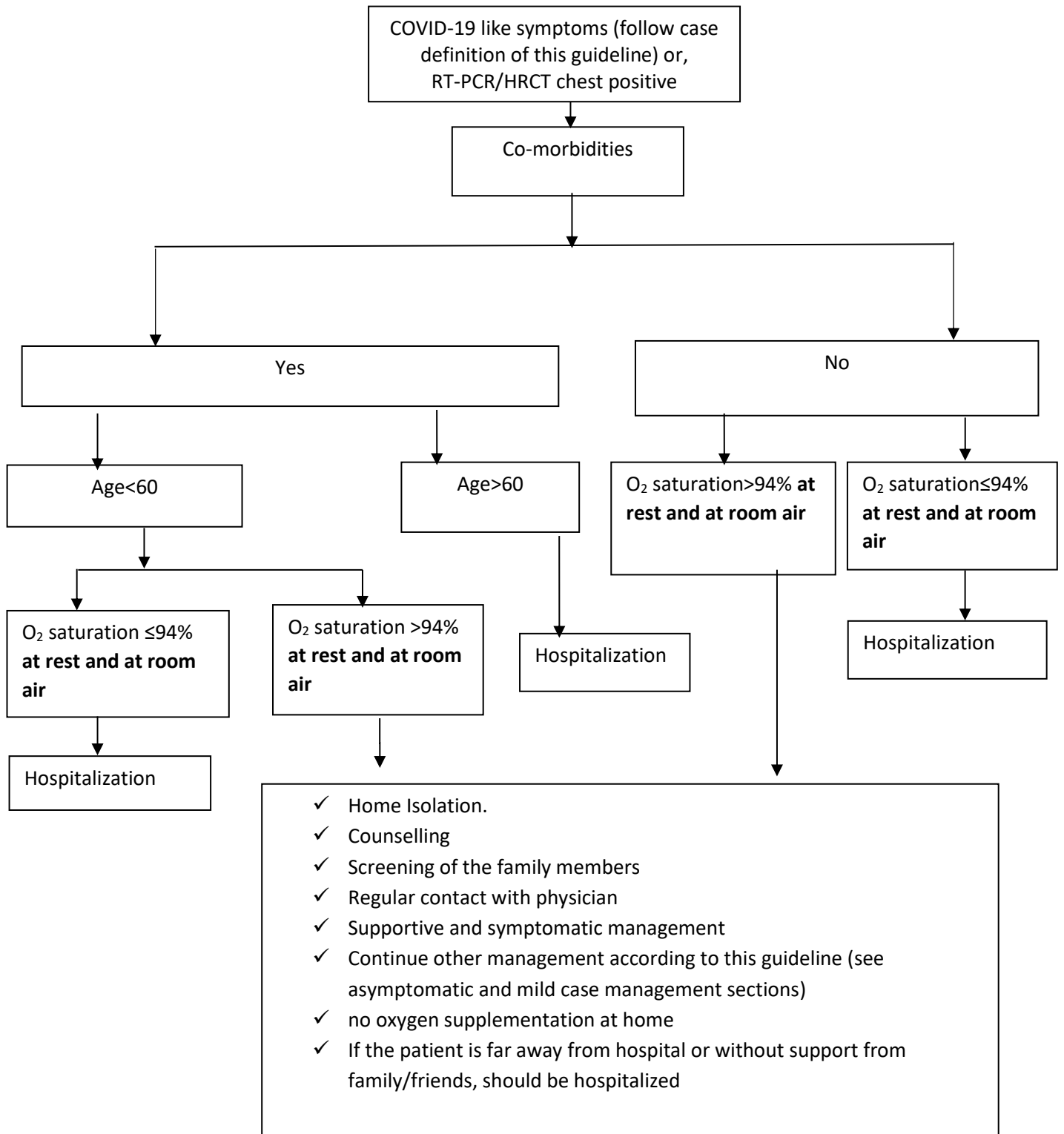
কোভিড-১৯ প্রমাণিত না হলে এবং রোগীর অন্য জটিল সমস্যা না থাকলে চিকিৎসা প্রটোকল অনুযায়ী রোগীকে ১৪ দিনের জন্য বাসায় অবস্থান (হোম কোয়ারেন্টাইন) করতে পরামর্শ দিন।

- কোভিড-১৯ প্রমাণিত হলে রোগীকে চিকিৎসা প্রটোকল অনুযায়ী চিকিৎসা প্রদান অব্যাহত রাখুন
- মৃদু উপসর্গ বিশিষ্ট কোভিড-১৯ রোগের ক্ষেত্রে বিশেষ কোন চিকিৎসা প্রয়োজন হয় না। জ্বরের বা অন্যান্য উপসর্গের সাধারণ চিকিৎসা করুন
- কোভিড-১৯ এর সাথে অন্য রোগ থাকলে (যেমন- ডায়বেটিস, উচ্চ রক্তচাপ, COPD, CKD, CLD, ক্যান্সার, গর্ভাবস্থা ইত্যাদি) এবং বয়স > ৬০ এর বেশি হলে বিশেষ সাবধানতা অবলম্বন করুন
- অন্যান্য পরীক্ষার প্রয়োজন হতে পারে যেমন রক্ত পরীক্ষা, এক্সরে, সিটি স্ক্যান ইত্যাদি। উক্ত হাসপাতালে পরীক্ষার ব্যবস্থা না থাকলে অথবা নিউমোনিয়া বা অন্যান্য জটিলতা সৃষ্টি হলে প্রয়োজনে উচ্চতর হাসপাতালে বা আইসিইউ তে স্থানান্তর করুন

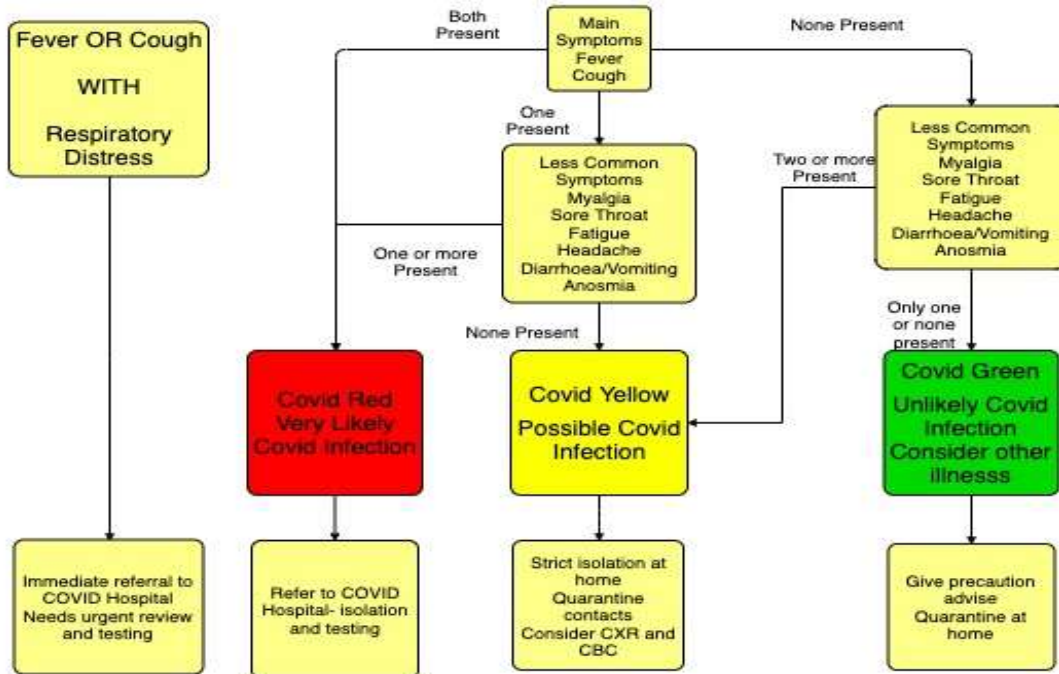
নিউমোনিয়া, সেপটিক শক বা অন্যান্য জটিলতার চিকিৎসা প্রচলিত প্রটোকল অনুযায়ী করুন

পর পর দুইদিন জ্বরের ওষুধ ছাড়াই জ্বর না থাকলে এবং পর পর দুই দিন কোভিড-১৯ এর RT-PCR পরীক্ষার নেগেটিভ হলে বা চিকিৎসকের পরামর্শমতে রোগীকে হাসপাতাল থেকে ছেড়ে দেয়ার জন্য ছাড়পত্র দিন।

Annex 2: COVID-19 telemedicine flow chart for physicians



Annex 3: Telemedicine service likelihood tool and color coded pathway for patients (all hospital will deal COVID and NONCOVID cases and hence every hospital is COVID hospital now)



Annex 4- Serological test in COVID- 19

Serological tests: The antigen based and antibody based serological test is important in context of COVID-19 in Bangladesh.

Antigen based: This antigen based point of care test (with sensitivity of more than 80%) can be a useful tool for diagnosing COVID-19 in community setting (where RTPCR is lacking). Symptomatic suspected patient with positive antigen based test is excellent test for early detection of COVID-19. If test is negative and suspicion remain high, then patient can be sent for RT-PCR. Point of care test with ICT for antigen is available and deployment in all community can be done with quick effect.

Antibody Based: The most sensitive and earliest serological marker is total antibodies, levels of which begin to increase from the second week of symptom onset. Although IgM and IgG ELISA have been found to be positive even as early as the fourth day after symptom onset, higher levels occur in the second and third week of illness.

Serological diagnosis is especially important for patients with mild to moderate illness who may present late, beyond the first 2 weeks of illness onset. Serological diagnosis also is becoming an important tool to understand the extent of COVID-19 in the community and to identify individuals who are immune and potentially “protected” from becoming infected. ELISA-based IgM and IgG antibody tests have greater than 95% specificity for diagnosis of COVID-19. Testing of paired serum samples with the initial PCR/ Antigen test and the second 2 weeks later can further increase diagnostic accuracy.

Rapid point-of-care tests for detection of antibodies have been widely developed and marketed. These tests are purely qualitative in nature and can only indicate the presence or absence of SARS-CoV-2 antibodies.

Rapid point of care test for antigen and antibody can be used in triage area of hospital for quick diagnosis and allocation of patient for red, yellow and green zone of hospital.

Annex 5: Extended Use of N95 respirator/mask and eye shield

○ Extended use

- When N95 and eye shield is used for multiple patients without removal between each patient care

Healthcare workers (HCW) can reuse n95 masks in following way. If an HCW is supplied with 6 N-95/FFP2 masks, they can re-use them up to 2 months, recommended by the CDC without damage or changing its functional integrity.

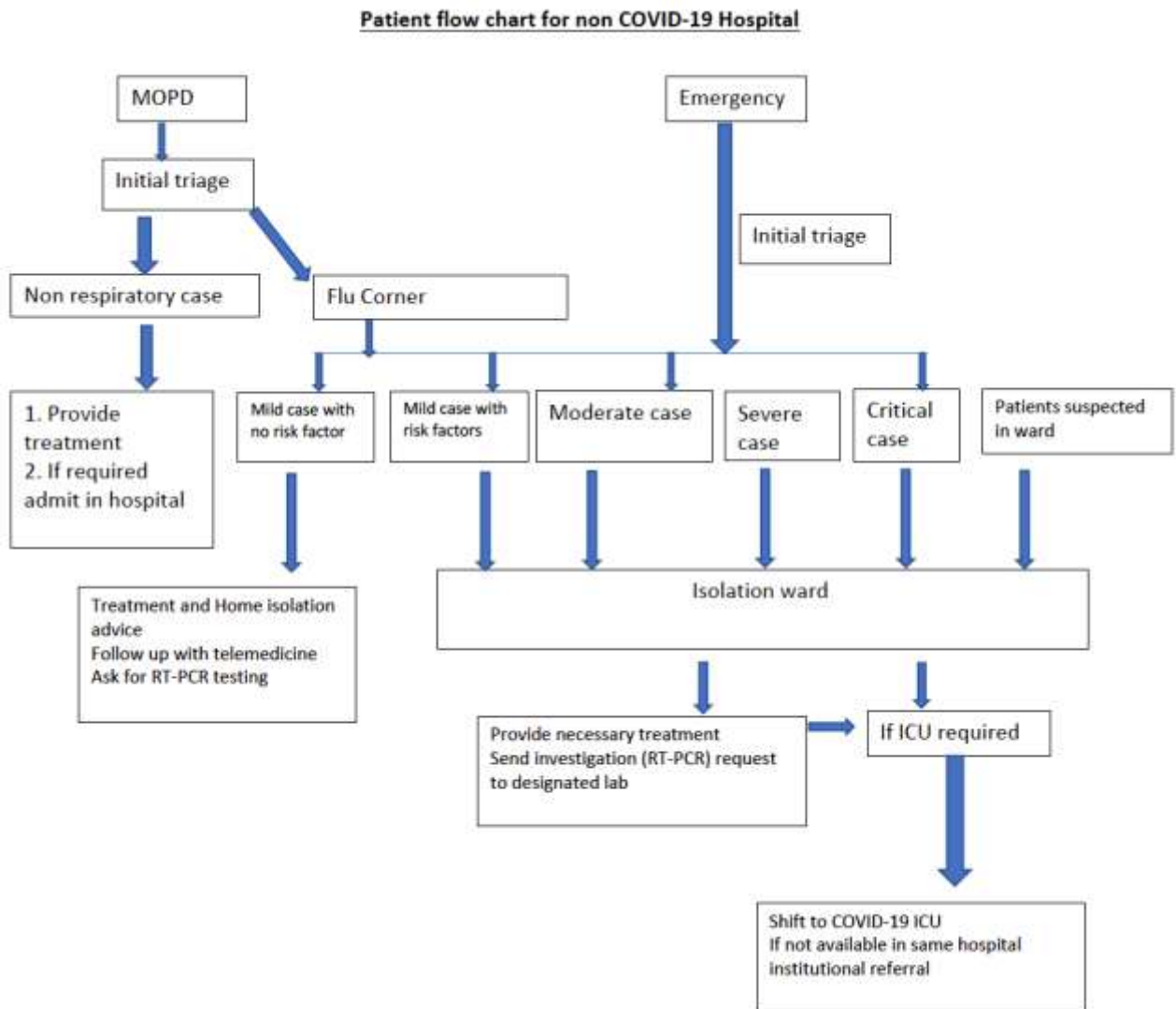
Key Points:

- It's important to discard N95/FFP2 masks contaminated with blood, respiratory or nasal secretions.
- A cleanable face shield or surgical mask on top of this mask to prevent spilling of bodily fluids can be used.
- Clean hands with soap and water or an alcohol-based hand sanitizer before and after touching or adjusting the respirator (if necessary, for comfort or to maintain fit).
- Avoid touching the inside of the respirator. If inadvertent contact is made with the inside of the respirator, discard the respirator and perform hand hygiene as described above.
- Recommended max continuous use of 8 hours in one day between breaks for these masks is extended use. Taking it off(doffing) in the same day during meal break/toilet break and wear it back(donning) after break with precautions is of crucial importance

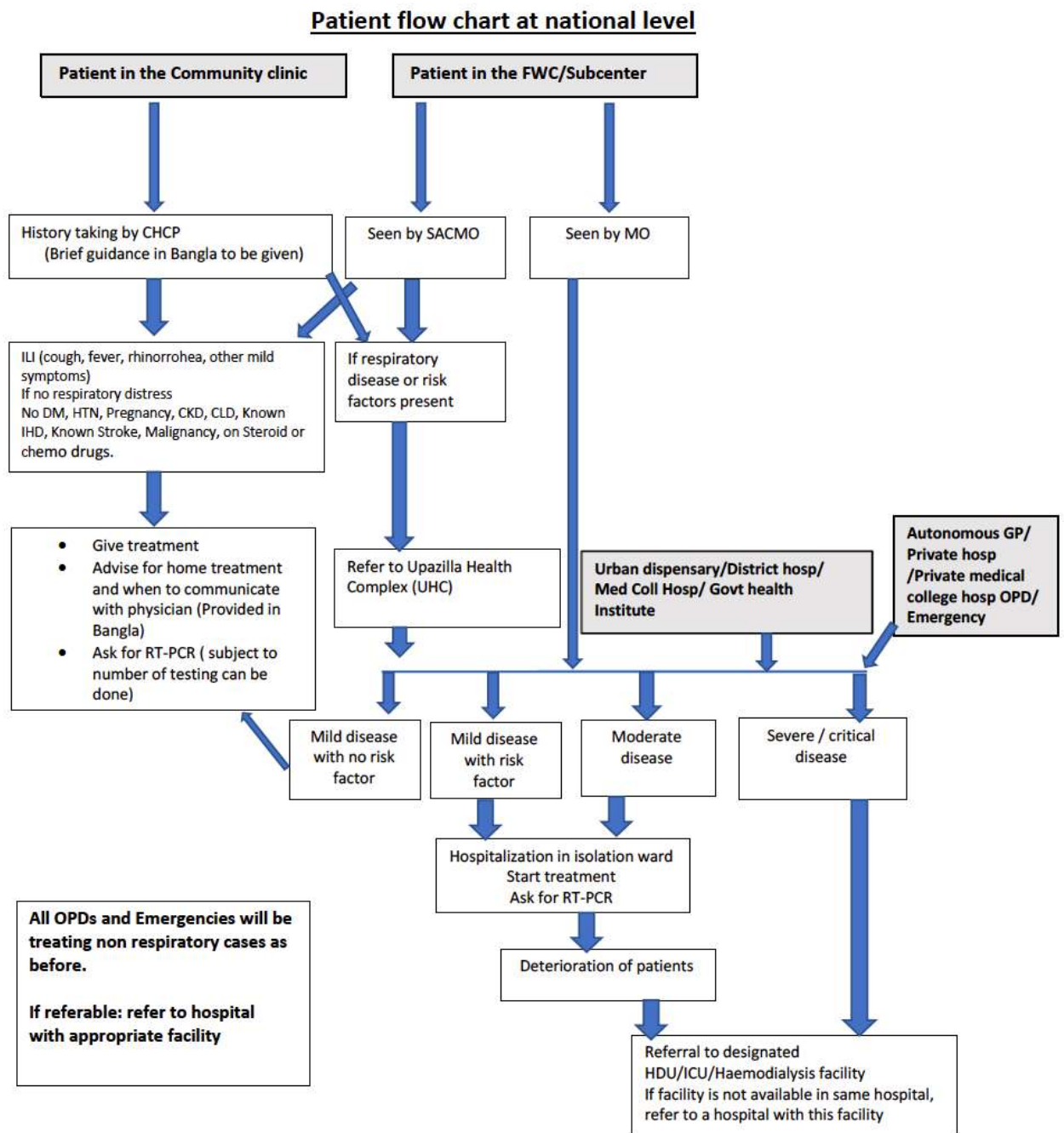
Detail procedure:

- Day 1- Doffing mask no. 1 using the ribbon attached on the edge of mask, put it in paper bag, write 1 on bag for mask no.1, put it away in well-lit area for next re-use on day 7
 - Day 2-Use the mask no.2 on day 2, doffing after hand wash and with precautions, put it in paper bag, write No. 2 on it, keep it away in well-lit area for re-use on day 8. Repeat same cycle for the mask no. 3, 4 and 5, after using them accordingly on day 3,4, 5 and 6.
 - Day 7- you will wear the mask you have worn on day 1, as kept it no. 1 labeled bag, re-use as you will use a new one as there is no viable virus attached to its surface.
- Surgical masks may also be worn in extended use up to 6 hours as long as the outer surface of the mask is not touched by the healthcare worker
 - Extended use is preferred over reuse to minimize potential contamination during donning and doffing

Annex 6: Patient flow chart for non COVID-19 hospital



Annex 7: Patient flow chart at national level



Annex 8: Case Report Form for COVID-19 patients



COVID-19 CRF



Case No.:.....

Date of Entry:...../...../2020

Patient code number/Hospital registration number:.....

Name (name will not be used in public domain):.....

Age (years or month): |__| |__| Y/M Sex: Male / Female

Address: Division:....., District:....., Upazaila:.....

Union:....., Ward no:....., Road no:....., House no:.....

National ID if known:.....

Occupation:....., Contact No:.....

Date of symptom onset:...../...../2020; Date of sample collection:...../...../2020

Date of admission (Only for admitted patient):...../...../2020

Any contact of COVID-19 patient in last 14 days: Yes / No

Any history of travelling or residing in an area reporting COVID-19: Yes / No

Family members affected: Yes/ No; If Yes number:.....

Diagnosis (clinical syndrome) (see NGL for definition): Asymptomatic / Mild / Moderate / Severe / Critical

1. General Symptoms: (Please Tick all symptoms present in the patient)

Fever / Cough / Dyspnoea / Altered sense of smell / Altered sense of taste / Fatigue / Sore throat/ Diarrhoea/ Vomiting / Anorexia / Headache / Confusion / Nasal congestion / Conjunctivitis / Dizziness/ Chest pain / Others (Mention):

2. Signs (Tick): (Please Tick all symptoms present in the patient) Cyanosis/ Crackles / Wheeze /Bronchial breath sound on auscultation SpO2: %; GCS:...../15

3. Vital signs during admission:

Temp (axillary):..... °F, Heart rate:..... /min, BP:..... /..... mmHg; Resp rate:..... /min

4. RT-PCR test: Positive /Negative

Date of sample collection:...../...../2020; Date of result:...../...../2020

5. Lab investigations:

Hb%:....., TC-WBC:....., Neu:.....%, Lymph:.....%, Platelet:....., RBS:....., ALT:....., AST:....., CRP titre:....., D-dimer:....., Procalcitonin:....., Serum creatinine:....., HbA1C:....., Serum electrolyte: Na⁺:....., K⁺:....., Cl⁻:....., HCO₃⁻:....., ABG:pH:....., HCO3:.....,CO2:.....,Alkalosis/Acidosis Tropini n.....

6. Imaging: CXR P/A view (Pneumonitis): Yes / No

ECG:.....

CT Chest: Yes / No, Report:.....

7. Risk factors of co-morbidities (PI Tick): DM/ HTN/ Bronchial asthma/ Chronic heart disease/ CVD/ COPD/CKD/CLD/ Smoking/ Obesity/ Chemotherapy Surgery/ HIV/TB/Malnutrition/Dengue/.....

8. Treatment (PI Tick): Oxygen therapy/ IV Fluid/ BI Pressure support required/ Mechanical Ventilation required/ Dialysis required/ Steroid

O2 therapy duration:.....hrs/days; Mechanical Vent duration:..... hrs/days

Drug: Azithromycin / HCQ/.....

9. For mild / moderate cases (If not admitted): Home isolation: Yes / No, Institutional isolation: Yes / No;

Date of end of isolation:...../...../2020

10. Repeat PCR: Yes / No

1 st Date:...../...../2020	Result:
2 nd Date:...../...../2020	Result:

11. Date of discharge:...../...../2020;

12. Date of end of isolation:...../...../2020

13. Outcome: Recovered / Referred to higher center / Left by own / Death

14. Contact tracing (to be done by the local health authority): Informed: Yes/ No

Signature of the concerned physician

Annex 9: 'CARING FOR CRITICALLY ILL COVID- 19 PATIENT: QUICK GUIDE FOR ICU CARE'

DGHS website have a guideline named 'CARING FOR CRITICALLY ILL COVID- 19 PATIENT: QUICK GUIDE FOR ICU CARE' which can be followed for detailed management strategies. The link to this document-

https://dghs.gov.bd/images/docs/Notice/27_04_2020_Annex%20Critically%20ill%20COVID19%20management.pdf