

National Guidelines on Clinical Management of Coronavirus Disease 2019 (Covid-19)

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Disease Control Division Directorate General of Health Services Ministry of Health & Family Welfare Government of the People's Republic of Bangladesh





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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 National Preparation and Response Plan. As a part of the preparation process, a guideline on clinical management was developed by Bangladesh Society of Medicine late January, 2020. To further update the document with the latest evidence 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 evidence 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	
САР	Community Acquired Pneumonia	
СВС	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	
НСР	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	
МАР	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) pandemic declared by the World Health Organization (WHO) on 11th March 2020, caused by SARS CoV 2 virus is at exponentially rising state across the globe. Bangladesh is also facing the toll of this highly transmissible zoonotic disease with hint of community transmission in some places. 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 the 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 strategy is containment. The pick can be delayed or more precisely flattened by isolation of cases, quarantine of contacts and social distancing of non-infected people. Early diagnosis can help by identifying cases and areas for individual and group isolation. From 'draconian' process of complete lockdown to confirmatory diagnosis and isolation should be practiced by every nation. Bangladesh has already started the mitigation process and this guideline is a part of the strategy, addressing the case management of COVID-19 cases in Bangladesh with specific recommendations:

- Case definition of suspect, probable and confirmed COVID-19 will be followed by every physicians of Bangladesh which will be updated regularly. All cases to be reported to the health authority (civil surgeon, DGHS)
- The concept of testing, tracking, tracing, isolation of cases and quarantine of close contacts will be followed
- 3. The clinical syndrome ranges from mild illness, pneumonia, severe pneumonia, ARDS and sepsis and septic shock
- Specific test for confirmation will be done by RT-PCR taking samples from upper and lower respiratory tract unless rapid nucleic acid test (NAT) and other WHO recommended tests are available
- All suspected, confirmed and probable COVID-19 cases will be managed (according to severity) in designated COVID-19 hospitals and every measure will be taken to keep the other health facilities free from Corona virus infected patients to maintain the ongoing health service of other Non COVID patients.
- An effective patient transportation system among different health facilities at local and central levels has to be established.
- 7. The mild case of influenza like illness (ILI) can be managed by telephone/telemedicine service
- 8. The severe and critical cases will be admitted and treated in COVID-19 designated hospitals.

- 9. The principles of management will be appropriate supportive therapy in pneumonia case ranging from empirical antibiotic, antiviral oseltamivir to high flow oxygen and mechanical ventilation for ARDS cases.
- This guideline recommends the use of Hydroxychloroquine/chloroquine and azithromycin in the treatment of covid-19 cases. For prophylaxis, this guideline recommends the use of Hydroxychloroquine
- 11. A comprehensive infection prevention and control (IPC) is important in every aspects of case management from community to hospital ICU. A national guideline is available in this aspect.

Introduction

COVID-19 is the pandemic disease declared by World Health Organization (WHO) on 11th March 2020 which is 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. 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.

Globally 209 countries are reported to have the pandemic going on and the situation is evolving rapidly with global case counts and deaths increasing each 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.

In Bangladesh, COVID 19 infections are being reported from Directorate General of Health Service on daily basis. So far, total 218 confirmed cases and 20 deaths are reported (dated 8 April, 2020).

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

There are no specific treatments found to be effective for COVID-19 yet; 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 with mild illness unless there is concern about rapid deterioration or an inability to promptly return to hospital if necessary. If self-isolation at home is not possible because of lack of care giver, overcrowding at home or any other cause, patient should be brought to the hospital for institutional isolation in a designated area

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 as 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 situation of the epidemic in the country, availability of new scientific knowledge, 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 cause 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.

A preliminary study suggests that there are two major types (or strains) of the SARS-CoV-2 virus in China, designated L and S. The L type was found to be more prevalent during the early stages of the outbreak in Wuhan City and may be more aggressive (although this is speculative), but its frequency decreased after early January. The relevance of this finding is unknown at this stage and further research is required as the virus is still evolving.



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

Suspect case

a. A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), AND a history of travel to or residence in a Country/location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset.

OR

 A patient/ health care worker with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case (see definition of contact) in the last 14 days prior to symptom onset

OR

c. A patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.

Probable case:

a. A suspect case for whom testing for the COVID-19 virus is inconclusive. Inconclusive being the result of the test reported by the laboratory.

OR

b. A suspect case for whom testing could not be performed for any reason.

Confirmed case:

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

Definition of contact:

- a. A contact is a person not having symptoms at present but who has been exposed to probable case or confirmed case.
- b. Contact timing: 2 days before and the 14 days after the onset of symptoms of a probable or confirmed cases
- c. Contact pattern
- Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes.
- Direct physical contact with a probable or confirmed case
- Direct care for a patient with probable or confirmed COVID-19 disease without using proper personal protective equipment1, OR
- Other situations as indicated by local risk assessments.

Note: 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 was taken* which led to confirmation.

 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-duringhealth-care-when-novel-coronavirus-(ncov)- infection-is-suspected-20200125

COVID-19 is a notifiable disease. Please report all cases (confirmed or suspected) to health authority (civil surgeon, DGHS).

Clinical syndromes associated with COVID-19

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

Mild illness	Patients with uncomplicated upper respiratory tract viral infection may have non-		
(ILI)	specific symptoms such as fever, fatigue, cough (with or without sputum production),		
	sore throat, nasal congestion, anorexia, malaise, or headache. Rarely, patients may also		
	present with diarrhoea, nausea, and vomiting.		
	The elderly and immunosuppressed may present with atypical symptoms. Symptoms		
	due to physiologic adaptations of pregnancy or adverse pregnancy events, such as		
	dyspnea, fever, GI-symptoms or fatigue, may overlap with COVID-19 symptoms		
Pneumonia	Adult with pneumonia but no signs of severe pneumonia and no need for		
	supplemental oxygen.		
	Child with non-severe pneumonia who has cough or difficulty breathing + fast		
	breathing: fast breathing (in breaths/min): < 2 months: \geq 60; 2–11 months: \geq 50; 1–5		
	years: \geq 40, and no signs of severe pneumonia		
Severe	Adolescent or adult: fever or suspected respiratory infection, plus one of the		
pneumonia	following:		
	Respiratory rate > 30 breaths/min.		
	Severe respiratory distress; or		
	SpO2 ≤ 93% on room air.		
	Child with cough or difficulty in breathing, plus at least one of the following: central		
	cyanosis or SpO2 <90%.		
	severe respiratory distress (e.g. grunting, very severe chest indrawing);		
	Signs of pneumonia with a general danger sign:		
1			

	Other signs of pneumonia may be present: chest indrawing, fast breathing (in		
	breaths/min): <2 months: \geq 60; 2–11 months: \geq 50; 1–5 years: \geq 40 (16). While the		
	diagnosis is made on clinical grounds; chest imaging may identify or exclude some		
	pulmonary complications.		
Acute	Onset: within 1 week of a known cli	nical insult or new or worsening respiratory	
respiratory	symptoms.		
distress	Chest imaging (radiograph, CT scan or l	ung ultrasound): bilateral / unilateral opacities,	
syndrome	not fully explained by volume overload, lobar or lung collapse, or nodules. Patient with		
(ARDS)	pleural effusion unlikely to be COVID.		
	Pulmonary infiltrates/ respiratory failure not fully explained by cardiac failure or fluid		
	overload.		
	Need objective assessment (eg echocardiography or USG) to exclude hydrostatic cause		
	of infiltrates/oedema if no risk factor present.		
	Oxygenation impairment in adults:		
	> Mild ARDS: 200 mmHg < $PaO_2/FiO_2 \le 300$ mmHg		
	(with PEEP or CPAP \geq 5 cmH ₂ O, or non-ventilated)		
	> Moderate ARDS: 100 mmHg < $PaO_2/FiO_2 \le 200$ mmHg		
	(with PEEP \geq 5 cmH ₂ O, or non-ventilated)		
	> Severe ARDS: $PaO_2/FiO_2 \le 100 \text{ mmHg}$		
	(with PEEP \geq 5 cmH ₂ O, or non-ventilated)		
	> When PaO_2 is not available, $SpO_2/FiO_2 \le 315$ mmHg suggests ARDS		
	(including in non-ventilated patients)		
Sepsis	Sepsis: adults		
	Life-threatening organ dysfunction c	aused by a dysregulated host response to	
	suspected or proven infection.		
	Signs of organ dysfunction	Laboratory evidence of:	
	Altered mental status	Coagulopathy	
	Difficult or fast breathing	Thrombocytopenia < 50,000/cmm	
	Low oxygen saturation	Raised lactate	
	Reduced urine output	Hyperbilirubiemia	
	Fast heart rate, weak pulse, cold		
	extremities or low blood pressure,		
	skin mottling		
	Children: suspected or proven infectio	on and \geq 2 age- based systemic inflammatory	
	response syndrome criteria, of which	one must be abnormal temperature or white	
	blood cell count.		

Septic shock	Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to	
	maintain MAP \geq 65 mmHg and serum lactate level > 2 mmol/L.	
	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).	

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

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.

NAAT can be done (rapid test) once it is readily available in Bangladesh.

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
 - o Crazy paving appearance (GGOs and inter-/intra-lobular septal thickening)
 - Bronchovascular thickening in the lesion
 - o Traction bronchiectasis

- Chest Xray- Is not as sensitive as HRCT. However, this can be done where CT is not available or after doing CT scan if facility is available. 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.





HRCT findings of a COVID-19 patient (Left- ground glass opacities, Right- Bilateral pneumonia) (@ Md Robed Amin)





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

Supportive investigations

CBC: lymphopenia (83%), leukopenia (9–25%), leukocytosis (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 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 rapid 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 are significantly elevated in severe cases, which is a potential risk factor for poor prognosis).

Treating clinician may order relevant investigations if required

N.B: Normal or low TC of WBC, Lymphopenia, High CRP, Low Procalcitonin.if these are associated with bilateral pneumonia in Chest x-ray or GGO in CT scan of Chest- Diagnosis is COVID 19 in this current time

Management/Treatment

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

Clinical criteria 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.

All suspected, confirmed and probable COVID-19 cases will be managed (according to severity) in designated COVID-19 hospitals and every measure will be taken to keep the other health facilities free from Corona virus infected patients to maintain the ongoing health service of other Non COVID patients. An effective patient transportation system among different health facilities at local and central levels has to be established.

Admission criteria

- 1. All suspect/ confirmed cases of COVID-19 presenting with
 - Pneumonia with CRB 65 score 1 or more (Please see figure 1)
 - Severe Pneumonia
 - ARDS, Sepsis, Septic shock
 - Hypoxia (SpO2 <94%) in the absence of any clinical signs
- 2. All cases with respiratory distress should be admitted for further evaluation and testing

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



Figure 1: CRB65 Scoring system

Treatment Protocol of COVID-19 infection in Bangladesh

Mild and Moderate cases can be managed at home and Severe and Critical patients should be receive hospital care

1. Mild illness [Influenza Like Illness (ILI)] - Patient with one or more features (fever, cough, sore throat, malaise, nasal congestion).

To avoid diseases transmission and reduce the burden on hospitals, patients with ILI should stay at home and consult doctors through different telephone/telemedicine services provided by various government and non-government organisations. (Annexure- tool use for COVID-19 in telemedicine)

Advice for ILI patients

- Rest in home as self- isolation (If self-isolation at home is not possible because of lack of care giver, overcrowding at home or any other cause, patient should be brought to the hospital for institutional isolation in a designated area.)
- Social distancing with family members (If possible, in a 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
- Symptomatic treatment
 - Tab Paracetamol 500 mg 1+1+1
 - Tab antihistamine (Fexofenadin) 0+0+1

- Steam inhalation/Gurgle of Lukewarm water
- Chloroquine/Hydroxychloroquine and Azithromycin (see page. 22 for detail dosage and instruction)
- Follow up
 - Self-home isolation for 14 days after clinical recovery
 - Ask about: Dyspnoea, chest pain, persistent or worsen dry or productive cough, Haemoptysis
- When patient should immediately seek hospital care?
 - Respiratory distress
 - Worsening cough and fever
 - o Altered mental status
 - Extreme lethargy

2. Moderate

- o Pneumonia
- No signs of severe pneumonia (CRB 65 score 0)
- No need for supplemental oxygen

Management of moderate group

The patient will be managed as like as Mild illness (ILI). However, the patient should receive broad spectrum oral antibiotics as for uncomplicated community acquired pneumonia (CAP)

Hospital care Principles

- 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 measures.
- Patients with severe disease often need oxygenation support.
- Aerosol generating procedures such as endotracheal intubation, bronchoscopy, nebulization, cardiopulmonary resuscitation, open suctioning 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. Oxygen hood is suitable if patient needs oxygen in general ward.
- 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.
- ECMO (extracorporeal membrane oxygenation) may be indicated in patients with refractory hypoxia in ICU setting

3. Severe

- Severe pneumonia
- o Sepsis

These patients should be managed preferably in a High Dependency Unit (HDU) based on availability.

Management

- o Give immediate supplemental oxygen for the following patients
 - If SPO₂<94%
 - Respiratory rate >30 breaths/ minute
 - Shock
- Initiate oxygen at 5 litres/min and titrate flow to reach target $SPO_2 \ge 94 \%$
- Use face mask with reservoir bag (at oxygen at 10–15 L/min) if patient in critical condition.
- Once patient is hemodynamically stable, the target is SpO₂ ≥ 90% in non-pregnant adults and ≥ 92–95% in pregnant patients
- Patients with severe pneumonia or sepsis should be treated cautiously with intravenous fluids, because aggressive fluid resuscitation may worsen oxygenation, especially in settings where there is limited availability of mechanical ventilation
- Chloroquine/Hydroxychloroquine and Azithromycin (see page. 22 for detail dosage and instruction)
- Give empiric antimicrobials to treat all likely pathogens causing severe pneumonia and sepsis as soon as possible, within 1 hour of initial assessment for patients with sepsis.
- Closely monitor patients with COVID-19 for signs of clinical deterioration, such as rapidly progressive respiratory failure and septic shock and respond immediately with supportive care interventions
- Management of co-morbid conditions

N.B. Adults with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma, or convulsions) should receive airway management and oxygen therapy during resuscitation to target SpO2 \geq 94%.

4. Critical

- o ARDS
- \circ Septic shock

Critically ill patients should be managed in intensive care unit (ICU). They should be managed based on following Recommendations. Along with standard management, these patients should also receive combination of Chloroquine/Hydroxychloroquine and Azithromycin (see page. 22 for detail dosage and instruction).

Recommendations of care of patient of COVID-19 in ICU

This recommendation is standard recommendation for survival sepsis campaign for COVID 19 in ICU setting. There is variable grade of recommendation from strong to weak and adjustment is advised through risk benefit in working team of ICU of COVID 19 hospitals in Bangladesh

Haemodynamic

- In adults with COVID-19 and shock, use dynamic parameters like skin temperature, capillary refilling time, and/or serum lactate measurement over static parameters in order to assess fluid responsiveness.
- 2. For the acute resuscitation of adults with COVID-19 and shock, use a conservative over a liberal fluid strategy.
- 3. For the acute resuscitation of adults with COVID-19 and shock,
 - i. use crystalloids over colloids.
 - ii. use buffered/balanced crystalloids over unbalanced crystalloids.
 - iii. avoid using hydroxyethyl starches.
 - iv. avoid using gelatins.
 - v. avoid using dextrans.
 - vi. avoid the routine use of albumin for initial resuscitation.
 - vii.
- 4. For adults with COVID-19 and shock,
 - i. use norepinephrine as the first-line vasoactive agent, over other agents.
 - ii. If norepinephrine is not available, use either vasopressin or epinephrine as the first-line vasoactive agent, over other vasoactive agents, for adults with COVID-19 and shock.
 - iii. avoid using dopamine if norepinephrine is available.
 - iv. add vasopressin as a second-line agent, over titrating norepinephrine dose, if target mean arterial pressure (MAP) cannot be achieved by norepinephrine alone.
 - v. titrate vasoactive agents to target a MAP of 60-65 mmHg, rather than higher MAP targets.
- For adults with COVID-19 and shock with evidence of cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation and norepinephrine, add dobutamine, over increasing norepinephrine dose.
- For adults with COVID-19 and refractory shock (when patient do not respond to fluid and inotrope therapy), use low-dose corticosteroid therapy ("shock-reversal").

Remark: A typical corticosteroid regimen in septic shock is intravenous hydrocortisone 200 mg per day administered either as an infusion or intermittent doses.

Ventilation

- In adults with COVID-19, start supplemental oxygen if the peripheral oxygen saturation (SPO2) is < 94%
- 2. In adults with COVID-19 and acute hypoxemic respiratory failure on oxygen, SPO2 be maintained no higher than 96%.
- 3. For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, use HFNC (high flow nasal canula) over conventional oxygen therapy.
- 4. In adults with COVID-19 and acute hypoxemic respiratory failure, use HFNC (high flow nasal canula) over NIPPV (non-invasive positive pressure ventilation)..
- 5. In adults with COVID-19 and acute hypoxemic respiratory failure, if HFNC is not available and there is no urgent indication for endotracheal intubation, a trial of NIPPV with close monitoring and short-interval assessment for worsening of respiratory failure.
- 6. The use of helmet NIPPV compared with mask NIPPV is an option but there is lack of evidence.
- 7. In adults with COVID-19 receiving NIPPV or HFNC, close monitoring for worsening of respiratory status is crucial, and early intubation in a controlled setting if worsening occurs.
- In mechanically ventilated adults with COVID-19 and ARDS, use low tidal volume (Vt) ventilation (Vt
 4-8 mL/kg of predicted body weight), over higher tidal volumes (Vt>8 mL/kg).
- For mechanically ventilated adults with COVID-19 and ARDS, target plateau pressures (Pplat) of < 30 cm H2O.
- 10. For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, we suggest using a higher PEEP strategy, over a lower PEEP strategy.

Remarks: If using a higher PEEP strategy (i.e., PEEP > 10 cm H2O), clinicians should monitor patients for barotrauma.

- 11. For mechanically ventilated adults with COVID-19 and ARDS, use a conservative fluid strategy over a liberal fluid strategy.
- 12. For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, we suggest prone ventilation for 12 to 16 hours, over no prone ventilation.
- 13. For mechanically ventilated adults with COVID-19 and moderate to severe ARDS: use, as needed, intermittent boluses of neuromuscular blocking agents (NMBA), over continuous NMBA infusion, to facilitate protective lung ventilation.
- 14. In the event of persistent ventilator desynchrony, the need for ongoing deep sedation, prone ventilation, or persistently high plateau pressures, use a continuous NMBA infusion for up to 48 hours.

- 15. In mechanically ventilated adults with COVID-19 ARDS, avoid the routine use of inhaled nitric oxide.
- 16. In mechanically ventilated adults with COVID-19, severe ARDS and hypoxemia despite optimizing ventilation and other rescue strategies, start a trial of inhaled pulmonary vasodilator as a rescue therapy; if no rapid improvement in oxygenation is observed, the treatment should be tapered off.
- 17. For mechanically ventilated adults with COVID-19 and hypoxemia despite optimizing ventilation, use recruitment manoeuvres, over not using recruitment manoeuvres.
- 18. If recruitment manoeuvres are used, we recommend against using staircase (incremental PEEP) recruitment manoeuvres.
- 19. In mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimizing ventilation, use of rescue therapies, and proning, use venovenous (VV) ECMO if available, or referring the patient to an ECMO center.

Remark: Due to the resource-intensive nature of ECMO, and the need for experienced centers and healthcare workers, and infrastructure, ECMO should only be considered in carefully selected patients with COVID-19 and severe ARDS.

Therapy

- 1. In mechanically ventilated adults with COVID-19 and respiratory failure (without ARDS), avoid the routine use of systemic corticosteroids.
- 2. In mechanically ventilated adults with COVID-19 and ARDS, use systemic corticosteroids.
- 3. In mechanically ventilated patients with COVID-19 and respiratory failure, use empiric antimicrobials/antibacterial agents.

Remark: if the treating team initiates empiric antimicrobials, they should assess for deescalation daily, and re-evaluate the duration of therapy and spectrum of coverage based on the microbiology results and the patient's clinical status.

- 4. For critically ill adults with COVID-19 who develop fever, use acetaminophen/paracetamol for temperature control, over no treatment.
- 5. In critically ill adults with COVID-19, avoid the routine use of standard intravenous immunoglobulins (IVIG), avoid the routine use of convalescent plasma and avoid the routine use of lopinavir/ritonavir.
- 6. There is insufficient evidence to issue a recommendation on the use of recombinant rIFNs, alone or in combination with antivirals, in critically ill adults with COVID-19.
- 7. There is insufficient evidence to issue a recommendation on the use of tocilizumab in critically ill adults with COVID-19.

Infection Control and Testing

1. For healthcare workers performing aerosol-generating procedures on patients with COVID-19 in the ICU, use fitted respirator masks (N95 respirators, FFP2, or equivalent), as opposed to surgical/medical

masks, in addition to other personal protective equipment (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles)

- 2. Perform aerosol-generating procedures on ICU patients with COVID-19 in a negative pressure room.
- For healthcare workers providing usual care for non-ventilated COVID-19 patients, use surgical/medical masks, as opposed to respirator masks, in addition to other personal protective equipment (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles)
- 4. For healthcare workers who are performing non-aerosol-generating procedures on mechanically ventilated (closed circuit) patients with COVID-19, use surgical/medical masks, as opposed to respirator masks, in addition to other personal protective equipment (i.e., gloves, gown, and eye protection, such as a face shield or safety goggles).
- 5. For healthcare workers performing endotracheal intubation on patients with COVID-19, use videoguided laryngoscopy, over direct laryngoscopy, if available.
- 6. For COVID-19 patients requiring endotracheal intubation, perform endotracheal intubation by the healthcare worker who is most experienced with airway management in order to minimize the number of attempts and risk of transmission.
- 7.1 For intubated and mechanically ventilated adults with suspicion of COVID-19: For diagnostic testing, obtain lower respiratory tract samples in preference to upper respiratory tract (nasopharyngeal or oropharyngeal) samples.
- 7.2 For intubated and mechanically ventilated adults with suspicion of COVID-19: With regard to lower respiratory samples, obtain endotracheal aspirates in preference to bronchial wash or bronchoalveolar lavage samples.

Pharmacotherapy

Pharmacological drug

Based upon limited in vitro and anecdotal clinical data in several case series, and observational studies, a combination of hydroxychloroquine/chloroquine and azithromycin is currently recommended for treatment of all **confirmed** and **probable** COVID-19 patients (see case definition).

Drug	Dose and duration	Remarks	
lydroxychloroquine 400mg-BID-D1 and then		Caution : Elderly, Diabetics (may lower	
	200 mg -TID-D2-D10	blood glucose). children below 9 years	
	(11mg/kg/dose BID-D1 & 5.5mg/kg/dose TID- D2-10 for Children over	May aggravate: Myasthenia Gravis,	
		Psoriasis, Epilepsy. The drug should be	
		withheld in patients with baseline QT	
	9 years)	prolongation	
		Before treatment: ECG and Serum	
		electrolytes should be measured. Assess	
		Renal and Liver Function (Adjust Dose)	
		Assess any Visual Impairment	
Chloroquine (if	500mg BID for 7 days	Caution: Elderly, Diabetics (may lower	
Hydroxychloroquine is	(5mg/kg/dose BID for 7	blood glucose), Ocular toxicity (usually after	
unavailable)	days for Children over 9	prolonged usage), children below 9 years	
	years)	May aggravate: Myasthenia Gravis,	
		Psoriasis, Epilepsy. Dose adjustment in	
		Severe Hepatic and Renal Impairment.	
		Prohibit to combine with the chloroquine	
		drugs that may lead to the	
		phosphate - prolonged Q-T interval (such as	
		moxifloxacin, azithromycin,	
		amiodarone, etc).	
		Before treatment: ECG and Serum	
		electrolytes should be measured.	
Azithromycin	500mg OD for D1, then	Caution: Electrolyte imbalance (may cause	
	רמ-צם צוווסרצ	prolonged QT). The drug should be	

(10mg/kg/day for D1, then	withheld in patients with baseline QT
5mg/kg/day D2-D5 in	prolongation
children over 9 years)	Associated Ischemic Heart Disease
	Other drugs causing prolonged QT
	May aggravate Myasthenia Gravis

N.B: If cloroquine is used in high dose, use it singly and do not combine with azythromycin. Hydroxychlorquine and azythromycin can be used together but with precaution of QT prolongation ECG is a must in patient with heart condition before starting HCQ+Azythromycin and repetition of ECG should also be considered.

Corticosteroids: Dose:

Indication for Corticosteroids

- for those in severe and critically ill stage;
- al for those with persistent high fever (temperature above 39°C) even after treatment for severe pneumonia
- for those whose computerized tomography (CT) demonstrated patchy ground-glass attenuation or more than 30% area of the lungs are involved;
- for those whose CT demonstrated rapid progression (more than 50% area involved in pulmonary CT images within 48 hours);
- for those whose IL-6 is above

Initial routine methylprednisolone at a dose of 0.75-1.5 mg/kg intravenously once a day (nearly 40 mg once or twice a day).

- The WHO and CDC recommend corticosteroids are not to be used in patients with COVID-19 pneumonia unless there are other indications (eg exacerbation of COPD).
- Corticosteroids have been associated with an increased risk of mortality in patients with influenza and delayed viral clearance in patients with Middle East respiratory syndrome coronavirus (MERS-CoV) infection.
- Though widely used in management of severe acute respiratory syndrome (SARS), there was no good evidence for benefit, and there was persuasive evidence of adverse harm in the short and long term
- Corticosteroid can be used in septic shock patient according to survival sepsis guideline hydrocortisone 200/day in divided doses.

Other antiviral drugs that are being used in different countries:

Lopinavir-ritonavir:

Investigators in China report the results of an open-label, randomised clinical trial of lopinavir–ritonavir for the treatment of COVID-19 in 199 infected adult patients. There was no difference in the primary end point, time to clinical improvement.



Remdesivir:

- Several randomised trials are under way to evaluate the efficacy of remdesivir for moderate or severe COVID-19.
- It has activity against SARS-CoV-2 in vitro, SARS and MERS-CoV, both in vitro and in animal studies.
- The compassionate use of remdesivir through an investigational new drug application was described in a case report of one of the US patients with COVID-19.
- Any clinical impact of the drug on COVID-19 is awaited.

Favipiravir (starting dose of 1600mg followed by 600 mg tid)

- Japan based treatment option for CoVID 19 cases when the early regimen fails
- No high-quality based data

Ribavain: Dose IV 4 gm – Stat and then every 8 hourly 8mg/kg IV for 14 days

• No high-quality based data

Tocilizumab:

- Treatment guidelines from China's National Health Commission include the IL-6 inhibitor tocilizumab for patients with severe COVID-19 and elevated IL-6 levels.
- A clinical trial is under way.

Uncertainty about NSAID use

- Some clinicians have suggested that the use of NSAIDs early in the course of disease may have a negative impact on disease outcome (Day *BMJ* 2020;368:m1086. Epub 17 Mar 2020). These are based on anecdotal reports of a few young patients who received NSAIDs early during infection and experienced severe disease. There is also the concern that the anti-inflammatory properties associated with NSAIDs could have a negative impact on the patient's immune response.
- Use paracetamol (acetaminophen) in place of NSAIDs for reduction of fever.

Interleukin: Interferon nebulization is recommended in COVID-19. It should be performed in negative-pressure wards

Important Information of using Pharmacological agents:

- May consider for Flu Shot, Zinc, Melatonin, Vit C, Oseltamivir (75 mg twice daily for 5 days)
- Empirical antibiotics when Procalcitonin is high, Neutrophilic leucocytosis
- Treat each syndrome accordingly.
- Use paracetamol as fever-lowering agent. (if temperature is more than 102oF)
- Avoid steroids (From mild cases to severe pneumonia cases but may be given as indicated above) and NSAID
- WHO has started Solidarity trial giving importance on 4 drugs (Chlorquine, Remdesavir, Interleukin and Iopinavir-ritonavir)
- As there is no high- quality data regarding antiviral agent, use of these agents (as repurpose drug) should be use judiciously (by judging risk benefit) by consultant while working in COVID 19 hospital

Chemoprophylaxis

The following recommendation for the use of hydroxychloroquine as a prophylactic agent against SARS-CoV-2 infection is based on limited in vitro and anecdotal clinical data in several case series, and observational studies, as well as risk-benefit consideration, under exceptional circumstances that call for the protection of high-risk individuals: frontline healthcare workers.

Dosage:

Candidate	Drug, Dose and Duration	Remarks
Asymptomatic healthcare	Hydroxychloroquine	To be taken with meals
workers involved in the care of	400 mg BD on Day 1, followed	
suspected or confirmed cases of	by 400 mg once weekly for next	
COVID-19	7 weeks	

N.B: HCW with pre-existing heart condition, should do ECG before starting HCQ and also repeat it every week

Caring for infants and mothers with COVID-19: IPC and breastfeeding

- 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.

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, 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

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: Lopinavir/ritonavir tablets could be used. Favipiravir and chloroquine phosphate are prohibited.
- 2. Patients with hepatic insufficiency Drugs that are excreted unchanged through the kidney are preferred, such as penicillin and cephalosporins, etc.
- 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.

Discharge Criteria

- 1. Body temperature remains normal for at least 3 days (ear temperature is lower than 37.5 °C).
- 2. Respiratory symptoms are significantly improved.
- The nucleic acid is tested negative for respiratory tract pathogen twice consecutively (sampling interval more than 24 hours); the nucleic acid test of stool samples can be performed at the same time if possible.
- 4. Lung imaging shows obvious improvement in lesions.
- 5. There is no comorbidities or complications which require hospitalization.
- 6. SpO₂, >93% without assisted oxygen inhalation.
- 7. Discharge approved by multi-disciplinary medical team.

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.

Antiviral drugs can be used after discharge for patients with multiple lung lesions in the first 3 days after their nucleic acid are tested negative.

Home isolation

Patients must continue two weeks of isolation after discharge. 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 week, 2 weeks, and 1 month after discharge.

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 6months 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 in China, after being discharged based on the standards of 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. 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 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.

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Annex1: হাসপাতালে কোভিড-১৯ রোগের ব্যবস্থাপনা



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: Patient flow pathway for designated COVID-19 hospital



Patient flow pathway for designated COVID-19 Hospital



Patient flow chart for non COVID-19 Hospital

SOP- Patient flow chart

