



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

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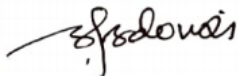
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Preface

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
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
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 put the scientific authority in a puzzle. The epidemic curve observed in the last three months starting at Wuhan of China towards rest of the globe is similar which showed slow to start the cases with steep doubling in three to five days and then leading to quick upsurge and collapsing the health system of a country very quickly. The number of cases affected and death both 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, delay the peak of epidemic curve by diagnosis & treatment, and mitigation through various process including non therapeutic interventions are crucial. 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 case management of COVID-19 in Bangladesh with specific consideration:

1. Case definition of suspect, probable and confirmed COVID-19 will be followed by every physicians of Bangladesh which will be updated regularly
2. The concept of testing, tracking, tracing, isolation 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
4. 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
5. The mild case of influenza like illness (ILI) will be managed by telephone/telemedicine service
6. The severe and critical cases will be treated in COVID-19 designated hospitals.
7. 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.
8. Currently antiviral (single or combination) or auxiliary drugs (Chloroquine, hydroxychlorquine) for COVID-19 is not recommended
9. A comprehensive infection prevention and control (IPC) is important in every aspects of case management from community to hospital ICU.

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 199 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.

Bangladesh is also declared the COVID 19 infection reported from Directorate General of Health Service on daily basis with 48 confirmed case and 5 death having community transmission (dated 28th March, 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 is 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

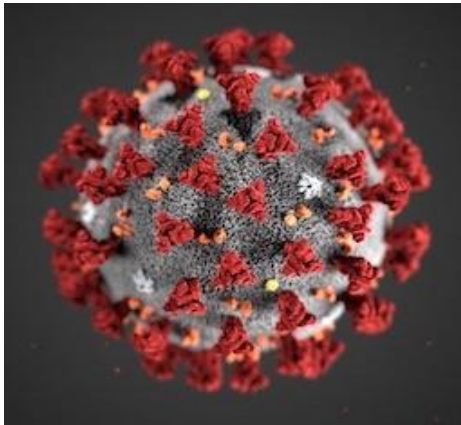
A surveillance based case definition and approach to diagnose and management principles are highlighted in this guideline. This version will time to time updated according to need of the country.

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 this book content. Readers are requested to acquire the knowledge in this regard from peer reviewed sources from biomedical journals

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

- b. 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. Who is contact? 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
- 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.

1. 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)

Clinical syndromes associated with COVID-19:

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

Mild illness (ILI)	<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, 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 dyspnea, fever, GI-symptoms or fatigue, may overlap with COVID-19 symptoms</p>
Pneumonia	<p>Adult with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen.</p> <p>Child with non-severe pneumonia who has cough or difficulty breathing + fast breathing: fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40, and no signs of severe pneumonia</p>
Severe pneumonia	<p>Adolescent or adult: fever or suspected respiratory infection, plus one of the following: Respiratory rate > 30 breaths/min. Severe respiratory distress; or SpO₂ $\leq 93\%$ on room air.</p> <p>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: Inability to breastfeed or drink, lethargy or unconsciousness, or convulsions. Other signs of pneumonia may be present: chest indrawing, fast breathing (in breaths/min): <2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 (16). While the diagnosis is made on clinical grounds; chest imaging may identify or exclude some pulmonary complications.</p>
Acute respiratory distress syndrome (ARDS)	<p>Onset: within 1 week of a known clinical insult or new or worsening respiratory symptoms.</p> <p>Chest imaging (radiograph, CT scan or lung ultrasound): bilateral / unilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules. Patient with pleural effusion unlikely to be COVID.</p>

	<p>Pulmonary infiltrates/ respiratory failure not fully explained by cardiac failure or fluid overload.</p> <p>Need objective assessment (eg echocardiography or USG) to exclude hydrostatic cause of infiltrates/oedema if no risk factor present.</p> <p>Oxygenation impairment in adults:</p> <ul style="list-style-type: none"> > Mild ARDS: $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$ (with PEEP or CPAP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated) > Moderate ARDS: $100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}$ (with PEEP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated) > Severe ARDS: $\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mmHg}$ (with PEEP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated) > When PaO_2 is not available, $\text{SpO}_2/\text{FiO}_2 \leq 315 \text{ mmHg}$ suggests ARDS (including in non-ventilated patients) 												
Sepsis	<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> <tr> <td>Low oxygen saturation</td> <td>Raised lactate</td> </tr> <tr> <td>Reduced urine output</td> <td>Hyperbilirubiemia</td> </tr> <tr> <td>Fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling</td> <td></td> </tr> </table> <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>	Signs of organ dysfunction	Laboratory evidence of:	Altered mental status	Coagulopathy	Difficult or fast breathing	Thrombocytopenia $< 50,000/\text{cmm}$	Low oxygen saturation	Raised lactate	Reduced urine output	Hyperbilirubiemia	Fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling	
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Septic shock	<p>Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain $\text{MAP} \geq 65 \text{ mmHg}$ and serum lactate level $> 2 \text{ mmol/L}$.</p> <p>Children: any hypotension ($\text{SBP} < 5\text{th centile}$ or $> 2 \text{ SD}$ below normal for age) or two or three of the following: altered mental state; tachycardia or bradycardia ($\text{HR} < 90 \text{ bpm}$ or $> 160 \text{ bpm}$ in infants and $\text{HR} < 70 \text{ bpm}$ or $> 150 \text{ bpm}$ in children); prolonged capillary refill ($> 2 \text{ sec}$) 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 non-covid hospital after proper evaluation.

Testing for COVID-19

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.

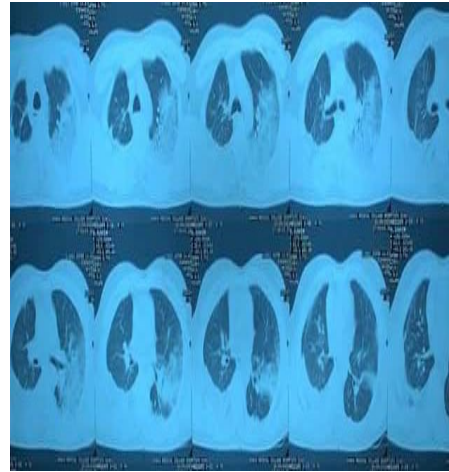
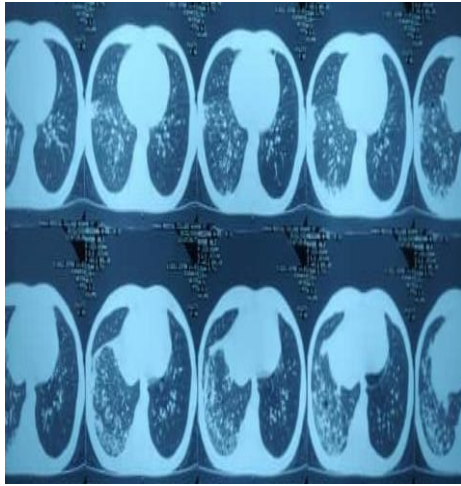
➤ Detection of viral nucleic acid

Nucleic acid testing is the preferred method for diagnosing COVID-19. In our country viral nucleic acid is detected by RT-PCR (Real time- Polymerase Chain Reaction)

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
 - 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. 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



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. D-dimer levels are significantly elevated in severe cases, which is a potential risk factor for poor prognosis.

Blood culture: to detect secondary bacterial infection.

Liver and renal function test, Arterial blood gas analysis.

Serum Ferritin, S.LDH, D-dimer.

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

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
2. All cases with respiratory distress should be admitted for further evaluation and testing

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

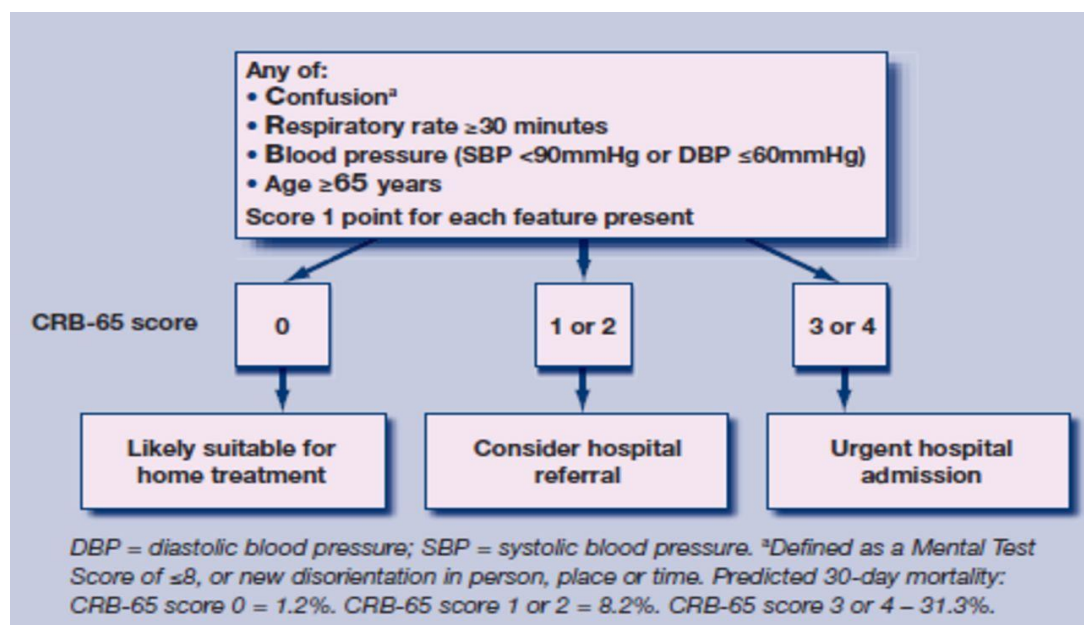


Figure 1: CRB65 Scoring system

Treatment Protocol of COVID-19 infection in Bangladesh

Mild and Moderate cases should 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

1. 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.**)
2. Social distancing with family members (If possible, in a single room)
3. No visitor
4. Hand wash (20 seconds each time) (Repeated hand wash is beneficial)
5. Cough etiquette (use tissue paper or elbow followed by hand wash)
6. Medical mask
7. Symptomatic treatment
 - Tab Paracetamol 500 mg 1+1+1
 - Tab antihistamine (Fexofenadin) 0+0+1
 - Steam inhalation/Gurgle of Lukewarm water
8. Follow up
 - Self-home isolation for 14 days after clinical recovery
 - Ask about: Dyspnoea, chest pain, persistent or worsen dry or productive cough, Haemoptysis
9. When patient should immediately seek hospital care?
 - Respiratory distress
 - Worsening cough and fever
 - Altered mental status
 - Extreme lethargy

2. Moderate

- 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
- Sepsis

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

Management

- Give immediate supplemental oxygen for the following patients
 - If $SPO_2 < 93\%$
 - Respiratory rate ≥ 30 breaths/ minute
 - Shock
- Initiate oxygen at 5 litres/min and titrate flow to reach target $SPO_2 \geq 93\%$
- Use face mask with reservoir bag (at 10–15 L/min) if patient in critical condition.
- Once patient is stable, the target is $\geq 90\%$ SpO₂ in non-pregnant adults and $\geq 92-95\%$ 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
- 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 ≥ 94%.

4. Critical

- ARDS
- Septic shock

Critically ill patients should be managed in intensive care unit (ICU). They should be managed based on following Recommendations

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

1. In adults with COVID-19 and shock, use dynamic parameters 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, use crystalloids over colloids.
4. For the acute resuscitation of adults with COVID-19 and shock, use buffered/balanced crystalloids over unbalanced crystalloids.
5. For the acute resuscitation of adults with COVID-19 and shock, avoid using hydroxyethyl starches.
6. For the acute resuscitation of adults with COVID-19 and shock, avoid using gelatins.
7. For the acute resuscitation of adults with COVID-19 and shock, avoid using dextrans.
8. For the acute resuscitation of adults with COVID-19 and shock, avoid the routine use of albumin for initial resuscitation.
9. For adults with COVID-19 and shock, use norepinephrine as the first-line vasoactive agent, over other agents.
10. 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.
11. For adults with COVID-19 and shock, avoid using dopamine if norepinephrine is available.

12. For adults with COVID-19 and shock, add vasopressin as a second-line agent, over titrating norepinephrine dose, if target mean arterial pressure (MAP) cannot be achieved by norepinephrine alone.
13. For adults with COVID-19 and shock, titrate vasoactive agents to target a MAP of 60-65 mmHg, rather than higher MAP targets.
14. 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.
15. For adults with COVID-19 and refractory shock, use low-dose corticosteroid therapy (“shock-reversal”), over no corticosteroid.

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

Ventilation

1. In adults with COVID-19, start supplemental oxygen if the peripheral oxygen saturation (SPO₂) is < 92%, and recommend starting supplemental oxygen if SPO₂ is < 90%
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 over conventional oxygen therapy.
4. In adults with COVID-19 and acute hypoxemic respiratory failure, use HFNC over NIPPV.
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.
8. In mechanically ventilated adults with COVID-19 and ARDS, use low tidal volume (V_t) ventilation (V_t 4-8 mL/kg of predicted body weight), over higher tidal volumes (V_t>8 mL/kg).
9. For mechanically ventilated adults with COVID-19 and ARDS, target plateau pressures (P_{plat}) 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, over not using corticosteroids.
3. In mechanically ventilated patients with COVID-19 and respiratory failure, use empiric antimicrobials/antibacterial agents, over no antimicrobials.
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).
6. In critically ill adults with COVID-19, avoid the routine use of convalescent plasma.
7. In critically ill adults with COVID-19: avoid the routine use of lopinavir/ritonavir.

8. There is insufficient evidence to issue a recommendation on the use of other antiviral agents in critically ill adults with COVID-19.
9. 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.
10. There is insufficient evidence to issue a recommendation on the use of chloroquine or hydroxychloroquine in critically ill adults with COVID-19.
11. 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.
3. 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 video-guided 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:

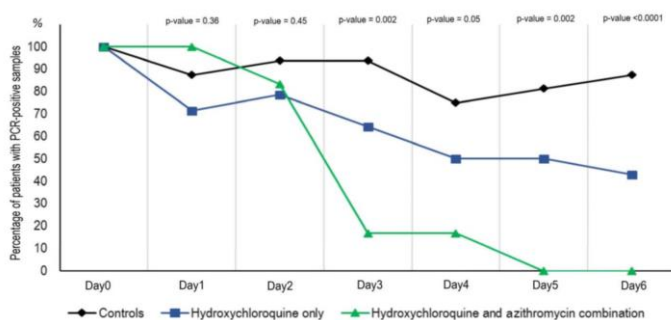
Pharmacological drug

Indicated only for pulmonary syndrome without hypoxia

Chloroquine: Dose: 500mg BID for 7 days

- Use of chloroquine is included in treatment guidelines in China's National Health Commission at Wuhan and was observed to be associated with reduced progression of disease and decreased duration of symptoms.
- However, there is no published data.

Hydroxychloroquine: 400mg-BID-D1 and then 200 mg –TID-D2-D10



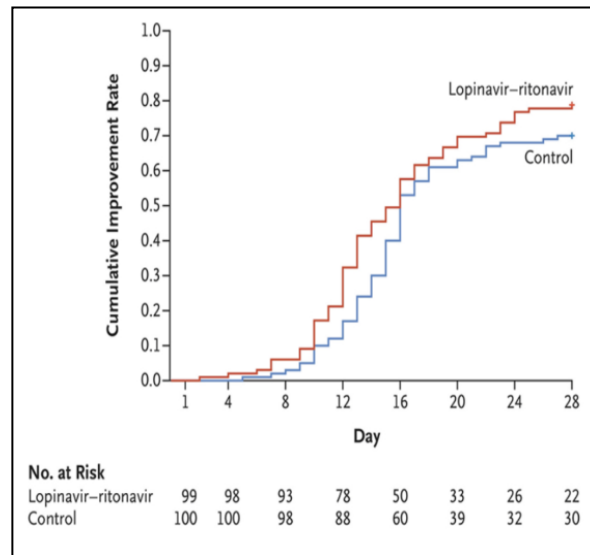
- Hydroxychloroquine (200 mg tds for 10 days) was associated with a higher rate of undetectable viral RNA on nasopharyngeal specimens at day 6 compared with no specific treatment (70 vs 12.5%).
- In this study, the use of azithromycin in combination with hydroxychloroquine appeared to have additional benefit, but there are methodological concerns about the control groups for the study, and the clinical basis for using azithromycin is not clear.
- Very recent analysis from big cohort of China patient showed no benefit of Hydroxychloroquine in COVID 19 patient (27th March report)

Corticosteroids: Dose: 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.

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 leukocytosis
- Treat each syndrome accordingly.
- Use paracetamol as fever-lowering agent.
- Avoid steroids (in mild to severe pneumonia), NSAID
- WHO has started Solidarity trial giving importance on 4 drugs (Chlorquine, Remdesavir, Interleukin and lopinavir-ritonavir)
- As there is no high- quality data regarding pharmacological agent, use of these agents (as repurpose drug) should be use judiciously (by judging risk benefit) by consultant while working in COVID 19 hospital
- No drug is recommended as chemoprophylaxis as there is no quality evidence of efficacy and safety in COVID 19

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.
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.2

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.
3. 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 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 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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- WHO

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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

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 রোগীকে ১৪ দিনের জন্য বাসায় অবস্থান (হোম কোয়ারেন্টাইন) করতে পরামর্শ দিন।

- কোভিড-১৯ প্রমাণিত হলে রোগীকে চিকিৎসা প্রটোকল অনুযায়ী চিকিৎসা প্রদান করুন
- 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।