Guidelines for the Management of COVID-19 (Coronavirus Disease 2019)
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ABSTRACT

The clinical manifestations of COVID-19 vary widely, ranging from asymptomatic/asymptomatic to very severe respiratory distress. Both the body's immune response, both the natural body's immune response and the adaptive body's immune response, play a very important role in the course of COVID-19. Most patients infected with SARS-CoV-2 show symptoms of the respiratory system such as fever, coughing, sneezing, and shortness of breath. The most common symptoms are fever, dry cough, fatigue, and anosmia or ageusia. The management of COVID-19 focuses on isolation, improving the immune system, and handling comorbid patients.

Keywords: COVID-19, SARS-CoV-2, management; disease degree.
Introduction

In December 2019, there were reports of the Coronavirus from the city of Wuhan, Hubei province, China.1 This virus has become a pandemic that has spread throughout the world until now.2 The name COVID-19 stands for coronavirus diseases 2019 or also known as SARS-CoV-2.3 The clinical manifestations of COVID-19 vary widely, ranging from asymptomatic/asymptomatic to very severe respiratory distress. Both the body's immune response, both the natural body's immune response and the adaptive body's immune response, play a very important role in the course of COVID-19.4 Most patients infected with SARS-CoV-2 show symptoms of the respiratory system such as fever, cough, sneezing, and shortness of breath. The most common symptoms are fever, dry cough, fatigue, and anosmia or ageusia. Other symptoms that can be found are productive cough, shortness of breath, sore throat, headache, myalgia/arthralgia, chills, nausea/vomiting, nasal congestion, diarrhea, abdominal pain, hemoptysis, and conjunctival congestion. A study concluded that more than 40% of fevers in COVID-19 patients had peak temperatures between 38.1-39°C, while 34% had fevers over 39°C.5,6

The course of the disease begins with an incubation period of about 3-14 days (median 5 days). At this time, leukocytes and lymphocytes are still normal or slightly decreased, and the patient is asymptomatic. In the next phase (early symptoms), the virus spreads through the bloodstream, presumably mainly in ACE-2-expressing tissues such as the lungs, gastrointestinal tract, and heart. Symptoms in this phase are generally mild. The second attack occurs four to seven days after the initial symptoms appear. At this time, the patient is still feverish and starting to have shortness of breath. The lesions in the lungs are getting worse. The lymphocytes are decreasing. Inflammatory markers begin to increase, and hypercoagulability begins to occur. If not resolved, the next phase of inflammation is increasingly uncontrolled. A cytokine storm occurs, which results in acute respiratory distress syndrome (ARDS), sepsis, and other complications.7,8

Management of asymptomatic COVID-19 confirmed patients

Individuals with confirmed asymptomatic COVID-19 are required to self-isolate at home for 10 days from specimen collection. Self-isolation can be done at home or in public facilities prepared by the government. Patients are monitored by telephone by first-level health facility officers (FKTP). Control at the nearest FKTP after 10 days of quarantine for clinical monitoring.9
Health workers provide education regarding self-isolation and the actions that need to be taken. Education for patients: always use a mask when leaving the room and when interacting with family members, wash your hands with running water and soap or hand sanitizer as often as possible, keep your distance from family (physical distancing), try to sleep alone/separately, apply cough etiquette (taught by medical personnel), eating and drinking utensils are immediately washed with water and soap, sunbathing for at least 10-15 minutes every day (before 9 am and after 3 pm), clothes that have been worn should be put in plastic bags/containers separated from other family's dirty clothes before washing and immediately put in the washing machine, measure and record body temperature 2 times a day (morning and night), immediately inform the monitoring officer/FKTP or family if there is an increase in body temperature > 38º C. Education for the environment/room: pay attention to ventilation, light and air, open the bedroom window regularly, if possible using a safety device protect yourself when cleaning the room (at least a mask, and if possible gloves and google, wash your hands with running water and soap or hand sanitizer as often as possible, clean the room every day, either with soapy water or other disinfectants. Education for families: family members who are in close contact with patients should check with the FKTP/Hospital. Family members always wear masks, keep a minimum distance of 1 meter from the patient, always wash their hands, do not touch the face area if you are not sure your hands are clean, remember always open the windows of the house so that air circulation is exchanged, clean as often as possible areas that may be touched by patients such as doorknobs and others.

If there are comorbidities, it is recommended to continue the Treatment that is routinely consumed. If the patient is routinely taking antihypertensive drug therapy with ACE inhibitors and angiotensin receptor blockers, it is necessary to consult an Internal Medicine Specialist or Cardiologist. Vitamin C (for 14 days), with a choice of non-acidic vitamin C tablets 500 mg/6-8 hours orally (for 14 days), lozenges 500 mg/12 hours orally (for 30 days), or a multivitamin containing vitamin C 1-2 tablets / 24 hours (for 30 days). The recommended multivitamin is a multivitamin that contains vitamins C, B, E, and zinc. Supportive medicines, both traditional (phytopharmaceuticals) and modern Indonesian medicines (OMAI), which are registered with BPOM, can be considered to be given but with due regard to the development of the patient's clinical condition. Drugs that have antioxidant properties can be given as supportive Treatment in COVID-19 patients.
Management of patients with confirmed mild COVID-19

Self-isolation at home/quarantine facilities for a maximum of 10 days from the onset of symptoms plus 3 days free of symptoms of fever and respiratory problems. Isolation can be done independently at home or in public facilities prepared by the government. FKTP officers are expected to be proactive in monitoring the patient's condition. After passing the isolation period, the patient will be controlled to the nearest FKTP. Education regarding what to do (same as asymptomatic education).  

Vitamin C with a choice of non-acidic vitamin C tablets 500 mg/6-8 hours orally (for 14 days), lozenges 500 mg/12 hours orally (for 30 days), multivitamins containing vitamin C 1-2 tablets/24 hours (for 30 days). It is recommended that the composition contains vitamins C, B, E, and zinc. Azithromycin is given at a dose of 1 x 500 mg per day for 5 days.

The antivirus given during the Treatment of mild COVID-19 can be one of the following: Oseltamivir (Tamiflu) 75 mg/12 hours/orally for 5-7 days or a combination of lopinavir + ritonavir (Aluvia) 2x 400 mg/100 mg for 10 days or Favipiravir (Avigan) 600 mg/12 hours/oral for 5 days. Chloroquine phosphate 500 mg/12 hours orally (for 5-7 days) or hydroxychloroquine (available in 200 mg) at a dose of 400 mg/24 hours/orally (for 5-7 days) may be considered if the patient is hospitalized and does not there are contraindications.

Symptomatic Treatment such as paracetamol, given if the fever. Supportive medicines, both traditional (Fitofarmaka) and original Indonesian modern medicines (OMAI), which are registered with BPOM, can be considered to be given but with due regard to the development of the patient's clinical condition.  

Management of patients with moderate COVID-19

Patients with moderate COVID-19 confirmed cases must be referred to a hospital (COVID-19 treatment room/emergency hospital). Patient management in the form of isolation in the COVID-19 treatment room/intensive care unit, total bed rest, adequate caloric intake, electrolyte control, monitoring hydration status, and fluid and oxygen therapy. Investigations can be done in the form of a complete peripheral blood examination, including a type count. If possible, additional evaluation should be carried out, plus regular CRP, kidney function, liver function, and chest X-ray examinations.

Pharmacological management of moderate COVID-19 patients in the form of vitamin C 200-400 mg/8 hours in 100 cc, 0.9% NaCl exhausted in 1 hour given intravenous drips (IV) during Treatment. Chloroquine phosphate 500 mg/12 hours orally (for 5-7 days) or
Hydroxychloroquine (available in 200 mg) given on the first day at 400 mg/12 hours/oral, then 400 mg/24 hours/oral (for 5-7 days). Azithromycin 500 mg/24 hours given intravenously or orally (for 5-7 days). Levofloxacin can be given as an alternative to antibiotics if a bacterial infection is suspected; a dose of 750 mg/24 hours iv or orally (for 5-7 days).13

One of the following antivirus; Oseltamivir 75 mg/12 hours orally for 5-7 days or a combination Lopinavir + Ritonavir (Aluvia) 2 x mg for 10 days or Favipiravir (Avigan 200 mg preparation) loading dose 1600 mg/12 hours/ orally on day 1 and then 2 x 600 mg (days 2-5) or Remdesivir 200 mg IV drip/3hours followed by 1x100 mg IV drip/3 hours for 9-13 days. LMWH/UFH anticoagulation was given based on the doctor's evaluation. Symptomatic Treatment can be given if there is fever (paracetamol).14

Management of patients confirmed with severe COVID-19

Treatment of severe COVID-19 patients in the form of isolation in the isolation room of a referral hospital or cohorting care, periodic swabs for PCR examination, complete rest, adequate calorie intake, electrolyte control, hydration status (fluid therapy), and oxygen. Complete laboratory monitoring of peripheral blood following with type count, if possible supplemented with CRP, renal function, liver function, hemostasis, LDH, and d-dimer. Serial chest X-ray examination if the patient's condition is getting worse.

Monitoring the patient in the form of tachypnea (respiratory rate 30x/min), oxygen saturation by pulse oximetry on the finger (SpO₂ 93%), PaO₂/ FiO₂ 300 mmHg, >50% increase in lung area involvement in the chest within 24-48 hours, progressive lymphopenia, progressive increase in CRP and progressive lactic acidosis.

Monitor critical conditions, namely respiratory failure requiring mechanical ventilation, shock, or multi-organ requiring ICU care. If respiratory failure is accompanied by ARDS, consider the use of a mechanical ventilator.

An important step in preventing disease exacerbation is the following: use of a high flow nasal cannula (HFNC) or non-invasive mechanical ventilation (NIV) in patients with ARDS or extensive pulmonary effusion. HFNC is preferred over NIV. Restriction of fluid resuscitation, especially in patients with pulmonary edema. Position the conscious patient in the prone position.

Oxygen therapy guidelines are in the form of NRM 15 liters per minute, then titrate according to SpO₂, HFNC (high flow nasal cannula), FiO₂ 100%, then titrate according to SpO₂, health workers must use a respirator (PAPR, N95). Give HFNC for 1 hour, then evaluate.
If the patient improves and meets the criteria for safe ventilation (ROX index $>4.88$ at 2, 6, and 12 hours indicates that the patient does not require invasive ventilation, while ROX $<3.85$ indicates a high risk for the need for intubation).

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\text{ROX Index} = \frac{\text{SpO}_2/ \text{FiO}_2}{\text{breath rate}}
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NIV (non-invasive ventilation) guidelines; health workers should wear a respirator (PAPR, N95). Administer NIV for 1 hour, then evaluate. Suppose the patient improves and meets the criteria for safe ventilation (tidal volume [VT] < 8 ml/kg, no symptoms of respiratory failure or an increase in FiO$_2$/ PEEP), then continue ventilation and reassess 2 hours later. In cases of severe ARDS, it is recommended for invasive ventilation not use NIV in patients with shock. Combination of awake prone position + HFNC / NIV 2 hours twice daily can improve oxygenation and reduce the need for intubation in mild to moderate ARDS. Avoid using this strategy in severe ARDS if the prone position is intended to delay or prevent intubation. NIV and HFNC have a risk of aerosol formation, so if they are to be applied, preferably in a negative pressure room (or in a room with normal pressure, but the patient is isolated from other patients) with complete PPE standards. If the patient still does not experience clinical improvement or oxygenation after oxygen therapy or non-invasive mechanical ventilation, further assessment should be carried out.$^{15,16}$

Invasive mechanical ventilation (Ventilator): the management of ventilator settings in COVID-19 is the same as the ARDS ventilator protocol where Tidal volume < 8 mL/kg, P plateau < 30 cmH$_2$O, PEEP titration and recruitment maneuver, and low target driving pressure.

ECMO (extracorporeal membrane oxygenation): COVID-19 patients can receive ECMO therapy in type A hospitals that have their own services and resources to perform ECMO. Critical COVID-19 patients can receive ECMO therapy if they meet ECMO indications after the patient has received therapy in the prone position (unless contraindicated) and maximal ARDS ventilator therapy, according to the clinician. ECMO indications are $\text{PaO}_2/\text{FiO}_2 < 60$ mmHg for $>6$ hours, $\text{PaO}_2/\text{FiO}_2 < 50$ mmHg for $>3$ hours, pH $< 7.20 + \text{Pa CO}_2 > 80$ mmHg for $>6$ hours. Relative contraindications of ECMO include age over 65 years, obesity with a BMI of 40, immunocompromised status, no valid informed consent permit, chronic systolic heart failure, and there are potentially reversible causes (pulmonary edema, bronchial mucus obstruction, abdominal compartment syndrome). Absolute contraindications: clinical frailty
scale category 3, mechanical ventilation > 10 days, presence of significant comorbid disease (grade III chronic kidney failure, liver cirrhosis, dementia, chronic neurological disease that does not allow rehabilitation, metastatic malignancy, end-stage lung disease, diabetes not controlled with chronic organ dysfunction, severe peripheral vascular disease). 

Conclusion

The management of COVID-19 focuses on isolation, improving the immune system, and treating comorbid patients.

References