

COVID-19: APPROACH TO DIAGNOSIS AND TREATMENT STRATEGY IN VIETNAM

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ABSTRACT

Introduction: the Coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to spread all over the world. This situation brings medical facilities into an emergency state and the huge need for medical staff in the diagnosis and treatment of infected patients. Therefore, it is necessary to standardize knowledges and therapeutics agents of hospitalized patients or field hospitals. The article was aimed to summarize the clinical progression, risk factors and treatment protocols for COVID-19 patients around the world and practical guidelines in Vietnam. These help new medical staff that update knowledges quickly. **Methods:** review the latest approaches and guidelines of the Vietnamese Ministry of Health on the diagnosis and treatment of Covid-19 patients. **Results:** we summarize specific treatment guidelines for Covid-19 patients into treatment protocols according to the level of severity. The regimen is being applied at medical facilities, field hospitals, and Covid-19 treatment hospitals in Vietnam. **Conclusion:** the strategy of COVID-19 treatment is monitoring and detecting cases with signs of severe progression and limiting mortalities. Management protocols according to the level of severity provides

standardized regimens and comprehensive information of COVID-19.

Keywords: SARS-CoV-2, Covid-19 management, antiviral drugs.

I. INTRODUCTION

During the fourth Sars-Cov-2 wave in Vietnam, the number of infected patients has increased dramatically. According to data from the Ministry of Health (MoH - Vietnam), until August 28th, the number of infections was 410,366 with 10,053 fatalities. This has been the largest outbreak since the beginning of the pandemic and the reported cases have gone up over time without any sign of stopping. The urgent situation has caused the national health system, particularly intensive care units, being overload. Almost all healthcare personnels, either with intensive care profession or not, have been immediately involved in the national battle. Hence, it is crucial to have a standardized multidisciplinary approach to manage COVID-19 patients. The MoH has published a management guideline so as to limit complications and reduce mortality.

II. CLINICAL PROGRESSION OF COVID-19 PATIENTS [1],[3],[5]

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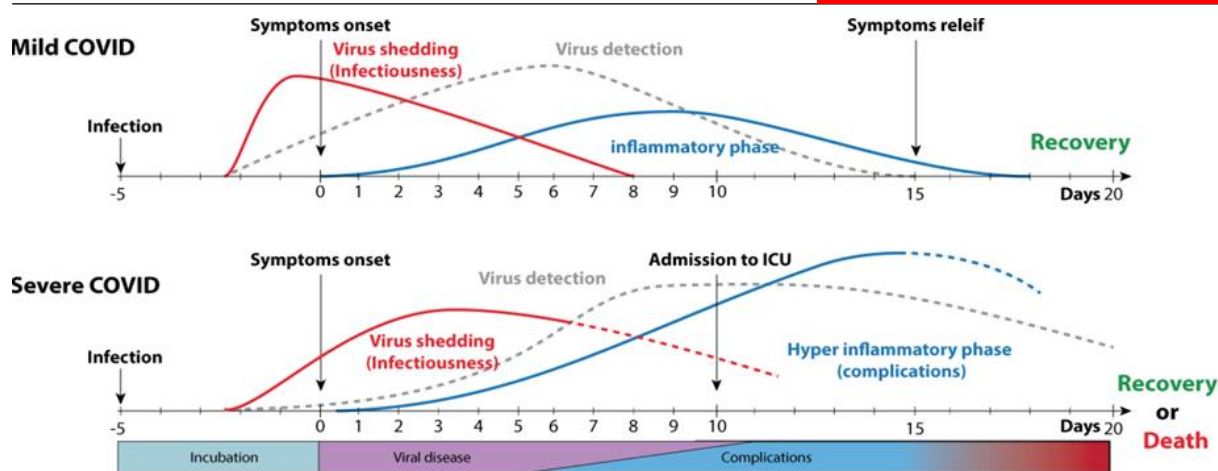
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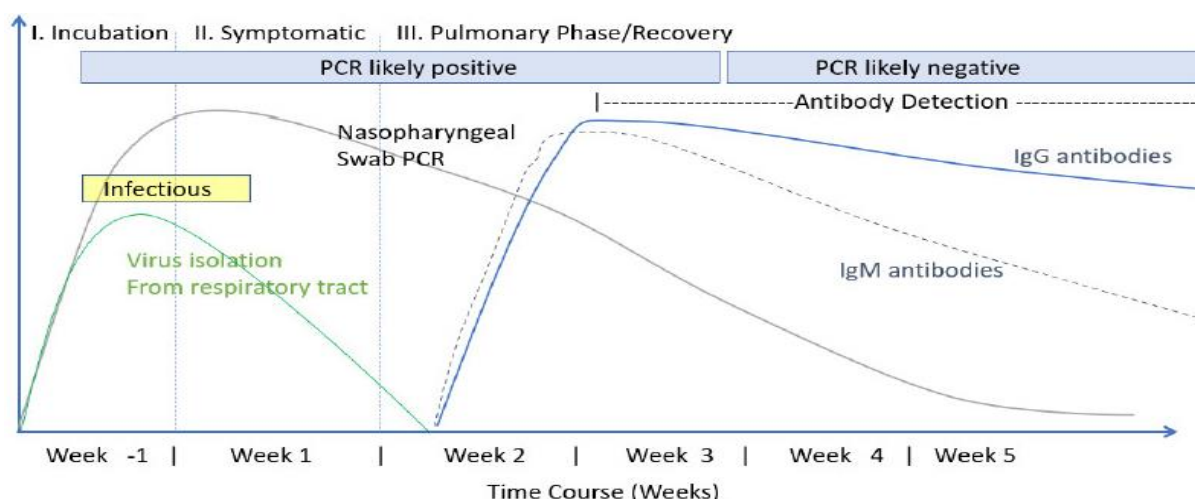


Picture 1: Clinical progression of covid-19 patients [1][3]

- Incubation period: usually lasts 2-5 days without symptoms.
- Symptomatic period: patients represent symptoms of fever, headache, muscular pain, sore throat ... and usually lasts for 1-2 weeks, this is the most contagious phase. During this time, the disease can get worse, especially in the second week. SARS-CoV is involved with the renin-angiotensin-aldosterone system (RAAS) through ACE2. When the virus enters the cell, this leads to the activation of the body immunity system

mediated by B cells and T cells. T helper cells are responsible for the release of cytokines and chemokines. The uncontrolled activation of inflammatory response could lead to cytokine storm syndrome and tend to create thrombosis. This causes to multi-organ dysfunction, most commonly affecting the lungs, heart, and kidneys, which can lead to death.

- Recovery period: symptoms improve and patients recover from the disease and creating antibody to protect body.



Picture 2: Recovery period [1],[3]

III. SEVERITY CLASSIFICATION AND RISK FACTORS

3.1. Severity staging [1],[2]

According to IDSA (2021), infected patients can be classified into 5 stages.

* Asymptomatic infection: positive SARS-CoV-2 Realtime PCR without any associated symptoms.

* Symptomatic infection:

- Mild: clinical symptoms of SARS-CoV-2 include fever, sore throat, fatigue, headache, myalgia or arthralgia, nausea, diarrhea, anosmia and ageusia which are similar to other virus infection. Patients at this stage do not present shortness of breath or abnormal pulmonary imaging.

- Moderate: lower respiratory tract infection symptoms are the dominant expressions with diffuse interstitial infiltration on chest x-ray. Although pulmonary damage is found, oxygen saturation level remains stable at least over 94% with room air.

- Severe: diffuse alveolar damage continues to develop which leads to increased respiratory rate up to more than 30 times per minute, SpO₂ < 90% with room air or PaO₂/FiO₂ ratio below 300 mmHg. Radiological findings in this stage represent diffuse ground-glass opacities affecting both lungs.

- Critical ill: as the disease progresses, acute respiratory distress syndrome, multiple organ failure and septic shock are the major fatal complications.

3.2. Risk factors associated with severe disease in infected patients [1],[3],[5]

- Diabetes melitus.
- Chronic obstructive pulmonary disease or other chronic lung disease.
- Cancer, especially malignant tumor of the lungs, leukemia, or metastatic tumor.
- Chronic kidney disease.
- Organ transplant or hematopoietic stem cell transplant.
- Obesity.
- Cardiovascular disease (heart failure, coronary artery disease, myocardial disease).
- Cerebrovascular disease
- Down syndrome.
- HIV/AIDS
- Neuropathy, including dementia.
- Sickle cell disease
- Asthma.
- Hypertension
- Immunocompromised disease.
- Liver disease
- Substance abuse disorders.
- Ongoing use of corticosteroids or other immunosuppressive drugs.
- Systemic disease.
- Unvaccinated individuals

IV. STEPWISE TREATMENT STRATEGY [2],[5],[6]

- Symptomatic treatment and improvement of physical condition.
- Early detection and treatment of complications.
- Follow closely the clinical progression.
- Manage underlying medical comorbidities.
- Infection control.

Plasma exchange	CRRT ± Cytokine blood filtration	Oxygen supplement		Immuno-therapy	Anti-biotics	Antithrombotic therapy			Anti-inflammatory	Antiviral therapy	Supplementary treatment
		General	Pregnant			Low dose	Moderate dose	High dose			
Consider combine with CRRT Exchange daily with high flow within consecutive 5 days Multi-organ failure (high SOFA scores) Severe ARDS Acute kidney damage	Cytokine storm syndrome (positive cytokine storm syndrome scoring system and invasive ventilation) Multi-organ failure (high SOFA scores) Severe ARDS Acute kidney damage	SpO ₂ > 90%	SpO ₂ > 94%	Positive cytokine storm syndrome scoring system <i>or</i> disease progresses rapidly.	Empirical anti-biotics if there is evidence of super-imposed infection.	BMI < 30: <i>Enoxaparin</i> 40mg subcutaneously once a day	BMI < 20: <i>Enoxaparin</i> 40mg subcutaneously once a day.	<i>Enoxaparin</i> 40 - 60 mg subcutaneously twice a day (1mg/kg per 12h)	<i>Dexamethasone</i> : 6mg once a day, and 10 – 12 mg per day if disease progresses. <i>Hydrocortisone</i> : 50mg x 3 per day or 100mg x 2 per day <i>Methylprednisolone</i> : 16mg x 2 per day <i>Prednisolone</i> : 40mg once a day Consider prescribe <i>Pulse Corticoid dose</i> in critical ill.	<i>Molnupiravir</i> : 200mg x 2 oral per day <i>Remdesivir</i> : loading dose of 200mg parenteral on the 1 st day and 100mg parenteral at least 5 consecutive days. Continue antiviral therapy if disease progresses.	Vitamin C: 500mg x 4 oral per day <i>Zinc</i> : 75 – 100mg oral per day <i>Rhino-throat rinse, comorbidities management.</i> Justify serum glucose level, maintain acid-base balance, homeostasis and nutrients. PPI addition if needed.
		1 st step: nasal oxygen 1-5L/m 2 nd step: non rebreather mask 10 – 15 L/m; 3 rd step: HFNC or NIV (non-invasive); 4 th step: intubation and invasive ventilation. 5 th step: ECMO				BMI ≥ 30: <i>Enoxaparin</i> 40mg subcutaneously twice a day <i>or</i> <i>Heparin</i> if CrCl <30 ml/min	BMI ≥ 20: <i>Enoxaparin</i> 40mg subcutaneously/12h (0.5mg/kg twice a day) <i>or</i> <i>Heparin</i> if CrCl <30 ml/min	MILD GRADE			
		MODERATE GRADE									
SEVERE GRADE											
CRITICAL GRADE											

Picture 3: Stepwise treatment strategy

4.1. Antiviral therapy [1]

* Oral antiviral drugs can be used according to the manufacturer's instructions with the approval of the MoH.

* Indications of Remdesivir: in hospitalized COVID-19 patients with the need for oxygen supplement, mechanical ventilation or ECMO, IDSA suggests the routine use of Remdesivir within 10 days since the onset of the disease.

- Consider to combine remdesivir and dexamethasone.

- Therapeutic treatment with remdesivir is prioritized in patients with risk factors, including patients older than 65 years old, underlying medical comorbidities or obesity.

* Dose:

- First day: 200mg IV within 30 - 120 minutes.

- Days after: 100mg IV in 2 - 5 days.

- In patients without any clinical improvement after a 5-day course, continue 100mg dose up to 10 days.

* Instructions: adding 19 mL of distilled water into 100 mg Remdesivir, then put the solution in 230 mL of normal saline, intravenous infusion in 30 - 120 mins.

* Contra-indications:

- Hypersensitivity reaction with any drug components.

- Impaired renal function with eGFR < 30 mL/min.

- Elevated alanine aminotransferase (ALT) 5 times above the upper limit.

- Severe multiple organ failure.

4.2. Anticoagulants [1],[2],[3]

In patients with lung damage (in chest xray or having respiratory rate more than 20 times per minute or rales findings), subcutaneous inject low molecular weight heparin immediately with therapeutic dose (2mg/kg per 24 hours) combined with Dexamethasone 6 mg per day.

4.3. Monoclonal antibodies [1],[3],[5]

These antibodies are under trials. The MoH has not approved their use in clinical practice. Several researches suggested:

- Tocilizumab: 8 mg/kg for patients weighed more than 30 kg or 12 mg/kg for those less than 30 kg, maximum dose is 800 mg, a repetitive dose after 8 hours can be used in case of no clinical improvements. Doses are adjusted according to liver transaminase.

- REGEN-COV: casirivimab 600mg and Imdevimab 600mg intravenous injection, one dose only.

4.4. Antibiotics [4]

- Empirical antibiotics are used if there is evidence for superimposed pulmonary infection.

- Empirical antibiotics:

- + Hospitalized patients not in ICUs: a quinolone with good efficacy in respiratory tract (moxifloxacin, gemifloxacin, levofloxacin) OR a anti-streptococcal beta-lactam (cefotaxime, ceftriaxone, ampicillin-sulbactam, ertapenem) plus a macrolide (azithromycin, clarithromycin, erythromycin).

- + Hospitalized patients in ICUs: a beta-lactam plus a macrolide OR a beta-lactam plus a quinolone OR a quinolone plus aztreonam (in those who have allergy with penicillin).

- Modify the appropriate antibiotics according to the microbiology results.

4.5. Follow [1]

- Vital signs, respiratory signs, alertness and complications.

- Early detect complications.

- For critical ill patients, following the A (airway), B (breathing), C (circulation), D (disability), E (Electrolyte), F (Fluid), G

(Gastrointestinal system), H (hematology), I (infection), K (kidney), L (liver), M (metabolism), N (nutrition) rule.

V. CONCLUSION

COVID-19 is a multiple-organ disease, which can lead to death. Up to now, there is still no specific therapy. Treatment mainly focuses on symptoms and complications. Therefore, strategy is to follow and early detect severe cases in order for on-time intervention and mortality reduction.

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