

COVID-19 Clinical Practice Guidelines

Hadhramout Initiative Against Corona Group (HIAC Group)

Abdulla A. Baradwan, Khalid H. Ba-Msahell, Iman A. Ba-Saddik, Ibrahim Albakri,
Hassan O. Batis, Ahmed Babiqai, Ahmed Al habshi, Shaker Bajaber, Ahmed M. Badheeb
(HIAC Clinical Scientific Committee)

Abstract

Hadhramout Initiative Against Corona (HIAC) formed a working group of clinicians relevant to the management of COVID-19 to formulate clinical practice guidelines (CPG) for clinicians caring for the patients infected with COVID-19 in Yemen.

The regional guidelines on the management of COVID-19 were thoroughly reviewed and its applicability was assessed for Yemen. HIAC's recommendations covered (2) sections: the first one is the diagnosis, including case definition, risk stratification of the affected cases, investigations (prioritization of reverse transcription-polymerase chain reaction (RT-PCR) testing, D-dimer, chest x-ray, and chest computed tomography, while the second part covers the treatments (mainly Favipiravir, Remdesivir, Hydroxychloroquine, and Glucocorticoid, Anticoagulants, and Supportive measures).

In conclusion, the adoption of cost-effective and evidence-based guidelines in Yemen will standardize the management of the patients infected with COVID-19 and protect both the patients and the health care workers from malpractice.

Keywords: COVID-19, SARS-CoV-2, HIAC Recommendation, Diagnosis, Treatment, Discharge Management.

Introduction

On March 11th, 2020, the World Health Organization (WHO) declared Coronavirus Disease 2019 (COVID-19) a pandemic. Given the current global public health threat and economic impact, it is of paramount importance to urgently move and work towards rapid diagnosis, therapeutic measures, and management on discharge.

In Yemen, the identification of public health risks and prioritization of resources are still uncertain, a few public hospitals and medical wards together with isolation units have been designated to receive patients. Fear is increasing among healthcare staff due to the lack of personal protective equipment and the massive shortage of equipment and medicines.

This article is presented as a possible cost-effective guideline designed for Yemen, aiming to standardize the management of the COVID-19 patients based on the best available evidence.

Definitions:**High-Risk Groups****Epidemiological criteria**

- Age more than 60 years
- Smoking
- Pregnancy
- Obesity with BMI > 40 and/or
- Comorbidities as Diabetes Mellitus, Hypertension, Cardiac disease, Chronic lung disease, Cerebrovascular disease, Chronic kidney disease, Chronic liver disease, Chronic endocrine diseases, Immunosuppression and Cancer

Clinical criteria

- Respiratory rate >24
- Heart rate >125b/m
- And or Saturation of peripheral oxygen (SpO₂ < 94% on room air

Laboratory criteria:

- D-Dimer > 1mg/L
- Creatinine Phosphokinase (CPK) more than > twice normal upper limit
- Elevated Troponin I and 0.4 ng/mL
- C-reactive protein (CRP) > 75mg/dL
- Lactic dehydrogenase (LDH) > 245 U/L
- Ferritin > 500 ug/L, and/or
- Admission absolute lymphocyte < 0.8 lymphocytes/mcL

Laboratory work-up

- COVID-19 Polymerase Chain Reaction (PCR)
- Chest X-ray as a baseline test
- Chest Computed tomography (CT) scan if indicated (suspicion of pulmonary embolism (PE), worsening in patient's condition and unclear diagnosis from CXR and PCR)
- Complete Blood Count (CBC), Urea, Creatinine, Liver function test (LFTs), Electrolytes, CRP, and LDH initially.
- And Ferritin and D-Dimer if available and accessible.
- Electrocardiogram (ECG): should be done as a baseline for severe and critical patients and if the treating physician suspects ischemia or arrhythmias.
- Malaria, Dengue, and Chikungunya are endemic infectious diseases that should be tested and treated per routine protocols. Co-infection with COVID-19 may occur.

Management

Suspected patients

❖ Mild to Moderate Symptomatic patient:

- Strict Home isolation for 10 days after onset of symptoms, plus at least 3 days without symptoms (fever and respiratory symptoms).
- High-risk group patients should be monitored closely and may require hospitalization due to the risk of rapid clinical deterioration.
- Adequate nutrition and appropriate hydration.
- Symptomatic treatment: Paracetamol is the preferred antipyretic agent for fever and pain.
- Azithromycin can be used as an immune-modulatory agent for only 5 days duration.
- Other Antibiotics are not recommended for therapy or prophylaxis in patients with mild or moderate COVID-19 unless there is a clinical suspicion of a bacterial infection.

PCR Confirmed Cases

Asymptomatic patient

Individuals who test positive for SARS-CoV-2 by using a molecular diagnostic test (e.g. polymerase chain reaction) or antigen test, but have no symptoms.

- Strict Home isolation for 10 days after a proven positive test.
- Adequate Nutrition and Appropriate Hydration.
- No need for specific treatment.

Mild to Moderate infected patient

Patient with any of the various symptoms and signs of COVID 19 but without dyspnea and SpO₂ ≥ 94% on room air at sea level but does not require O₂ supplementation.

Symptomatic meeting the case definition for COVID-19, but do not require O₂ supplementation.

- Strict home isolation for 10 days after symptom onset, plus at least 3 days without fever and respiratory symptoms.
- Unless High-risk group patients should be monitored closely and may require hospitalization due to the risk of rapid clinical deterioration.
- Adequate Nutrition and Appropriate Hydration.
- Symptomatic treatment:
 - **Paracetamol** is the preferred antipyretic agent for fever and pain (
 - **Azithromycin** is used as an immune-modulatory agent for only 5 days duration.
 - Other **Antibiotics** are not recommended as therapy or prophylaxis for patients with mild or moderate COVID-19 unless there is clinical suspicion of bacterial infection.

Severely infected patients

- Symptomatic patient meeting the case definition for COVID-19, with ≥ 1 of the following signs: Respiratory rate $\geq 30/\text{min}$ (adults), $\geq 40/\text{min}$ (children < 5 years), Oxygen saturation 'SpO₂' $< 94\%$, Partial pressure of oxygen/Fraction of inspired oxygen (PaO₂/FiO₂) ratio < 300 mmHg and/or Lung infiltrates $> 50\%$ and requires O₂ supplementation.
- Strict Hospital Isolation and decision for Intensive Care Unit (ICU) admission taken by ICU team.
- **Oxygen supplementation** either by nasal prong, face mask, venturi mask, or face mask with reservoir bag to reach target SpO₂ $\geq 94\%$. Once the patient is stable, target 'SpO₂' is $> 90\%$; while in pregnant women target oxygen saturation is $\geq 92 - 95\%$.
- Consider an awake **prone position** for a spontaneously breathing patient.
- Adequate **Nutrition** and **Appropriate Hydration**.
- Early patient mobilization.
- **Symptomatic treatment: Paracetamol** is the preferred antipyretic agent for fever and pain (Adjust the dose in patients with hepatic impairment).
- **Corticosteroids:** Should be used for all patients who require oxygen supplementation for 10 days duration. Monitor and treat hyperglycemia, hypernatremia, and hypokalemia if corticosteroids are prescribed.

Different corticosteroid forms are available:

- **Dexamethasone:** 6 mg once daily oral or IV preparation
- **Methylprednisolone sodium succinate** 0.8mg IV once daily
- **Hydrocortisone:** Adult Dose: 80 mg IV twice daily
 Preterm dose: with a corrected GA > 40 weeks 0.5mg/kg every 12 hours
 Infant dose: 1-2 mg/kg/day
 Children under 12 years dose: 1 -5 mg/kg/day
- **Prednisolone:** Adult Dose: 40 mg PO twice daily
 Pediatric Dose: 1 mg/kg once daily (max: 40 mg)
- **Antibiotics:** Empirical use of antimicrobials are discouraged. Antibiotics are used if there is an indication. Selection of antibiotics will be based on the type of infection, severity and suspected organisms that cause the infection.
- Consider antiviral '**Remdesivir**' (once available) in the first 10 days of symptoms
 - Adult Dose: 200 mg loading (IV within 30 min), followed by 100 mg once daily for 5 days in a non-mechanically ventilated patient and extend to 10 days in the mechanically ventilated patient.
 - Pediatric dose: $< 40\text{kg}$: 5 mg/kg IV load, then 2.5 mg/kg q24h for 5 to 10 days.
 $\geq 40\text{kg}$: 200 mg IV load, then 100 mg IV q24h for 5 to 10 days.

Critical patients

Patients who have respiratory failure, ARDS, Septic shock, and Multi-organ failure with Altered Conscious level and/or High Risk for Cytokine Release Syndrome.

- Strict Hospital Isolation and ICU admission and management by ICU team.
- Oxygen supplementation either by Non-rebreather mask (NRFM)/ High-flow nasal cannula (HFNO), Non-invasive ventilation (NIV), invasive ventilation or Extracorporeal membrane oxygenation (ECMO) according to patient condition to reach target SpO₂ ≥ 94%. Once the patient is stable, target 'SpO₂' is > 90%; while in pregnant women target oxygen, saturation is ≥ 92-95%.
- Consider a prone position for 12-16 hours if there is no contraindication.
- Adequate Nutrition and Appropriate Hydration.
- Early patient mobilization.
- **Symptomatic treatment: Paracetamol** is the preferred antipyretic agent for fever and pain (Adjust the dose in patients with hepatic impairment).
- **Corticosteroids:** Should be used for all patients who require oxygen supplementation Monitor and treat hyperglycemia, hypernatremia, and hypokalemia if corticosteroids are prescribed. Patients on chronic steroids, follow the usual recommendation of doubling steroids dose.

Different corticosteroid forms are available:

- **Dexamethasone:** 6 mg once daily oral or IV preparation
- **Methylprednisolone sodium succinate (IV):** 0.8mg/kg
- **Hydrocortisone:** Adult Dose: 80 mg IV twice daily
 - Preterm dose: with a corrected GA > 40 weeks 0.5mg/kg every 12 hours
 - Infant dose: 1-2 mg/kg/day
 - Children under 12 years dose: 1 -5 mg/kg/day
- **Prednisolone:** Adult Dose: 40 mg PO twice daily
 - Pediatric Dose: 1 mg/kg once daily (max: 40 mg)
- **Antibiotics:** start empirical antibiotics if secondary infection is suspected.
- Antimicrobial selection will depend upon the assessment of the treating physician and type of infection and epidemiology of each institute.
- Consider the use of **Vancomycin** 15 mg/kg every 12 h, adjust in renal impairment patient if the patient shows:
 1. Prior respiratory sample culture isolation revealing Methicillin-resistant *Staphylococcus aureus* (MRSA).
 2. Recent use of IV parenteral antibiotics (in the last 90 days).
 3. The hemodynamically unstable patient, who shows no response to empirical antibiotics within 48 hours.

- Consider antiviral '**Remdesivir**' (once available) in the first 10 days of symptoms
 - Adult Dose: 200 mg loading (IV within 30 min), followed by 100 mg once daily for 5 Days in non-mechanically ventilated patients and extend to 10 days in mechanically ventilated patients.
 - Pediatric dose: < 40kg: 5 mg/kg IV load, then 2.5 mg/kg q24h for 5 to 10 days
 ≥ 40kg: 200 mg IV load, then 100 mg IV q24h for 5 to 10 days.
- Consider starting Favipiravir for mild-moderate cases
 - Adult Dosing: 1800 mg/dose twice a day on the first day; followed by 800 mg/dose twice a day for 7-10 days
- Consider **Tocilizumab** 'IL6' if cytokine release syndrome is suspected or confirmed (once available).
- **Criteria for using Tocilizumab.**
 - CRP > 75
 - SPO2 < 92%
 - Within 48 hours from ICU admission
 - Rapid respiratory deterioration
- Avoid in patients with active (bacterial infection, tuberculosis, and hepatitis).
 - Adult Dose: Single-dose 4-8 mg/kg (usual dose 400 mg; maximum 800 mg) by IV infusion; repeated within 24 hours for 2 maximum doses.
 - Pediatric Dose (<18 years): < 30 kg; 12 mg/kg repeated within 12 hours for 2 maximum doses and ≥ 30 kg; 8 mg/kg (max: 800 mg/dose) repeated within 24 hours for maximum of 2 doses.

Criteria for high-risk patients at risk for developing cytokine storm: 1 or more of the following:

- Serum IL-6 ≥ 3 x upper normal limit
- Ferritin > 300ug/L with double the level within 24 hours.
- Ferritin > 600ug/L at presentation and LDH > 250.
- Elevated D-dimer (>1 mcg/mL).

Do not stop Angiotensin-converting enzyme inhibitors/Angiotensin receptor blockers ACEI/ARBs or aspirin in a patient who is already on its use

Anticoagulant:

Thromboprophylaxis Recommendations:

- All admitted patients should be evaluated upon admission, and daily thereafter for both risks of thrombosis and bleeding.
- Laboratory evaluation and monitoring: Baseline CBC, PT, aPTT on admission" and CBC should be done serially twice weekly.

- If the patient is on heparin infusion, then it is advised to do aPTT according to the given protocol.
- Direct oral anticoagulant (DOAC) is an alternative therapy for patients who do not prefer to use injections, especially those who are treated on an outpatient basis.
- Antiplatelet medications are not recommended to be used as prophylaxis.
- Thromboprophylaxis should be continued until the time of discharge or if the patient becomes asymptomatic.
- Patients with Heparin-induced thrombocytopenia (HIT), please follow HIT standard institutional protocol for alternative anticoagulation.
- D- Dimer is not currently available in Hadhramout public governorate hospitals and with quite an expensive cost price of the test in private health care centers; thus the following advice is adopted to be undertaken locally.
- D- Dimer is not recommended as a mandatory test.
- Enoxaparin is used in patients with moderate COVID-19 pneumonia with high risk and immobile should use prophylaxis dose once daily.
- Enoxaparin used in patients with severe and critical COVID-19 pneumonia should use therapeutic dose twice daily.
 - **Enoxaparin Dose**
 Prophylaxis: 1mg/kg once daily.
 Therapeutic: 1mg/kg twice daily.
 The dose should be an adjustment on the infected patients with renal impairment.

Venous Thromboembolic Risk factors

- Altered Mobility
- Active cancer (receiving chemotherapy/radiation in previous 6 months)
- Burns: > 50% total body surface area
- Severe dehydration
- Severe systemic infection
- Inflammatory disorders
- Known acquired or inherited thrombophilia
- Obesity (BMI \geq 95 percentile)
- Protein-losing disorders
- Sickle Cell Disease
- Previous history of clots (DVT/PE)
- Family history of VTE in 1st-degree relative < 40 years old.

When to Consult Hematologist?

- Heparin-induced thrombocytopenia (HIT)
- Platelets below $50 \times 10^9/L$
- Unexplained bleeding

- Inherited bleeding disorder (Hemophilia, thrombasthenia), Inherited red blood disorder (sickle cell disease)
- Previously on anticoagulation therapy
- Radiological evidence of thrombosis.

Contraindication:

- Intracranial hemorrhage,
- Ongoing and uncontrolled bleeding /hematoma,
- Congenital bleeding disorder and
- Uncorrected coagulopathy: INR >1.5, APTT >44 seconds, Fibrinogen <100g/dl, or Platelet < 50000/microliter.

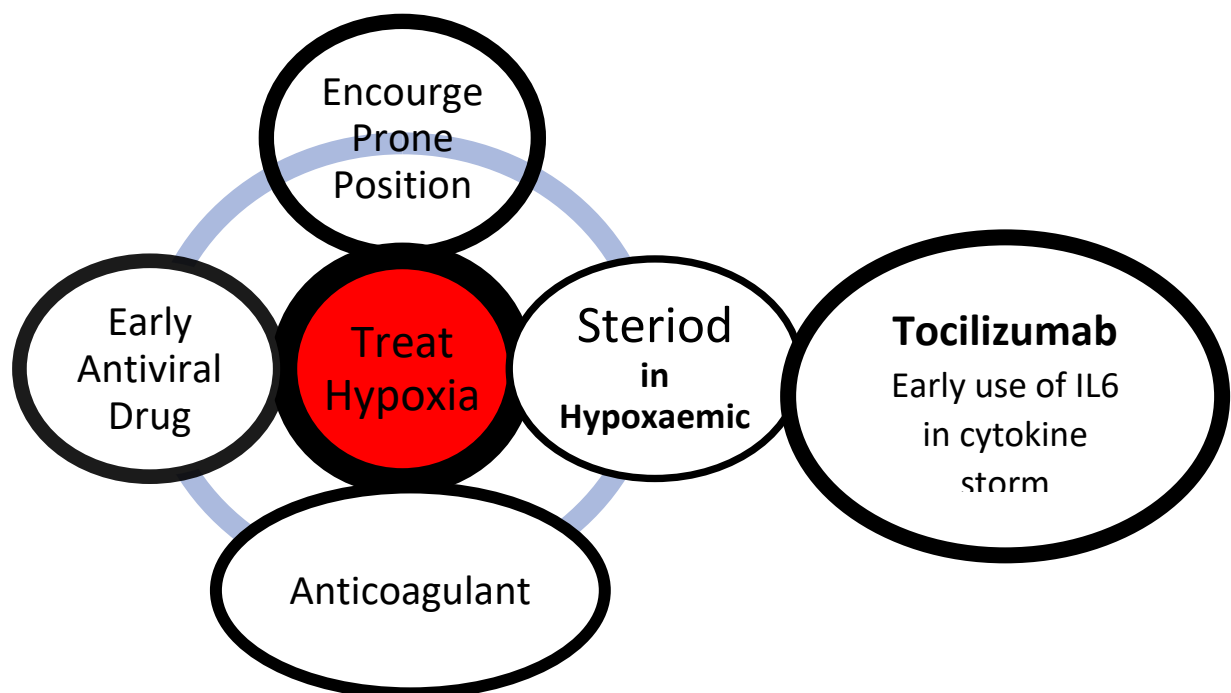


Figure1. Management Survival Chain in Severe and Critical COVID 19 Pneumonia

Discussion

The first case of COVID-19 in Yemen was declared in Hadramout governorate on 10 April 2020. Soon after, the Ministry of Public Health and Population began active search and contact tracing in all territories. COVID-19 isolation units were established with at least one in each governorate. The number of these units continues to expand as the number of patients infected with COVID-19 increases. All units have been supported by WHO with COVID-19 essential supplies and

equipment such as intensive care unit beds, oxygen, ventilators, personal protective equipment, essential medicines, laboratory supplies, and reagents.

In response to the above gaps, HIAC deployed a technical team to support the local health authority to enhance the clinical management practices in the country. Several virtual scientific meetings were held for physicians working in isolation units taking care of COVID-19 patients as well as on infection prevention and control measures. The trainees work at different departments, including intensive care units and emergency and internal medicine departments in all designated locations of the southern governorates. The discussion was based on regional and international CPGs and recommendations, as well as preparing for the discussion of the readiness for the different waves of the pandemic.

Challenges remain in the areas of surveillance, laboratory testing, reporting, community engagement, and case management, due to a long-standing conflict in the country. After 3 months of the weekly meetings, the group ended up with this protocol for the COVID-19, which will be submitted to the national COVID-19 task force before disseminating this CPGs to all health care workers.

Conclusions

HIAC guidelines are following the current evidence and cost-effective management to improve the outcome of Covid's victims, so as to safeguard and protect health in low-income countries.

Acknowledgments

The authors acknowledge Dr. Omer S. Alkhnbashi and Eng. Ahmed Ali Ahmed Bahashwan for their technical support for the completion of this work.

References:

1. WHO missions supporting Yemen to fight COVID-19. (2021). Accessed: 3/24/2021: <http://www.emro.who.int/pandemic-epidemicdiseases/news/who-missions-supporting-yemen-to-fight-covid-19.html>.
2. Dureab F, Al-Awlaqi S, Jahn A.: COVID-19 in Yemen: preparedness measures in a fragile state. Lancet Public Health. 2020;5(6):e311. . 10.1016/S24682667(20)30101-8
3. Hadhramout Initiative against Covid-19 (HIAC). (2020). Accessed: 3/25/2021: https://www.youtube.com/channel/UCJ4eT8pag_tuBSuRnKGyL BA.

4. Chemoprophylaxis, diagnosis, treatments, and discharge management of COVID-19: An evidence-based clinical practice guideline (updated version). *Mil Med Res.* 2020; 7: 41.. 2020, 10.1186/s40779-020-00270-8
5. COVID-19 Guidelines in Saudi Arabia.
<https://www.moh.gov.sa/en/Ministry/MediaCenter/Publications/Pages/covid19.aspx>.
6. WHO COVID-19 Case definition. (2021). Accessed: 3/25/2021:
https://www.who.int/publications/i/item/WHO-2019-nCoVSurveillance_Case_Definition-2020.2.
7. Clinical management of COVID-19. Geneva: World Health Organization; Interim guidance; 27 May 2020.
8. Egyptian Ministry of Health and population; management protocol for COVID-19 patients (diagnosis and treatment), Version 1.4; 30 May, 2020. . (2021). Accessed: 3/25/2021:
https://www.researchgate.net/publication/344078546_Management_Protocol_for_COVID-19_Patients_Version_1430th_May_2020_....
9. National Institutes of Health COVID-19 Treatment Guidelines. (2020). Accessed: 3/25/2021: <https://www.covid19treatmentguidelines.nih.gov/>.
10. Clinical care for severe acute respiratory infection: toolkit: COVID-19 adaptation. (2021). Accessed: 3/25/2021: <https://apps.who.int/iris/handle/10665/331736>.