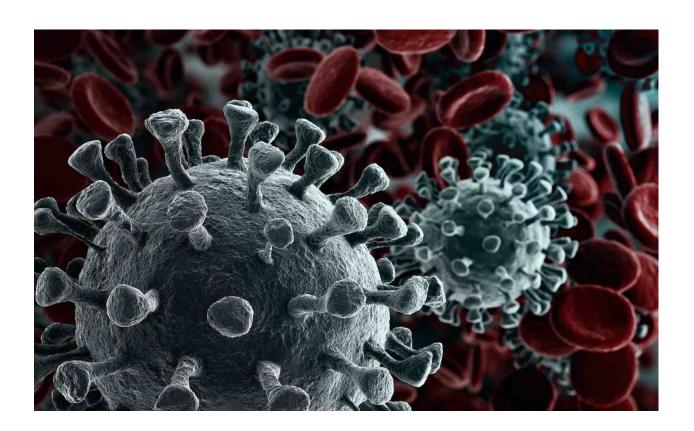


# COVID-19 Management Guidelines



**Message by President Pakistan Chest Society** 

Pandemic of Coronavirus disease 2019 (COVID-19) has grasped the world

including Pakistan. As the virus is new and the dynamic of human involvement is

not known so it is difficult to design strategy to overcome this threat. The country

is trying to follow the path of prevention (lockdown, physical but not social

distancing, hand washing, droplet and contact precautions etc) but at the same

time we need to devise concentrated efforts to treat the disease/infection.

Pakistan Chest Society (PCS) decided to take meaningful steps in this scenario and

the PCS guideline committee voluntarily took the lead. I would like to

congratulate PCS guideline committee for developing this guideline on "COVID-

19".

The guideline was prepared on war footing basis and the committee was able to

bring this guideline in just one week time. I appreciate the sincere efforts done by

each member.

I am hopeful that this concise guideline will be of great help and ready reference

for health care professionals involved in the management of such patients. It will

also be useful for under & postgraduate students and the nursing staff.

PROFESSOR. DR. NISAR AHMED RAO

President,

**Pakistan Chest Society** 

28 March 2020

1

# Guidelines on Management of Patients with COVID-19 March 2020

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## **Preface**

There have been various epidemics in different regions of the world during different time frames. Many were confined to specified regions like Dengue outbreak in Pakistan (2011), Yellow fever outbreak in Sudan (2012), Ebola virus epidemic in West Africa (2013-16), and 2019 measles outbreak in the Democratic Republic of the Congo. The world has also witnessed deadly pandemics like Spanish flu (1918–1920), Asian flu (Influenza A virus subtype H2N2) in 1957–1958, Seventh cholera pandemic (Cholera (El Tor strain) in 1961–1975, Swine flu pandemic (H1N1) in 2009, Middle East respiratory syndrome coronavirus outbreak during 2012 and the current ongoing 2019–2020 coronavirus pandemic (Covid-19).

This is an unprecedented global war, and the entire mankind is fighting against the same enemy identified as SARS CoV-2. This war commenced in December 2019 from Wuhan (China), and was declared a pandemic in March 2020 by the WHO. Every physician and epidemiologist is staring at the same question — how and when is will be eradicated from the world? It seems to be the beginning of the end or perhaps the end of the beginning in China, while in other regions like the USA and Europe and eventually Asia, the pandemic seems to be a harbinger of disaster.

The entire world was naïve about this novel disease's manifestations, complications, evaluation and management. Isolation, diagnosis, treatment, protective measures, and rehabilitation have all been implemented from scratch. This globally detrimental phenomenon has paved way towards the notion of joining heads and coming up with strategies to help the ailing humanity. At this moment, sharing success experiences and lessons, resources, and knowing what to avoid and what to adopt regardless of who you are, seems to be our only chance of winning this battle. The battle for which the health care facilities are battle fields and health care workers are soldiers. The remedy for this pandemic is not isolation, but cooperation.

This timely written guideline is a quick review for the pulmonary, medical, critical care and related specialties that are evaluating and providing care to suspected or confirmed COVID-19 patients. We strongly pray to Allah and looking forward to see an earlier end to this deadly pandemic from our homeland as well as the entire world.

Very sincerely,

Professor Talha Mahmud
On behalf of PCS Guidelines Working Group

## **Contents**

Message by president PCS	
PCS guidelines working group	2
Preface	
Contents	4
Dedication	5
Introduction	6
Definitions (WHO)	
Suspect Case	6
Confirmed Case	7
Contact	7
Clinical features of COVID-19	
Incubation period	
Spectrum of disease severity	
Frequently occurring presenting symptoms	7
Less common symptoms	
Disease categories: mild, moderate, severe and critically ill	8
Epidemiological risk factors for severity of disease	
Diagnosis of COVID-19	
Complete Blood Count (CBC)	
Serum biochemistry & inflammatory markers	
SARS-CoV-2 RNA detection by RT-PCR	
Serological testing	
Radiology (CXR & CT)	
Thoracic ultrasound	11
Electrocardiogram & echocardiography	12
Management of confirmed COVID-19 patients	-
Treatment guide for critically ill patients with covid-19	
Special considerations	
For intubation	
For bronchoscopy	
Noninvasive ventilation (NIV: BPAP and CPAP) and Hi-flow Nasal Cannula (HFNC)	
Bronchodilators	
Discharge Criteria	
Prevention in health care settings	
Regular hand washing	
PPE use in different clinical areas	
References	17, 18
Appendix	•
Advantages & disadvantages of various diagnostic interventions	20
Suggested reading	21

# Dedicated

to the Martyrdom of

## Dr. Osama Riaz



in the line of duty (Rest in Peace)

## Introduction

In December 2019, several cases of pneumonia due to some unknown pathogen were on the rise in Wuhan city, Hubei province of China. It was not till 31<sup>st</sup> of December 2019 that health authorities in China reported these cases to be investigated further. By this time a number of patients had become victim of severe illness. Soon a viral RNA was detected from bronchoalveolar lavage samples of some of the patients. The genome was sequenced and it was found to be closely related to SARS corona virus. The cases so far detected were linked to a seafood market and was thought to be a zoonotic, which could not be confirmed yet.

The disease was named by WHO as COVID-19 caused by SARS-CoV-2. It had started as a single patient on December 1, 2019, then increased rapidly, initially in China, thereafter affecting other countries particularly Iran, Italy, Spain and USA. WHO declared it as a worldwide pandemic on March 11, 2020. Pakistan was not exempted from this pandemic. Till date this potentially deadly virus has infected more than 595,000 people worldwide, and 1400 plus cases are already been reported from Pakistan.

The disease has variable clinical presentation. It can range from mild flu like symptoms to ARDS and sepsis. Mortality is more often reported in elderly population and those with comorbidities. In this situation Pakistan Chest Society is documenting the guidelines for diagnosis and treatment of the disease. Although we are still learning about the disease, Pakistan Chest Society (PCS) is playing its part in current situation.

## **Definitions (WHO):**

## **Suspect Case:**

- 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 location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset; OR
- A patient 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
- 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 suspect case for whom testing for the COVID-19 virus is inconclusive. OR
- A suspect case for whom testing could not be performed for any reason.

## **Confirmed Case:**

• A person with lab confirmation of COVID-19 infection irrespective of clinical signs and symptoms.

#### **Contact:**

A contact is a person who experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:

- 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 equipment; 2OR
- 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.

## **Clinical Features of COVID-19:**

## **Incubation Period:**

Incubation period varies from 1 to 14 days after exposure with most of the patient experiences symptoms on 5<sup>th</sup>day. In small number of patients, it can be longer than 14 days.

## **Spectrum of Disease Severity:**

Clinical Spectrum of disease ranges from asymptomatic to mild symptoms such as cough, fever, myalgias to pneumonia, acute respiratory distress syndrome, and sepsis with septic shock to multiorgan failure. Most of the cases are self-limiting (80%), however, elderly and patients with comorbidities tend to have more severe disease.

### Frequently occurring presenting symptoms are:

•	Fever > 100F	44-98%
•	Dry Cough (new or worsening)	46- 82%
•	Shortness of breath (new or worsening)	14-31%
•	Myalgia or Fatigue	11-52%

### Less common symptoms are:

- Sputum production
- Headache
- Sore throat
- Hemoptysis
- Rhinorrhoea

Gastrointestinal symptoms such as nausea & diarrhea may be seen in some as presenting symptoms. Anosmia (loss of smell) is being reported in some cohorts as a presenting symptom occurring even before any other clinical feature, although it has yet to be confirmed.

## Disease can be categorized into mild, moderate, severe and critically ill for appropriate management:

#### Mild Disease:

These patients usually present with symptoms of:

- An upper respiratory tract viral infection or
- Low grade fever, cough, malaise, rhinorrhea, sore throat without any warning signs and non immunocompromised.

#### **Moderate Disease:**

- Shortness of breath with respiratory rate > 25
- High grade fever > 100°F
- Hemoptysis (may be)
- Gastro-intestinal symptoms: nausea, vomiting, diarrhea
- Without change in mental status (i.e. confusion, lethargy)
- With or without comorbidities and chest radiograph suggestive of pneumonia

### **Severe Disease:**

- Respiratory rate > 30/min
- qSOFA score 2 or more
- SPO<sub>2</sub>  $\leq$  93%
- PaO<sub>2</sub>/FiO<sub>2</sub> <300</li>
- Confusion, agitation, restlessness
- Bilateral lung infiltrates >50% within 24- 48 hours

### **Critically ill:**

- Respiratory failure (need of mechanical ventilation)/ARDS
- Septic shock
- Multiorgan dysfunction syndrome (MODS)

## **Epidemiological risk factors for severity of disease:**

- Older Age
- Male gender
- Cancer
- Chronic pulmonary diseases
- Cardiovascular disease
- Chronic kidney disease
- Diabetes mellitus

## **Diagnosis of COVID-19:**

After initial evaluation of patients who meet the criteria for **suspect cases**, (see case definitions, clinical features and triage section) and taking decision for home care and quarantine versus hospitalization, in terms of isolation room/bay or ICU admission, the following diagnostic interventions should be considered:

## 1. Complete Blood Count (CBC):

- Leukopenia, leukocytosis, and lymphopenia (most common) can be seen.
- Hemoglobin and platelets count is mostly preserved.
- Thrombocytopenia and severe lymphopenia have been associated with mortality.

## 2. Serum Biochemistry & Inflammatory Markers:

- Elevated lactate dehydrogenase (LDH) and ferritin levels are common.
- Deranged LFTs (elevated aminotransferase levels) have also been described.
- Deranged renal functions (raised serum urea and creatinine levels, and altered electrolytes) are associated with acute kidney injury and are reflective of severe disease.
- **CRP** levels mirrors disease severity as are serum **procalcitonin** levels which may be normal at the time of hospitalization and are more likely to be elevated in subjects requiring critical care admission.
- High **D-dimer levels** (>1 mcg/mL), elevated troponin and elevated creatine phosphokinase have been associated with higher mortality.
- Coagulopathy (elevated prothrombin time), acidosis, raised lactate and hyperbilirubinaemia may be seen in life threatening cases associated with multiorgan dysfunction.

## 3. SARS-CoV-2 RNA detection by reverse-transcription polymerase chain reaction (RT-PCR): Can be done in any of the following respiratory specimens:

- a) Nasopharyngeal swab specimen (preferable as viral RNA levels may be higher in nasal compared with oral specimens).
- b) Oropharyngeal swab can be collected but is not essential; if collected, it should be placed in the same container as the nasopharyngeal specimen.
- c) Sputum collected only from patients with productive cough.
- d) Tracheal aspirate/bronchial washings/bronchoalveolar lavage: Can be evaluated from patients who are admitted in critical care and require intubation. Specimen can also be utilized to diagnose concomitant infection by other viruses/bacteria/fungi.

A positive RT-PCR test for SARS-CoV-2 confirms the diagnosis of COVID-19 although false-positive and false negative tests are possible. If initial testing is negative but the suspicion for

COVID-19 is high, it is recommended to resample and analyze specimen from multiple respiratory tract sites as above. Negative RT-PCR tests on oropharyngeal swabs despite CT findings suggestive of viral pneumonia have been reported in some patients who later on tested positive for SARS-CoV-2 PCR. The accuracy and predictive values of SARS-CoV-2 testing have not been systematically evaluated. In a recent study of 205 patients with COVID-19 who were sampled at various sites, the highest rates of positive viral RNA tests were reported from BAL (95%) and sputum (72%), compared with oropharyngeal swab (32%). So sputum specimen should be preferred to nasopharyngeal/oropharyngeal swab if patient is actively producing it but should be collected with caution.

Sputum induction is not recommended and droplet/aerosol and contact precautions must be followed when collecting respiratory specimen from suspected COVID-19 case. Ideally, all respiratory specimen collection procedures should be conducted in negative pressure room if available. For safety reasons, specimens from a patient with suspected or confirmed COVID-19 should **not** be submitted for viral culture.

## 4. Serological Testing:

The role of serology is currently unclear and once recommended and generally available, should be able to identify patients who have either current or previous infection but a negative RT-PCR testing. Large-scale serologic screening in near future may be able to provide a better sense of the scope of asymptomatic infections and inform epidemiologic analysis. In a recent Chinese study, the host humoral response against SARS-CoV-2 including IgA, IgM and IgG response were examined by using an ELISA based assay on the recombinant viral nucleocapsid protein. In confirmed and probable cases, the positive rates of IgM antibodies were 75.6% and 93.1%, respectively.

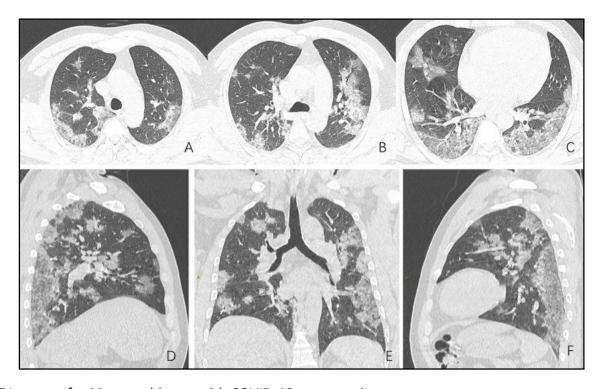
**COVID-19 rapid test kits** are also becoming available that qualitatively detects IgG and IgM antibodies (lateral flow immuno-chromatography) to SARS-CoV-2 in blood samples. Currently, there is no definitive evidence regarding the utility of rapid diagnostic kits.

## 5. Radiology:

**Chest radiograph** is usually the first radiological investigation. It may be normal in initial phases. It mostly reveals bilateral lung infiltrates and consolidation.

Chest CT, low dose non-contrast, may be helpful in making the diagnosis/follow-up and can also reveal presence of complications like ARDS and pleural effusions. No finding can completely rule in or rule out the possibility of COVID-19 pneumonia. Typical chest CT scans most commonly demonstrate ground-glass opacification with or without consolidative abnormalities, consistent with viral pneumonia. The abnormalities tend to be bilateral, exhibit a peripheral distribution, and predominantly may involve the lower lobes (see CT images below). Uncommon findings include pleural effusion and/or thickening, and mediastinal

lymphadenopathy. A "positive" chest CT for COVID-19 carries a sensitivity of 97 percent (using the RT-PCR tests as a reference standard) and specificity is around 25 percent as other etiologies may result in similar radiological findings. Timings of occurrence of radiological abnormalities may be variable; in some patients most severe abnormalities were detected approximately 10 days after symptom onset and in some with minimal respiratory symptoms and even prior to the detection of viral RNA from upper respiratory specimens and the CT findings can be categorized reflective of the disease stage. The provision of dedicated scanner and infection control protocols has to be followed.



CT Images of a 44-year-old man with COVID-19 pneumonia.

Source: Qian L, Yu J, Shi H.Severe acute respiratory disease in a Huanan seafood market worker: images of an early casualty. Radiology: cardiothoracic imaging. DOI: 10.1148/RYCT.20202000033. Published Online February 1, 2020.

**Thoracic ultrasound (TUS)** findings in COVID-19 arenon-specific and the role is not well established but it can still be used as a bedside modality without any radiations risk. It has the additional advantage of avoiding transportation of infectious, hypoxemic and hemodynamically unstable suspected or established COVID-19 patients for chest CT to radiology department. TUS findings may include thickening of the pleural line with pleural line irregularity, B lines in a variety of patterns including focal, multifocal, and confluent (interstitial edema), consolidations in a variety of patterns including multifocal small, non-translobar, and translobar with

occasional air bronchograms (pneumonia/ARDS), appearance of A lines during recovery phase and sometimes pleural effusions.

## 6. Electrocardiogram (ECG) & Echocardiography:

ECG is required for all hospitalized patients to measure baseline QT interval as some subjects may require drugs like chloroquine and/or azithromycin which may cause QT interval prolongation and cardiovascular events. Pre and post drug administration ECG can help recognize subjects who can develop QT interval prolongation as an adverse event related to offending drug. Besides, some very sick patients may develop or present with arrhythmias, acute cardiac injury, and shock and thus may require ECG and echocardiography.

## **Management of confirmed COVID-19 patients:**

Severity of Illness	General Management	Drugs*
Asymptomatic Cases	<ul> <li>Strict home isolation for a minimum of 14 days.</li> <li>if develops any symptoms ask to report on helpline.</li> <li>Repeat PCR on day-14 and If it is negative, discontinue isolation.</li> </ul>	Not needed.
Mild Disease	<ul> <li>Strict home isolation or if not available then in any health care facility with isolation facilities.</li> <li>Should be placed in a single room. Contact and droplet precautions should be instituted.</li> </ul>	Use paracetamol for fever and avoid ibuprofen or NSAIDs.
Moderate Disease	<ul> <li>Should be admitted in hospital and placed in a single room.</li> <li>Contact and droplet precautions should be instituted.</li> <li>Use paracetamol for fever and avoid ibuprofen or NSAIDs.</li> <li>Hydrate the patient preferably oral or IV fluid if required.</li> <li>Check oxygen saturation and if below 92% should administer oxygen via nasal cannula or face mask.</li> </ul>	Use paracetamol for fever and avoid Ibuprofen or NSAIDs.     Start     Hydroxychloroquine**loading dose 400 mg BD then 200 mg TDS for 10 days     OR     Chloroquine 500mg BD x 10 days.

Severe Disease	•Admit the patient preferably in	• Use paracetamol for fever and
	ICU with airborne isolation and	avoid ibuprofen or NSAIDs.
	strict PPE precautions.	Avoid systemic steroids.This
	<ul> <li>Hydrate the patient preferably</li> </ul>	can be used only if patient is in
	IV according to need and	septic shock requiring
	hemodynamic status of patient.	vasopressors (conditional
	<ul> <li>Oxygen administration via</li> </ul>	recommendation)
	face mask to keep oxygen	hydrocortisone 100 mg IV 8
	saturation > 92%.	hourly
	If unable to maintain saturation,	Give empiric antimicrobials to
	then can try Non Invasive	treat suspected pathogens
	ventilation (NIV) cautiously.	according to local settings
	<ul> <li>Regular assessment for need</li> </ul>	<ul><li>Start Hydroxychloroquine**</li></ul>
	of endotracheal intubation and	loading dose 400 mg BD then
	mechanical ventilation as delay	200 mg TDS for 10-14 days
	in intubation is associated with	OR
	unfavorable outcomes.	<b>Chloroquine</b> 500mg BD x 10-14
	<ul> <li>If mechanical ventilation is</li> </ul>	days
	needed, use ARDS NET protocol	If patient is not improving or in
	for ventilatory management.	ARDS, use one or more of the
	<ul> <li>Consider prone positioning</li> </ul>	following agents if available
	and ECMO (If available) for	with ID consultation:
	refractory hypoxemia.	1.Tab Lopinavir/Ritonavir
		400/100mg BID 14 days
		2. IV Remdesivir: loading dose
		200 mg followed by 100 mg
		once daily for 10 days
		3. IV Tocilizumab 4-8mg/kg

\*It has been clarified that there are currently no registered medicines for the treatment of COVID-19, because no treatment results from therapeutic research have been published. Based on currently available data, the options presented are for patients admitted with COVID-19 due to moderate and severe disease symptoms.

(max dose 800 mg)

\*\*Combination of Hydroxychloroquine (HCQ) and Azithromycin HCQ 200 mg TDS and Azithromycin 500 mg loading dose and 250 mg once daily for 4 days was used in one small study in moderate cases with favorable results. So far not enough data is available to recommend this combination therapy. Caution should be taken as this combination therapy can cause prolonged QT interval and Torsade de Pontes. Baseline and daily repeat ECG is recommended whenever this combination is used.<sup>17</sup>

\*\*\*Hydroxychloroquine (HCQ) Prophylaxis: In some countries like India, HCQ is being recommended for prophylaxis in health care workers involved in care of suspected/confirmed cases of COVID-19 (400 mg BD on day 1 followed by 400 mg once weekly for 7 weeks). There is no proven benefit/data available at this moment and most of the authorities are not recommending this prophylaxis.

## TREATMENT GUIDE FOR CRITICALLY ILL PATIENTS WITH COVID-19

## **Labs Indicating Severe Disease**

- D-dimer >1000
- CPK>2x ULN
- CPR>100
- LDH>245
- Troponin elevated/uptredending
- Abs lymphocyte count <0.8</li>
- Ferritin > 300

## **DIAGNOSTICS**

#### DAILY LABS

- CBC with diff (trend lymphocyte count)
- CPK

#### RISK START O2-3 DAY PRN

- D- dimer
- Ferritin/ CRP/ESR
- LDH
- EKG
- NO ROUTINE DAILY CXR

### **HEMODYNAMICS**

- · Norepinephrine first choice pressor
- If WORSENING:
- Consider myocarditis/ Cardiogenic shock
- Obtain echo, EKG, troponin

#### **THERAPEUTICS**

#### **ALL ICU ADMISSIONS**

- Empiric antibiotics
- Start Hydroxychloroquine\*\* 400 mg BID then 200 mg TID for 10-14 days OR
- Chloroquine 500mg BD
- If available use one of the following agents with ID consultation
- 1. IV Remdesivir: loading dose 200 mg followed by 100 mg once daily for 10 days
- 2.Tab Lopinavir/ritonavir (LPV/r)
- 400/100mg BID 14 days
- 3. IV Tocilizumab 4-8mg/kg two doses 12 hourly (max dose 800 mg)

## **RESPIRATORY FAILURE**

#### CONSIDER EARLY INTUBATION IN ICU

\*\*AVOID USING HFNC or NIV\*\*

WARNING SIGNS: INC Fi0<sub>2</sub>, DEC Sa0<sub>2</sub>, Worsening of lung infiltrates on CXR

#### LUNG PROTECTIVE VENTILATION

VT 4-6 ml/kg predicted body weight

 Plateau pressure <30</li>

 Driving pressure (Pplat-PEEP) <15</li>
 Target Sa02 90-96%. PaO2>60
 Starting PEEP 8-10 cmH20



#### CONSERVATIVE FLUID STRATEGY

Diuresis as tolerated by hemodynamics



### PEEP TITRATION

Best PEEP by tidal compliance or ARDS net low PEEP

#### **PRONE**

Early consideration if cont. hypoxemia or elevated airway pressures

#### ADDITIONAL THERAPIES

Paralytics for vent dysynchrony, not routine Inhaled NO up to 80 ppm (no epoprostenol)

IF WORSENING

## ECMO CONSULT (available at limited centers)

If continuous hypoxemia or elevated airway

## **Special Considerations:**

#### For intubation:

- Perform in negative pressure room whenever possible.
- PPE should include N95 respirator with face shield/protective eyewear (personal eyeglasses not adequate), isolation gowns (yellow gowns) for high risk aerosolizing procedures /impermeable to secretions and contact precautions. Intubate early/electively to avoid emergent intubation.
- Avoid noninvasive ventilation.
- Avoid bag mask ventilation of patients.
- Pre-oxygenate with nasal cannula and face masks as needed.
- Use rapid sequence induction and intubation with early use of paralytics.
- Consideration for shoe covers and surgical hoods or caps to avoid droplet contamination is reasonable.
- Avoid shortage of mechanical ventilators and crisis standard of care.

## For Bronchoscopy:

- Limit procedures, only perform if absolutely necessary.
- Perform in negative pressure room.
- PPE as per intubation.

## Noninvasive Ventilation (NIV: BPAP and CPAP) and Hi-flow Nasal Cannula

**(HFNC):** Noninvasive ventilation to be avoided because of it being highly aerosolizing.

- If NIV cannot be avoided due to respiratory distress or obstructive sleep apnea (OSA), a pulmonary/critical care consult is required for further recommendations.
- Patients on NIV should remain in a negative pressure room with all personnel using appropriate well fit N-95/PPE.
- This includes patients being transported between facilities.

### Hi-flow nasal cannula (HFNC) has conflicting literature:

- If patient dependent and appropriate for intubation, intubate
- Avoid hi flows of oxygen unless necessary.
- May consider use of hi oxygen flows (over 6 l/m) or HFNC in negative pressure room, with all personnel using appropriate well fit N-95/PPE.

### **Bronchodilators:**

 Avoid nebulization in non-intubated confirmed COVID-19 patients unless needed due to bronchospasm/asthmatic patients.

- Metered Dose Inhalers (MDIs) recommended for non-intubated patients, whether in ER or admitted.
- MDIs should be stored in wiped-clean closed plastic bag.
- Nebulization may be performed on intubated COVID-19 patients if the patient was prescribed an MDI prior to intubation.
- When administering an MDI, a face shield/protective eyewear (personal eyeglasses not adequate) and N95 mask are required.

## **Discharge Criteria:**

- Improvement of respiratory symptoms.
- Afebrile for at least 3 days.
- Chest x ray shows improvement in infiltrates.
- Documented virological clearance (negative PCR) in 2 samples at least 24 hours apart.
- Maintaining oxygen saturation >90% on room air.

## **Prevention in Health Care Settings:**

## **Regular Hand Washing:**

The CDC recommends regular hand washing with soap and water for at least 20 seconds and if soap and water are not available, use an alcohol-based hand sanitizer with at least 60% alcohol.

## PPE Use in Different Clinical Areas:

Screening areas at the entry of health care facility	Surgical mask
Health care providers in clinics	Gown and surgical mask
High risk screening areas/triage for COVID -19 suspect cases	Full sleeved impervious gowns, gloves, surgical mask
Areas where COVID - 19 suspected and positive patient admitted	Full sleeved impervious gowns, gloves, N95 mask and goggles/ full face wiser
Areas where aerosol generating procedures are performed like bronchoscopy, suctioning and nebulizations	Full sleeved impervious gowns, gloves, N95 mask and goggles/ full face wiser

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- **15.** Schwartz PJ, Woosley RL. Predicting the Unpredictable: Drug-Induced QT Prolongation and Torsades de Pointes. J Am CollCardiol 2016; 67:1639.
- **16.** Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, Shi Z, Hu Z, Zhong W, Xiao GRemdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro.Cell Res. 2020 Mar;30(3):269-271. doi: 10.1038/s41422-020-0282-0. Epub 2020 Feb 4
- **17.** Gautret P, Lagier J, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents 2020 Mar 20. [Epub ahead of print] PMID: 32205204
- **18.** WHO Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected. Interim guidance. WHO/2019-nCoV/clinical/2020.4

# **Appendix:**Advantages & disadvantages of various diagnostic interventions

	Advantages	Disadvantages	Remarks
History of travel from abroad	Easy to collect. Helpful in picking high risk people. Helpful in limiting the spread by self- quarantine measures.	People hide travel history. May be too late to self-quarantine as the disease has already spread. Not everyone will have the disease. Only 25% of Iran Zaireen had the disease.	Data should always be collected.
Contact with positive patient	Very helpful in identifying the high risk individual. Helpful in limiting the spread by selfquarantine measures.	Unknown contacts will be missed. People recall may not lead to listing of all. All contacts may not be traced.	Data should always be collected.
Typical flu symptoms	Can help in the picking of suspected cases	Not specific as other conditions may present like this.	
CBC	Easy to perform Widely available The changes due to Covid-19 are known	It is not specific. It can be higher or lower depending on individual patients. It does not confirm the diagnosis.	Must test in all the patients.
C-reactive protein (CRP)	Easy to do Widely available Varies in relation to the severity of the disease	It is nonspecific and non-diagnostic. Can be higher in other infections as well.	Useful test in admitted patients.
HRCT	Can be positive in the early stage It can show changes in almost all the cases There is good corelation with gold standard RT-PCR test It can show progression and improvement through serial scans	It is time consuming. Not widely available. It is non-specific as similar changes can be present in the other conditions. It will require dedicated CT scanner to prevent cross infection.	A very useful test where it can be performed safely.

SARS-CoV-2 RNA detection by reverse-transcription polymerase chain reaction (RT-PCR)	It is a diagnostic test when positive. Serial testing can declare patient cured. It can help in rapid diagnosis compared to gene sequencing.	Require invasive means to collect specimens. High chances of cross infection. Will need to be repeated as single specimen may not be positive. Multiple specimens will need to be tested from different sites. The Turn Around Time (TAT) will be in days. It will require specialized setup for reliable testing and safety measures. Kits supply can be the limiting factor.	It is a must test and gold standard at the moment.
Serological Testing	Quick to perform.  Does not require must expertise and special setups.  Different types of kits and methods available.	Not reliable. Can only show infection but not the active disease.	Not recommended.

## Suggested Reading:

- 1. https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19
- 2. Centers for Disease Control and Prevention (CDC): Coronavirus disease 2019 (COVID-19) Information for healthcare professionals (2020)
- 3. World Health Organization (WHO): Coronavirus disease (COVID-19) technical guidance (2020)
- 4. Public Health Agency of Canada (PHAC): Coronavirus infections For health professionals (2020)
- 5. Surviving Sepsis Campaign (SSC): Guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19) (2020)
- 6. European Centre for Disease Prevention and Control (ECDC): Scientific advice on coronavirus (2020)
- 7. Japanese Association for Infectious Diseases (JAID): New coronavirus infection (2020)
- 8. New South Wales Department of Health (NSW Health): COVID-19 Health professionals (2020)



COVID-19 Guidelines 2020
Pakistan Chest Society: www.pakistanchestsociety.pk