



Management of COVID-19 in Children (2022)



Kuwait

Pediatric Task Force Recommendations

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Coronavirus Disease 2019 (COVID-19) in Children: Kuwait Pediatric Task Force Recommendations

Jan. 1st, 2022



What is new in this version:

1. Update in COVID-19 testing section.
2. Update in COVID-19 (Sotrovimab Monoclonal Antibody section) and MIS-C management.
3. Addition to section XI (Special population and consideration in COVID-19): Addressing the Neuromuscular Disease (NMD) patients.

I. Background

SARS-CoV-2 has emerged to cause a global pandemic starting in late December 2019. The number of cases has been consistently increasing and reported in almost all countries. Observations so far indicate that pediatric COVID-19 diseases tend to be milder than the disease in adults^{1,2}. Nonetheless, severe pneumonia and respiratory failure do occur in children, albeit much less frequently than in adults.

This protocol aims to give guidance on the management of pediatric patients with suspected and confirmed SARS-CoV-2 infection.

II. Definitions

Pediatric population: We understand that, in Kuwait, the jurisdiction of the pediatric counsel is limited to patients less than 12 years of age. However, this statement of recommendation can be applied to all patients less than 18 years of age.

Suspected COVID-19 or persons under investigation (PUI) are patients who present with symptoms or signs compatible with COVID-19; however, their RT-PCR is pending or inconclusive. Higher suspicion should be exerted on a patient who was in direct contact with confirmed cases.

Confirmed COVID-19: Patients with positive SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR), regardless of symptoms³.

Severe Acute Respiratory Infection (SARI): is an acute respiratory infection with a history of fever and cough. Symptoms should have started within the last ten days and resulted in hospitalization⁴.

Multisystem Inflammatory Syndrome in Children (MIS-C): is a post-infectious inflammatory syndrome temporally related to SARS-CoV-2 infection.

III. Infection Control

General measures

This document does not intend to provide detailed recommendations for infection prevention and control (IPC) during the COVID-19 pandemic. Refer to the Ministry of Health published guidelines for more details.

The current evidence supports droplet and contact transmission being the predominant mode of transmission⁵. Airborne transmission by aerosols is possible in certain situations, mostly during aerosol-generating procedures (AGP)^{5,6}. Aerosol-generating procedures (AGP) include^{6,7}:

- Open suctioning of airway secretions
- Sputum induction
- Cardiopulmonary resuscitation
- Endotracheal intubation or extubation
- Tracheostomy procedure
- Non-invasive positive pressure ventilation (NIPPV) (e.g., BiPAP, CPAP)
- Bronchoscopy
- Manual ventilation (bag-and-mask ventilation)

The following are examples of procedures that may **provoke aerosolization**, as there is currently limited data on whether these procedures generate sufficient infectious aerosols and represent a transmission risk. Until more data is available, airborne precautions should be followed during the following procedures:

- Nebulizer administration
- Patient with tracheostomy (without manipulation or in-line suction)

AGP and aerosol provoking procedures, ideally, should be done in a negative pressure room. If a negative pressure room is not available, the procedure should be done in a single-patient room⁸. After the procedure, entry to the room should be limited for a period of time as directed by the infection control department. Then the room can then be cleaned as per ICP recommendations. All patients (2 years of age and older) and companions, regardless of symptoms, should be encouraged to wear an age-appropriate face mask⁹. All healthcare workers (HCW) are encouraged to wear medical masks at all times, as directed by MOH (table 1). The high-flow nasal cannula (HFNC) does not provoke aerosols like other modes of ventilation. Some studies have shown the HFNC, with good interface fitting, has limited aerosol depression (less than regular nasal cannula and nebulizer). For that reason, strict airborne precautions may not be needed for those patients^{10,11}.

SARS-CoV-2 can potentially be transmitted on fomites (e.g., gown)⁸. HCW should exert more attention during doffing to prevent self-infection. HCW should also change PPE between infected and non-infected patients. HCW should change PPE between seeing different in-patient COVID-19 cases after providing care to a patient with colonization or infection of a transmissible organism (e.g., MRSA, MDR, C. difficile, other respiratory viruses). The correct steps of PPE donning and doffing are listed in appendix 1.

Table 1. Indications and Types of Personal Protective Equipment (PPE)

Mode of transmission	Indication	Type of PPE
Contact and droplet	Regular care for patients with suspected or confirmed COVID-19 (within 2m of the patient or patient's environment)	Gloves Gown Eye protection Medical Mask
airborne	AGP COVID ICU	Gloves Gown Eye protection N95 mask

Reuse and extended use for N95 masks

Due to global shortages in PPE supply and increased demand, reuse and extended use of specific PPE, including N95, became a desirable intervention to overcome limited supply.

Extended use

This refers to wearing the same N95 for an extended period of time that involves a repeated encounter with several patients¹². There is no established consensus on an acceptable duration of a single extended use of N95¹³. Based on the available evidence,

and assuring the integrity of the mask, N95 should not be used beyond a single shift (8 hours)^{12,13}.

Due to the risk of contact transmission from the extended use of mask, the following steps should be taken to limit the risk of contact transmission (to the HCWs or the environment)¹²:

- Follow correct donning and doffing techniques (appendix 1)
- Discard N95 when it is contaminated with blood, respiratory secretions, or any other body fluids.
- Discard the N95 mask after AGP. HCWs working in the PICU and taking care of COVID-19 patients only, may keep wearing the mask until they leave the COVID-19 PICU.
- Discard N95 after being in close contact with a patient co-infected with an infectious disease requiring contact precaution.
- When possible, cover the N95 with either a face shield (preferred) or a medical mask¹⁴.
- Perform hand hygiene before adjusting the mask (to maintain a good seal or for comfort)

Limited Reuse

N95 reuse refers to the practice of using the same mask during several patient encounters but removing them between encounters. This practice has been followed previously in infection control guidelines for infections that do not require contact precautions (e.g., tuberculosis)¹⁵. However, the number of times the mask can be used before losing its integrity is limited, hence the term "limited reuse."

Because SARS-CoV-2 can be transmitted through fomites (surfaces), certain precautions should be followed when using the N95 mask multiple times. This includes¹²:

- Follow correct donning and doffing techniques (appendix 1)
- Discard N95 when it is contaminated with blood, respiratory secretions, or any other body fluids.
- Discard the N95 mask after AGP. HCWs working in the PICU and taking care of COVID-19 patients only, may keep wearing the mask until they leave the COVID-19 PICU.
- Discard N95 after being in close contact with the patient co-infected with an infectious disease requiring contact precaution.
- When possible, cover the N95 with either a face shield (preferred) or a medical mask¹⁴.

- Avoid touching the inside of the mask when duffing or donning. If the inside of the mask is touched, discard the mask.
- Between uses, store the mask in a clean and breathable container or bag (e.g., paper bag). Ensure appropriate labeling of the container to avoid using other's masks.
- Perform hand hygiene before adjusting the mask (to maintain a good seal or for comfort). Wearing new clean, nonsterile gloves can be considered.

Infection control considerations in specific respiratory procedures

Bronchoscopy

It is highly recommended to avoid routine bronchoscopy as it is AGP and subjects HCW to increase the risk of infection¹⁶. For severe and critical cases with obvious airway obstruction (mucus plug) that could not be managed conservatively or cases requiring bronchoalveolar lavage for cultures, bronchoscopies should be done under strict airborne precautions. Bronchoscopy can also be considered when sputum samples cannot be obtained to rule out alternative diagnoses like bacterial or fungal pneumonia, or tuberculosis in a selective population.

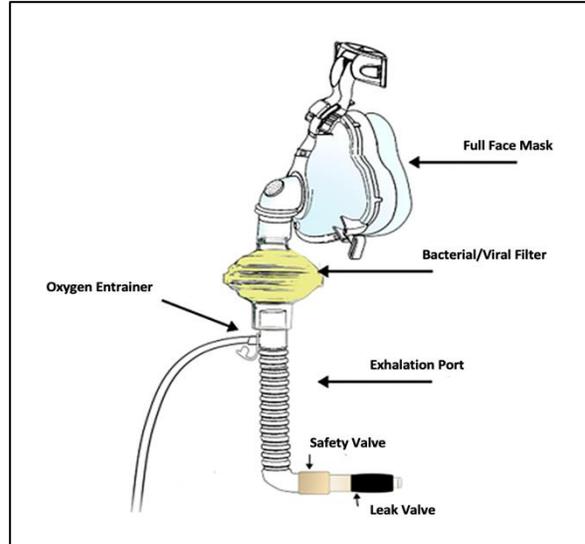
Nebulization

HCWs should be aware that nebulizing medication is a procedure that provokes aerosolization and can increase the risk of COVID-19 transmission¹⁷. A metered-dose inhaler (MDI) has been shown to be more effective than nebulization due to increased deposition and its portability. Therefore, it is **not** recommended to use nebulized medications in all patients regardless of their COVID-19 status in healthcare settings unless there are no other alternatives. Considerations for the use of nebulization:

1. Nebulization therapy should be provided in a single-patient room in the ER or the wards.
2. HCWs providing care during nebulization therapy should wear PPE in line with airborne precautions, including N95.

Non-invasive ventilation

Non-invasive positive pressure ventilation (NIPPV) is considered to be AGP⁸. The preferred interface will cover both mouth and nose (full face mask). Use a non-vented mask with an exhalation valve to minimize aerosolization. Avoid using wet humidifiers (water chambers) and use dry humidity (in-line HMEF). Heat and moisture exchanger filter (HMEF) should be placed between the patient's mask and the disposable exhalation port (figure 1). Monitor patients very carefully for both tolerance of the interface and setup (i.e., no hu-



midification).

Figure 1. Location of bacterial/viral filter in relation to the full-face mask (Adapted from: Pirzada, Abdul Rouf, et al. *Sleep and Vigilance* (2020)¹⁷

Tracheostomized patients

Invasive ventilation with a purposeful (unfiltered) leak should be treated as an AGP. Spacer with a mouthpiece could be connected directly to the tracheostomy tube to deliver MDI therapy (Figure 2). Use a dual-limb circuit with heated humidity and an expiratory viral filter. If unavailable, use a single-limb circuit (dry circuit, no humidity) with HMEF between the patient and disposable exhalation port. At all times, use inline suction (closed suctioning) system. Add a viral filter to the patient's bedside self-inflating bag for emergent use only.

Minimize the leak around the tracheostomy by inflating the cuff (for cuffed tubes) or using a tracheostomy tube size with the least leak. Also, remember that tracheostomy tube change is considered an AGP.

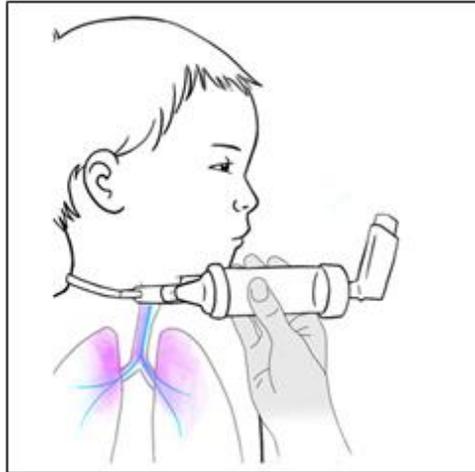


Figure 2. MDI administration through a spacer with a mouthpiece in tracheostomized patient (Adapted from <https://complexcareathomeforchildren.com>)

IV. Testing for COVID-19

Testing considerations

It is imperative to understand that SARS-CoV-2 is a lower respiratory tract virus. Obtaining an upper respiratory tract sample (e.g., nasopharyngeal) is associated with lower test sensitivity. The estimated sensitivity of detecting SARS-CoV-2 from nasal swabs was around 60-90% in adult patients¹⁸⁻²⁰.

The period of highest sensitivity for PCR testing on an upper respiratory tract specimen ranges between day 5-8 of SARS-CoV-2 exposure, which typically coincides with the first three days of symptoms^{18,21}. However, this fact should not limit testing to a specific period from exposure.

It is estimated that 85-90% of symptomatic COVID-19 patients would have positive PCR with a single nasopharyngeal specimen^{19,20}. Thus, SARS-CoV-2 PCR should be repeated in patients with high clinical suspicion of COVID-19, but the initial PCR was negative. Deeper specimens (e.g., deep tracheal suctioning) should be attempted in those patients in the PICU with appropriate infection control measures. To increase test sensitivity, consider doing paired nasopharyngeal and oropharyngeal sampling. Swabs may be placed in one viral transport media (VTM) tube.

Different types of swabs can be used to obtain a nasopharyngeal specimen. A flocked swab is considered the standard for respiratory specimen collection for the detection of respiratory viruses^{22,23}. Extra-caution should be

placed when using other swabs (viscose, rayon, etc.) when obtaining a nasopharyngeal specimen from infants as the nasal passage is smaller in this population and prone to trauma.

When an assessment of IgG is needed, a proper immunoassay should be done. This requires blood collection through venipuncture and may need an organization with a microbiologist or virologist. Rapid serological testing should not be done in children. The validity and performance of such a test were not assessed in the pediatric population.

Recently, commercial rapid antigen testing has been developed. In adults, the assay's sensitivity was highly dependent on the viral load in the tested clinical specimen. In symptomatic patients early in the illness course (high viral load), the test's sensitivity ranged from 77-82%^{24,25}. However, the interpretation of the result should consider the disease prevalence. In times when disease activity is low, a false-positive result is more likely. When available and at times of high disease prevalence, antigen testing would be ideal for identifying cases quickly; however, negative results may need a PCR to confirm negativity, especially in suspected cases.

Selection of appropriate SARS-CoV-2 test

PCR is the current gold-standard test for the diagnosis of acute COVID-19. It could be done on any respiratory specimen, including nasopharyngeal swab or aspirate, oropharyngeal swab, tracheal aspirate, and bronchoalveolar lavage. All commercial assays involve the detection of multiple SARS-CoV-2 gene targets. Occasionally, a single target is detected and results in an equivocal result. This can represent false-positive, or states with low viral load (very early infection, or late infection). In these cases, repeating the PCR in 24-72 hours is warranted.

Serology should only be used in patients with a suspected post-COVID-19 inflammatory process (a multisystem inflammatory syndrome in children, MIS-C).

Testing for other respiratory viruses can be done on the same sample collected for SARS-CoV-2 testing. The type of respiratory virus testing, if needed, can be decided based on the clinical syndrome, influence on management, and local hospital protocol.

Table 3. Test interpretation of PCR and Serology

Clinical status	PCR result	serology	Interpretation
Asymptomatic	PCR +	IgM+ IgG+	COVID-19 confirmed. Serology is not indicated in PCR+ patients.
		IgM+ IgG-	
		IgM- IgG+	
		IgM- IgG-	
	PCR -	IgM+ IgG+	Consider acute infection. PCR may be falsely negative with poor swab collection technique.
		IgM+ IgG-	Likely resolved infection.
		IgM- IgG-	Likely not infected.
Symptomatic Symptoms/ imaging con- sistent with COVID-19	PCR +	IgM+ IgG+	COVID-19 confirmed. Serology is not indicated in PCR+ patients. Some patients with MIS-C may have PCR+ results.
		IgM+ IgG-	
		IgM- IgG+	
		IgM- IgG-	
	PCR -	IgM+ IgG+	Consider acute SARS-CoV-2 infection or MIS-C, based on clinical presenta-
		IgM+ IgG-	tion. Consider repeating PCR. Also, review history and physical examina-
		IgM- IgG+	tion and consider alternate diagnosis for the clinical presentation.
		IgM- IgG-	Consider an alternate diagnosis. If COVID-19 is still suspected, repeat PCR.

V. Pediatric Emergency Room Care During COVID-19 Pandemic

The emergency physician should maintain a high index of suspicion for COVID-19. Signs and symptoms of SARS-CoV-2 infection could be nonspecific and non-respiratory in children. Fever and cough were the most commonly reported symptoms in pediatric COVID-19. However, gastrointestinal symptoms, rash, and nonspecific symptoms (e.g., fatigue) were reported in 5-10% of patients²⁶. Occasionally, these symptoms may be the sole presenting complaint.

Some of the entities mentioned below may not be caused by SARS-CoV-2. However, appropriate infection control consideration must be applied to those patients during the pandemic.

Emergency Triage and Recognition

In response to the pandemic, most emergency departments in the world divided their units into infectious/respiratory and clean zones. The main aim is to decrease the risk of SARS-CoV-2 transmission within the healthcare institution setting. In Kuwait, the effort was undertaken to maintain the separation of patients in emergency rooms (ER). Screening questions were implemented through a visual triage at the entrance of the ER. Detection COVID-19 cases in pediatrics require a high index of suspicions as symptoms vary in this population²⁷. We recommend referring to the flow diagram below (figure 3).

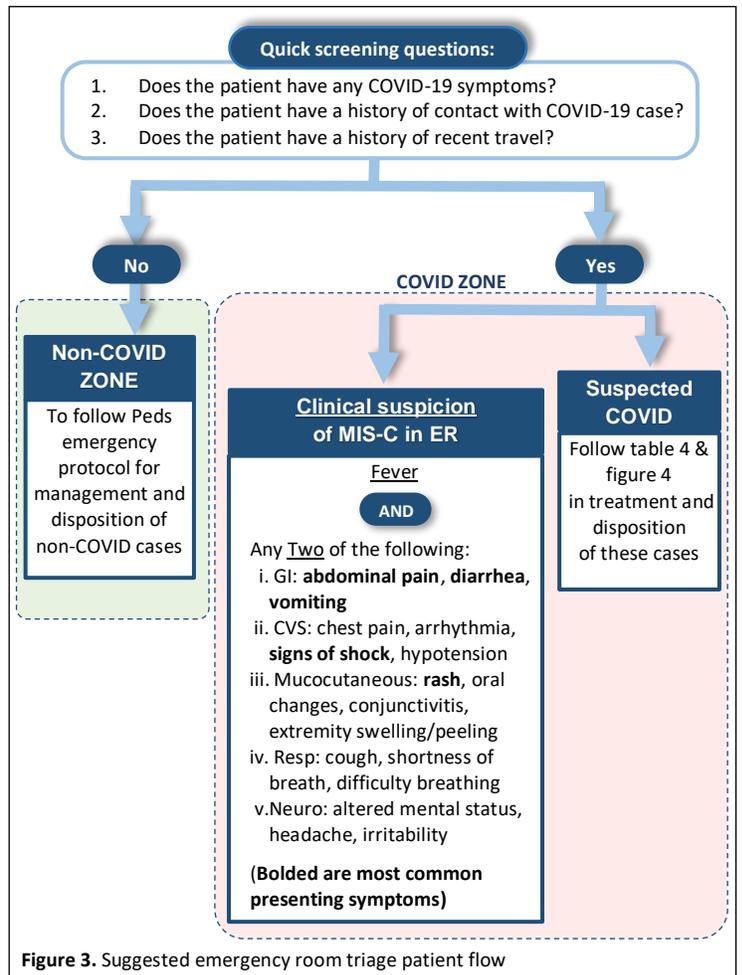


Figure 3. Suggested emergency room triage patient flow

Resuscitation for suspected or confirmed COVID-19 pediatric case

Cardiopulmonary Arrest

All HCWs who are present in the resuscitation room should follow airborne precautions. The resuscitation room door should be closed at all times to limit the potential spread of aerosols to other areas in the ER. If the resuscitation room contains more than one patient bed, all other patients should be immediately and safely moved out of the room. The Pediatric cardiopulmonary arrest algorithm was updated by American Heart Association in April 2020 to address infection control measures²⁸. They also recommended early intubation for suspected or confirmed COVID-19 cases if they present with cardiac arrest (appendix 2).

Shock

Early recognition and following PALS management guidelines are important in managing patients who present with shock. Those patients should be managed aggressively. Initial fluid boluses of 20 mL per kg of crystalloid fluid (0.9% NaCl or Ringer lactate) should be rapidly infused. Some COVID-19 patients may have cardiac dysfunction or myocarditis, requiring a frequent assessment before, during, and after the fluid bolus to detect any signs of cardiac failure or an overload state (e.g., hepatomegaly, pulmonary edema). Limit fluid resuscitation in children with signs of cardiac failure as recommended by PALS guidelines, and consider early inotropic support.

If the patient is suspected to have a bacterial infection (septic shock), the first dose of antibiotics should be given within the first hour of presentation. In the absence of risk factors for multidrug-resistant organisms, it is recommended to start ceftriaxone with or without teicoplanin (based on MRSA risk)²⁹.

For fluid refractory shock or in case of cardiac dysfunction with shock, early use of inotropic support peripherally (low dose epinephrine infusion of 0.05 mcg/kg/min, AND/OR dopamine infusion of 5-10 mcg/kg/min) is indicated. Early titration of inotropic support to achieve clinical response is essential. These medications should be infused through a central venous catheter once inserted.

Respiratory Failure

Although children have a higher risk of respiratory failure than adults, due to smaller airways and lung maturation, respiratory failure is uncommon in SARS-CoV-2 infected children³⁰.

Respiratory failure can be subclassified into hypoxic, hyper-carbic, or mixed type³⁰. Adults with COVID-19 commonly present with hypoxic type of respiratory failure, which improves with high flow nasal cannula (HFNC) or mechanical ventilation. The prevalence of hypoxemic respiratory failure in adult COVID-19 patients was reported in a Chinese study to be about 19%³¹. In children with hypoxic respiratory failure, a trial of HFNC might be considered if no contraindication (see section VIII below); however, if the patient presents with apnea, positive bag-mask ventilation with the use of bacterial/viral filter should be initiated. If invasive ventilation is needed, intubation should be performed under the infection control precaution mentioned in section III above.

Endotracheal Intubation

Endotracheal intubation is an AGP⁸. So, intubation should be performed by the most experienced physician in airway management to decrease the number of attempts and the risk of virus transmission. Moreover, minimizing members' numbers while intubating a COVID-19 patient is essential³². This procedure should be performed ideally in a negative pressure room. It is highly recommended to use a clear checklist for equipment and medication (appendix 3). Rapid sequence intubation is recommended with the judicious use of sedation and muscle relaxant agent to prevent coughing reflex during the procedure³². Minimize the use of the bag and mask ventilation as much as the situation allows. We recommend performing endotracheal intubation using a video laryngoscope if feasible. Always use a viral filter whenever bag-and-mask ventilation is required. In-line (closed) suction must be connected immediately to decrease the need for open suction.

Initial workup and management for suspected pediatric cases

Patient management will depend on the risk category as mentioned in table 4.

Table 4[‡]. COVID-19 disease severity definitions in pediatrics*

Disease Severity	Feeding and Hydration	Conscious State	Work of Breathing (WOB)	Oxygen Requirement [§]	Vital Signs
Mild illness	Normal or mildly reduced feeding	Normal	No or mild work of breathing	SpO ₂ > 92% in Room air	Normal for age
Moderate illness	Poor feeding AND unable to maintain hydration without nasogastric or IV fluids	Normal	Moderate work of breathing OR Brief self-resolving apnea (infants)	Requires O ₂ concentration (FiO ₂) of ≤ 50% ^Δ to maintain SpO ₂ > 90%	Tachycardia AND/OR tachypnoea for age
Severe illness	Poor feeding AND unable to maintain hydration without nasogastric or IV fluids	Drowsy OR Tired but easily rousable	Moderate-severe work of breathing OR Apnea needing support/stimulation (infants)	Requires O ₂ concentration (FiO ₂) of > 50% ^{ΔΔ} to maintain SpO ₂ > 90%	Tachycardia AND/OR tachypnoea for age
Critical illness	Poor feeding AND unable to maintain hydration without nasogastric or IV fluids	Altered Level of Consciousness OR Unconscious	Unable to maintain breathing or prevent apnea without advanced modes of support	Requires advanced Respiratory support (NIPPV or mechanical ventilation) to maintain oxygenation	Abnormal vital signs for age OR Hemodynamically unstable without inotropic or vasopressor support

[‡] Adapted and modified from Boston Children’s Hospital COVID-19 Treatment: Internal Guidance. Version 6/17/2020

* If signs and symptoms fall across different severity classifications, consider the patient under **the worse classification** to manage the illness.

[§] Oxygen saturation targets should be modified for patients with cyanotic heart disease.

^Δ In other words, oxygen via low flow system devices like nasal prong cannula or face mask.

^{ΔΔ} In other words, oxygen via high flow system devices like non-rebreathing face mask or high flow nasal cannula.

Asymptomatic or Mild Illness Cases

Most of those patients will not require close medical care. Home supportive care, hydration and antipyretics, if needed, are usually sufficient.

Perform laboratory tests or imaging only if clinically indicated. Avoid the use of routine blood cultures. Patients with mild illness may not require admission. However, instructions to the caregiver on when to seek medical attention should be provided (refer to the Ministry of Health published instructions).

Paracetamol is the preferred antipyretic of choice for pediatric patients. Ibuprofen can be given as a second-line agent. Currently, there is no clear evidence of harm when used in COVID-19 patients²⁷.

Moderate, Severe, and Critical Illness

Supportive care is the mainstay in the management of pediatric COVID-19 patients. Oxygen should be provided to maintain SpO₂ ≥ 90%.

Initial workup for those patients includes complete blood count (CBC), blood urea nitrogen (BUN), creatinine, electrolytes, liver function test (LFT), C-reactive protein (CRP), lactate dehydrogenase (LDH), creatine kinase (CK), ferritin, coagulation profile, D-dimer, troponin, blood culture, and chest X-ray.

Patients with moderate or severe presentation (those requiring oxygen) or clinical picture of bronchiolitis should have respiratory-virus multiplex PCR done (including as minimum influenza and RSV, but may include 15 or 22-pathogen panel respiratory virus

multiplex). If possible, this test could be done on the same sample provided for SARS-CoV-2 PCR. Suspected coinfecting patients being cohorted with other COVID-19 cases in a common room is another potential reason for performing respiratory virus multiplex PCR.

Empiric antibiotic therapy is not routinely indicated for all patients. It should only be considered in patients with suspected bacterial infection and should target the most common pathogens (e.g., use ampicillin for patients with lobar pneumonia²⁷).

Computed tomography (CT) scan of the chest should not be used as a first-line evaluation tool for children with suspected COVID-19. However, it may be used to aid in the diagnosis in select cases.

Bronchodilators are used only in cases with proven bronchoconstriction since they may cause tachycardia and worsening of V/Q mismatch. When needed, bronchodilators should be administered using MDI and spacer³³. If nebulization is used, airborne precautions should be implemented.

Croup in the setting of COVID-19 pandemic

For Mild Croup, consider avoiding corticosteroids; otherwise, use a lower dose of oral dexamethasone 0.15mg/kg/dose can be used as a single dose.

Moderate Croup, Administer oral corticosteroids (dexamethasone 0.6 mg/kg/dose, to a maximum of 10 mg). Intramuscular epinephrine (into the anterolateral thigh) could be used without the need for airborne precautions. Use the 1:1000 concentration (each mL contains 1 mg of epinephrine)²⁷.

Doses according to patient weight (Kg)*:

- 7.5 – 15 kg: 0.1 mg IM
- 15 – 30 kg: 0.15 mg IM
- >30 kg: 0.3 mg IM

*Could be repeated every 20 minutes for a maximum of 3 doses.

Nebulized epinephrine can be given if adequate airborne precautions (full PPE, including N95 and all airborne precautions) are available³³.

Severe Croup is considered as an emergency. It might progress to life-threatening upper airway obstruction, which may lead to a difficult airway condition. An early call to an experienced airway management team is highly recommended with the initiation of the previously mentioned interventions.

Asthma in the setting of COVID-19 pandemic

Salbutamol given via metered-dose inhaler (MDI) has been shown generally to be more effective than nebulization, due to increased deposition and its portability³⁴. Therefore, it is not preferred to use nebulized medications in all children, regardless of their COVID-19 status in health care settings^{33,35}. Valved-holding chambers, a type of spacers with a one-way valve, have been shown to be superior to un-valved spacers due to its capacity to trap the medication particles and provides time for slow and deep breaths, as well as ability to count effective breaths. For a patient with a tracheostomy, the spacer with a mouthpiece could be connected directly to the tracheostomy tube (figure 2).

For Mild asthma exacerbation, administer salbutamol via MDI and age-appropriate spacer (refer to dosing in appendix 3). Continue the use of regular inhaled corticosteroids (ICS) and review medication delivery techniques and triggers.

For Moderate asthma exacerbation, administer salbutamol and ipratropium bromide (MDI and spacer), and consider oral corticosteroids.

Multiple studies have shown a decrease in hospitalization among children with acute exacerbation of asthma when used a combination of beta-2 agonist and ipratropium bromide in the emergency room³⁶.

For Severe asthma exacerbation, administer salbutamol and ipratropium bromide by MDI and spacer. If ipratropium bromide is not available by MDI, use the nebulized form while adhering to the airborne precautions. Intravenous (IV) corticosteroids are added to the treatment regimen. Consider the use of magnesium sulfate IV with cardiorespiratory monitoring. Consider the use of salbutamol IV with cardiorespiratory monitoring.

Disposition from ER

The following illustration (figure 4) is not intended as a sole source of guidance on the choice of patient disposition. Instead, it is designed to assist clinicians in decision-making. Once COVID-19 severity has been assessed as aforementioned in table 4.

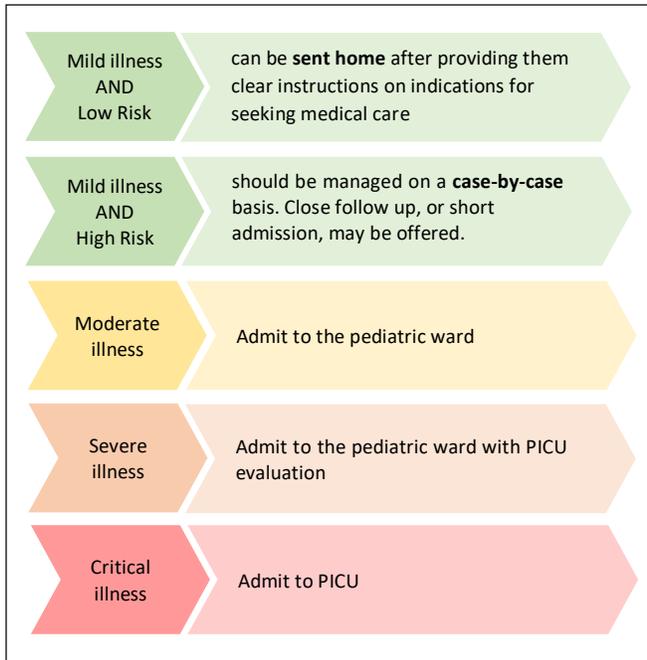


Figure 4. Patient disposition based on illness severity

Table 5. High-Risk Group in Pediatric for Severe COVID-19³⁷

- Immunocompromised state (chemotherapy or radiation therapy, transplant patients, high dose steroids, biologics)
- Obesity (weight >95th percentile for age and sex)
- Cardiac disease (Cardiomyopathy, unrepaired cyanotic heart disease, single ventricle physiology)
- Neuromuscular disease
- Chronic lung diseases (e.g., cystic fibrosis, interstitial lung diseases, severe asthma)
- Sickle cell disease
- Chronic Kidney or liver disease
- Poorly controlled DM
- Neonate less than 1 month of age
- Trisomy 21

VI. In-hospital investigation and management of confirmed or suspected COVID-19 patients

Laboratory Investigation

Patients with mild disease do not require routine investigations. However, those with severe and critical illness may require a repeat of inflammatory and biochemical markers for early identification of cytokine release syndrome (CRS). The frequency of repeating any specific test depends on the type of investigation and severity of illness. However, a daily repeat of

inflammatory markers (e.g., CRP) in clinically nonprogressive disease rarely affects patient management.

Imaging

In pediatric COVID-19 patients, chest X-ray (CXR) is the imaging modality of choice. Repeating CXR in stable patients without signs of progressive pneumonia is not recommended. CXR should be repeated in patients with worsening respiratory symptoms, or when a complicated disease is suspected (e.g., bacterial superinfection, pneumothorax).

Oxygen Therapy

Supplemental oxygen should be started for COVID-19 patients when SpO₂ is <90%. Target SpO₂ of 92% to 96% when treating hypoxemic patients with COVID-19³⁸. Indirect RCTs have shown that a liberal oxygen strategy is associated with high morbidity and increased hospital stay³⁹. Conventional oxygen therapy can be provided for pediatric cases via:

- **Nasal prong cannula** with a maximum flow of 4L/min. It can provide a maximum oxygen concentration of 40-50%
- **Face mask** with a flow rate of 5-10L/min. It can provide a maximum oxygen concentration of 40-60%; however, it is influenced by respiratory rate and tidal volumes.
- **Venturi mask** can give up to 50% oxygen, depending on adjusted flow. It provides an accurate and constant oxygen concentration despite varied respiratory rate and tidal volume.
- **Non-Rebreathing face mask** with a flow rate of 10-15 L/min. This can deliver up to 100% oxygen if the mask is well-fitting and valves are present.

If targeted SpO₂ is not achieved despite conventional oxygen therapy, and the patient does not have other indications for intubation, a high flow nasal cannula (HFNC) can be used⁴⁰.

Antibiotic Therapy

Routine empiric antibiotic therapy is not indicated in patients with COVID-19. If antibiotics were to be started, the need to continue antimicrobial therapy should be re-evaluated after 24-48 hours of admission. In patients with negative blood cultures and no specific imaging findings, antibiotics should be discontinued. If the blood culture results and/or imaging findings (e.g., CXR) are suggestive of bacterial infection, the narrowest spectrum antibiotic should be

used (e.g., ampicillin for uncomplicated community-acquired pneumonia)²⁷.

Management of influenza co-infection

It is difficult to distinguish influenza infection from COVID-19 based on clinical presentation. However, the suspicion for influenza should increase if the patient was a close contact to an individual with a proven influenza infection, regardless of the child's vaccination status.

Most children with influenza will improve without the use of oseltamivir. However, the maximum benefit of oseltamivir in children was observed in patients treated within 48 hours of symptom onset and those with risk factors for the development of severe influenza. Based on the available guidelines and evidence, table 6 summarizes the recommendations for oseltamivir use^{41,42}.

Table 6. Recommendation for the use of oseltamivir in a patient with confirmed or suspected influenza.

Influenza infection (one of the following): <ul style="list-style-type: none">- Proven infection by PCR or antigen detection- Close contact to an individual with proven or suspected influenza
AND
Clinical features (one of the following): <ul style="list-style-type: none">- Within 48 hours of symptoms and <2 years of age or medical comorbidity- Progressive severe influenza illness regardless of the duration of symptoms

Influenza treatment may be considered in special situations outside the listed indication and in patients beyond 48 hours of symptoms after discussion with an infectious diseases specialist

Oseltamivir has no activity on SARS-CoV-2. If it was started empirically for any patients, it should be stopped when the influenza PCR result comes negative.

Specific Anti-SARS-CoV-2 Therapy

Dexamethasone

Dexamethasone has shown in adults with acute SARS-CoV-2 infection to reduce mortality in severe COVID-19 cases⁴³. Dexamethasone may be considered in severe or critical illness with COVID-19 when PICU admission is required. However, to date, there is little evidence for the use of dexamethasone in children with COVID-19. Extrapolating data from adult studies may be difficult due to differences in disease

pathogenesis, pharmacokinetics and dynamics, and potential response⁴⁴.

Antivirals

To date, remdesivir is the only antiviral that has proven efficacy in COVID-19 patients in an RCT setting^{44,45}. Remdesivir has been shown to reduce hospital length of stay without significantly reducing mortality in adult COVID-19 patients. Its use might be considered in critical pediatric patients. Other antivirals (hydroxychloroquine, lopinavir/ritonavir) were found to be ineffective in managing SARS-CoV-2 infection and should be avoided.

Convalescent plasma:

At present, published data on the use of convalescent plasma is limited to small case series. The results of clinical trials and observational studies are conflicting. The standards and methods for screening donated plasma for SARS-CoV-2 binding and neutralizing antibodies have not been established. The variability in SARS-CoV-2 antibody levels in donor plasma may impact the product's efficacy^{46,47}. However, large clinical trials using high-titer SARS-CoV-2-specific IgG plasma failed to find a benefit of convalescent plasma in the treatment of severe COVID-19^{48,49}

The best timing to give convalescent plasma is unknown, and some patients may benefit from early administration of the plasma. Therefore, treatment may be considered on a case-by-case basis (e.g., patients rapidly deteriorating, increasing oxygen need, high-risk patients admitted to ICU) after discussion with infectious diseases service.

Sotrovimab Monoclonal Antibody

Sotrovimab is an anti-SARS-CoV-2 monoclonal antibody that targets a highly conserved epitope in the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein.

The US FDA and Ministry of Health in Kuwait (MOH) have issued an emergency use authorization (EUA) for the use of Sotrovimab as an early treatment for mild-moderate COVID-19 adult patients (≥ 12 years old AND weighing at least 40 kg) in late May 2021. Refer to the MOH Sotrovimab protocol for more details.

VII. Conditions related to COVID-19

Cytokine Release Syndrome (CRS)

CRS is an acute inflammatory storm that may occur with severe infection (figure 5). Usually, this phenomenon is seen in critical care units; however, a high index of suspicion is required when dealing with severe refractory cases. The diagnosis of CRS should be considered in patients who have rapid clinical deterioration, hemodynamic instability, and elevated inflammatory markers. More information is mentioned in the CRS section under the “Condition related with Critical COVID-19 infection” section.

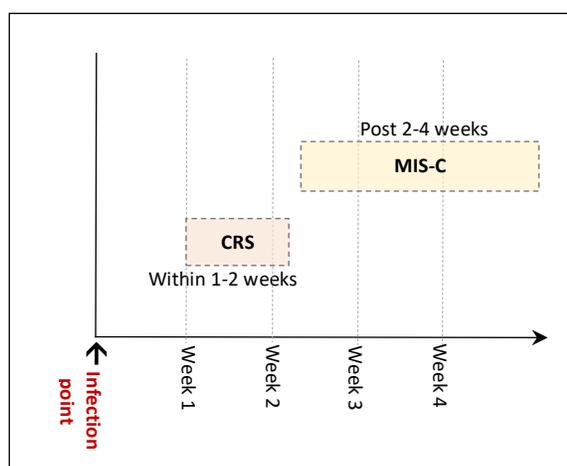


Figure 5. Timing of Cytokine Release Syndrome (CRS) and Multisystem Inflammatory Syndrome in Children (MIS-C) in relation to infection onset. CRS typically occurs earlier than MIS-C.

Multisystem Inflammatory Syndrome in Children (MIS-C)⁵⁰⁻⁵³

MIS-C is a rare syndrome (2:100,000 SARS-CoV-2-infected children). It was first described in April 2020 as a rare complication of SARS-CoV-2 infection. The symptoms of MIS-C occur 2-6 weeks following infection with the virus. More males are affected than females. Clinical symptoms frequently resemble features of Kawasaki disease.

A subset of these patients may present with hypotension and shock (20–100%) from either acute myocardial dysfunction or systemic hyperinflammation/vasodilation. Coronary artery dilation or aneurysms have been described in 6–24%, and arrhythmias in 7–60%. Most children who develop MIS-C have been previously healthy (78%), yet a majority of cases required ICU admissions (21–80%). Classification

criteria to aid in the diagnosis and classification have been proposed by the World Health Organization (WHO). Most cases worldwide have been described in children, with those between the ages of 5-15 years mostly affected. Children younger than five years of age are more likely to present with features akin to signs and symptoms of typical or atypical Kawasaki disease. About 15% of patients have mild illness and require no specific treatment. The majority, however, may present with multiorgan involvement and may require aggressive therapy. The course of MIS-C may show rapid deterioration with mortality up to 4% of all affected children. All patients suspected of MIS-C should be investigated for other infectious or non-infectious conditions that may mimic MIS-C. Most patients test positive for SARS-CoV-2 IgG, and more than a third are RT-PCR negative.

World Health Organization (WHO) Case Definition⁵⁴:

Children and adolescents 0–19 years of age with fever ≥ 72 hour
AND
Two of the following:
○ Acute gastrointestinal symptoms (diarrhea, vomiting, or abdominal pain).
○ Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet).
○ Hypotension or shock.
○ Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
○ Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
*Bolded symptoms are the most common presenting symptoms
AND
Elevated markers of inflammation such as ESR, C-reactive protein (CRP), or procalcitonin (PCT)
AND
No other apparent microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.
AND
Evidence of COVID-19 (RT-PCR, antigen test, or serology positive), or likely contact with patients with COVID-19

Management of MIS-C

(Guidelines presented here for MIS-C are based on expert opinion, the recommendations for Kawasaki disease are evidence-based)

Admit to the COVID ward and start monitoring using pulse oximetry, telemetry, and frequent blood pressure measurements. We recommend consulting rheumatology, cardiology, and infectious disease services, as well as consideration to involve the PICU team.

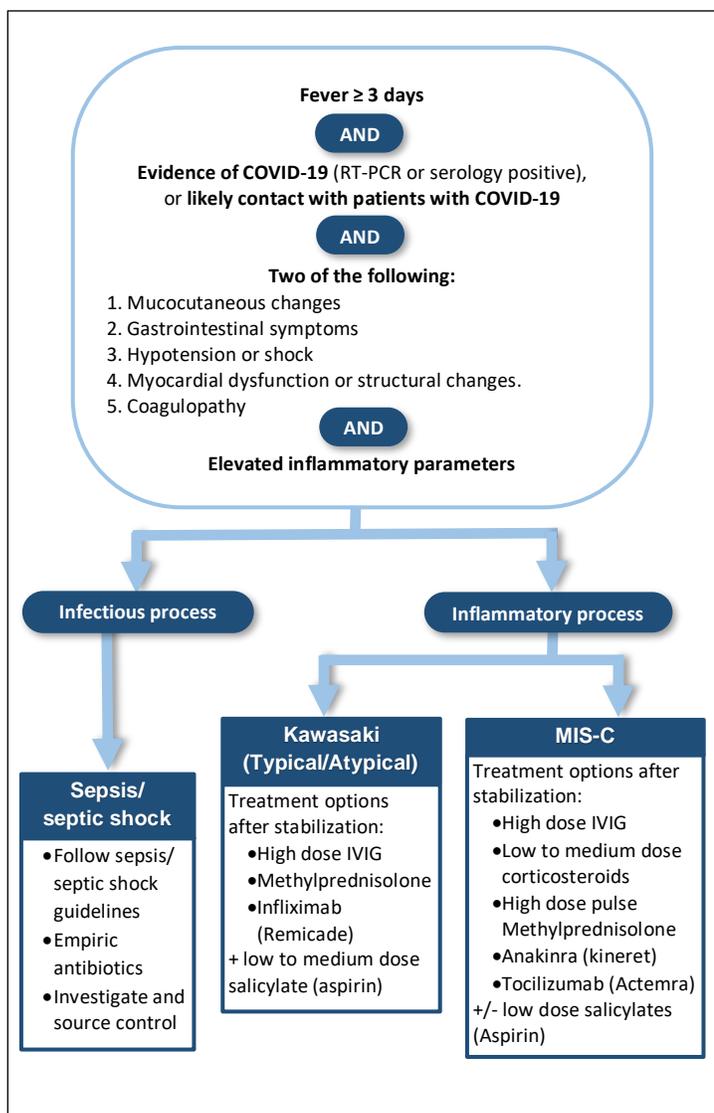


Figure 6. Conditions mimic MIS-C and possible therapy options for each. The management choices should be discussed with rheumatology or infectious diseases services.

Investigations

- CBC, ESR, CRP, Procalcitonin, ferritin, D-dimer, fibrinogen, triglycerides, LDH, Troponin level, and NT BNP.
- COVID-19 PCR and serology testing if serology is available).
- Blood culture and urinalysis and culture.
- ECG should be done at presentation and repeated every 48 hours.
- Consult cardiology and consider telemetry or Holter if cardiac rhythm abnormality is detected.
- Imaging: CXR, abdominal doppler for ectasia of blood vessels.
- Until further evidence emerges on the frequency and indication of coronary artery evaluation, an

echocardiogram should be done at the initial presentation, and 4-6 weeks after presentation. Patients with cardiac abnormalities may need more frequent examinations during and after hospital discharge. Also, hemodynamically unstable patients may need more frequent functional echocardiogram as indicated clinically⁵⁵.

- Cardiac CT may be considered in patients with suspicion of distal coronary artery aneurysms that are not well seen on echocardiogram.
- Cardiac MRI may be indicated 2-6 months after MIS-C diagnosis in patients who presented with significant transient LV dysfunction in the acute phase of the illness. The decision of cardiac MRI should be made after consulting a pediatric cardiologist.

Treatment of MIS-C: (Appendix 4. describes the treatment approach to MIS-C.)

Supportive treatment is the mainstay therapy for MIS-C, and it includes fluid management, inotropic support, respiratory support as needed. Extracorporeal Membrane Oxygenation (ECMO) may rarely be needed in severe cases. Empiric intravenous antibiotics are not indicated for MIS-C. However, broad-spectrum antibiotics (e.g., ceftriaxone) may be considered when bacterial infection or septic shock cannot be ruled out²⁷. Anticoagulation may be required as per the hematology consult.

Stepwise use of immunomodulators is recommended for the treatment of MIS-C. IVIG and/or steroids are the first-line immunomodulator therapy⁵⁶.

Managements of MIS-C patients may need to be done in a multidisciplinary approach with:

- Pediatric Rheumatologist
- Infectious diseases specialist
- Cardiologist
- Pediatric intensivist

Immunoglobulin (IVIG)

In patients with a clinical picture of Kawasaki or atypical Kawasaki without shock or coronary aneurysms, **IVIG alone 2 grams/kg infused over 12 hours** is the first choice of treatment. In obese patients, the dose of IVIG is calculated according to ideal weight with a maximum total dose of 100 grams. Infusion can be slower or split over two days in patients with a risk for fluid overload. In patients with high-risk Kawasaki disease (Kawasaki disease shock syndrome, fever > 10 days, age < one year, severe hemolysis, macrophage activating syndrome (MAS)), steroids may be

considered after the first dose of IVIG after discussion with a rheumatologist.

Salicylates (Aspirin)

Low dose oral salicylates (Aspirin) is indicated if Kawasaki is suspected or if MIS-C and echocardiogram showing left anterior descending (LAD) or right coronary artery (RCA) ectasia ≥ 2.5 . Salicylates should be avoided in patients with low platelet counts $< 50 \times 10^9$ /L. Also, it should be avoided in patients with G6PD due to the risk of hemolysis. Low-dose aspirin should be continued for at least 6 weeks in all patients with MIS-C53. A suggested approach to anticoagulation in the case of MIS-C is shown in figure 6.

Steroids

Systemic steroids Methylprednisolone 2 mg/kg in 2 divided doses may be considered for the treatment of mild-moderate MIS-C, including refractory Kawasaki phenotype. High dose pulse methylprednisolone (30 mg/kg/day) may be considered to treat patients with life-threatening complications, such as shock, and specifically, if the patient requires high dose or multiple inotropes and/or vasopressors. Patients on high-dose steroids gastric protection with a proton pump inhibitor. Once patients respond to treatment CS are switched to an equivalent oral dose and are tapered over a period of 3-4 weeks.

Steroids should be used with caution in patients who tested positive for SARS-CoV-2 by RT-PCR. In

those patients, acute SARS-CoV-2 infection should be ruled out before the use of steroids in patients not requiring oxygen.

Biological Therapy

Anti-IL-1 Ra (Anakinra) (used in 13% of patients) is an option in children with MIS-C patients refractory to IVIG and CS or with a contraindication to IVIG or CS.

Anti-IL-6 inhibitor (Tocilizumab) may also have a role in MIS-C patients.

Anti-TNF α (Infliximab) maybe be used for patients not responding to IVIG or systemic steroids as a last option.

Discharge Criteria for MIS-C

Patients with MIS-C can be discharged when all of the following are achieved: afebrile ≥ 24 hours, a downward trend of inflammatory markers, and resolution of symptoms. Patients should be discharged with a clear treatment plan and follow-up appointments. Follow-up should include as a minimum general pediatrician and cardiologist (for echocardiogram follow-up) and may include rheumatologist.

VIII. Pediatric critical care approach and management

Summary of critical care approach

Figure 7. describes the approach for most common COVID-19-related conditions requiring PICU care.

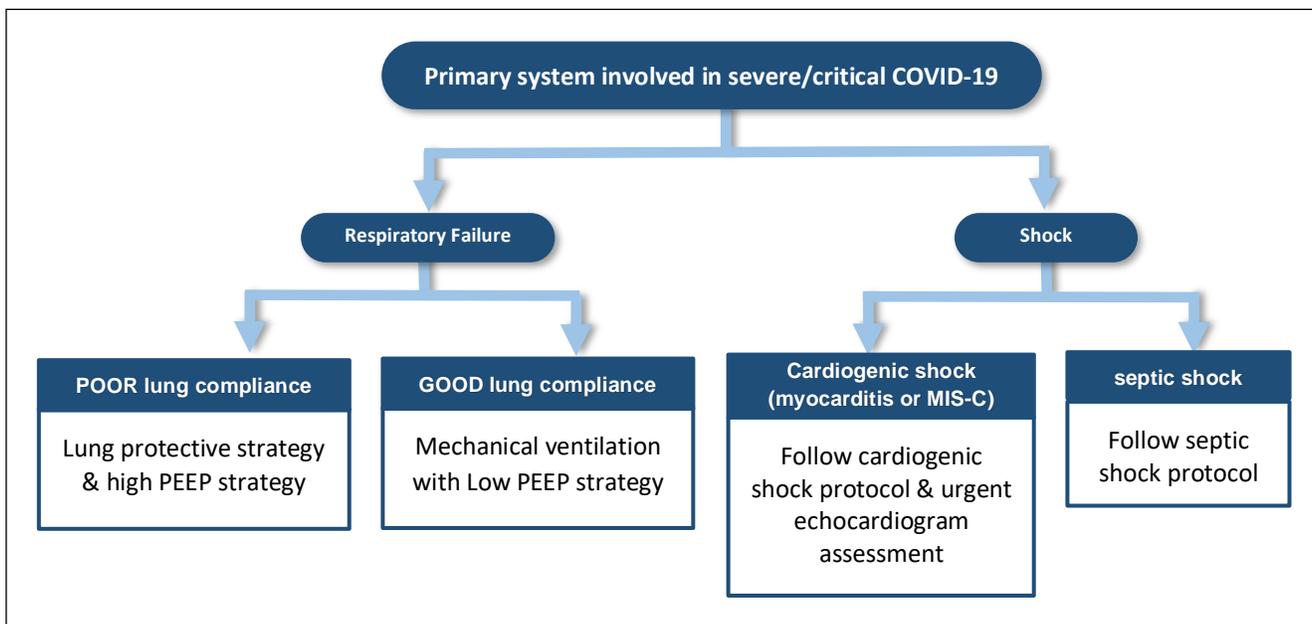


Figure 7. The approach to Severe/Critical COVID-19 in the intensive care unit. PEEP, positive end-expiratory pressure.

Respiratory support

High flow nasal cannula (HFNC)

HFNC is considered a good option for oxygenation in hypoxic COVID-19 patients as it imposes a lower risk of aerosolization compared to non-invasive ventilation and intubation^{40,44,57}. There is no evidence reported that HFNC is a risk factor for nosocomial transmission of respiratory pathogens. During the 2003 Toronto SARS-CoV-1 outbreak, HFNC was not found to be a risk for virus transmission to HCW. When HFNC is used, close monitoring of the patient is required. If no improvement is observed in the first 1-2 hours, intubation and invasive mechanical ventilation should be considered.

HFNC should not generally be administered to patients with a decreased level of consciousness, hemodynamic instability, and/or multiorgan failure³⁸. Since there is no consensus on HFNC failure, we suggest that failure to maintain SpO₂ ≥ 90% with FiO₂ of 60% for 1-2 hours is an indication to escalate respiratory care. A trial of non-invasive positive pressure ventilation (NIPPV) may be used in case HFNC is not available or fails to provide the necessary support, and immediate endotracheal intubation is not indicated. Close monitoring for clinical deterioration and the need for urgent intubation should be considered.

Non-Invasive positive pressure ventilation (NIPPV)

NIPPV should be used in a negative pressure room. HCW should use airborne precautions when giving care for such patients³⁸. When NIPPV is used, close patient monitoring is required, especially in the first two hours. Make sure of the availability of personnel capable of endotracheal intubation in close proximity. We recommend following a local PICUs guideline for NIPPV parameters and adjustment with caution to escalate to intubation whenever needed.

Mechanical ventilation (MV)

Proper understanding of lung dynamics is an integral part to properly manage MV settings. A lung-protective strategy should always be applied to prevent ventilator-associated lung injury, which may lead to multiorgan failure in patients with Pediatric Acute Respiratory Distress Syndrome (PARDS). Always consider using objective tools like the oxygenation index

(OI) or oxygen saturation index (OSI) to monitor the severity and progression of PARDS.

The hypoxemic state in patients with COVID-19 could be explained by two main pathophysiological processes; poor lung compliance, as seen in PARDS, or normal lung compliance, seen in pulmonary hemorrhagic infarcts, and micro-thrombosis formation. Consider the following ventilation strategy in these two entities³⁸:

1. Pulmonary hemorrhagic infarcts and micro-thrombi formations (**normal lung compliance**) and no/mild PARDS: a lower PEEP strategy to mitigate the unwanted effects of a higher PEEP is suggested.
2. PARDS (**poor lung compliance**): Apply a **high-PEEP strategy** with low tidal volume.
 - a. Target tidal volume of 4-6 ml/kg of predicted body weight (PBW).
 - b. Maintain plateau pressure ≤ 28 cm H₂O
 - c. If plateau pressure > 30 cm H₂O, decrease tidal volume by 1 ml/kg increments to a minimum of 4 ml/kg PBW.
 - d. The tidal volume of (3 ml/kg ideal body weight) can be considered for patients with poor respiratory system compliance or may accept plateau pressure of up to 30 cm H₂O.
 - e. Monitor the patient for signs of barotrauma, respiratory system compliance, and hemodynamics.
 - f. Adult evidence showed that the use of neuromuscular blocking agents' infusion for the first 48 hours improves the outcome of severe ARDS cases with poor lung compliance as it will decrease the negative effect of spontaneous breathing in lung injury.

Prone position

Prone positioning in an awake non-intubated adult with COVID-19 has been shown to improve oxygenation⁵⁸. However, it is difficult to be performed in a wakeful child. Besides, there is insufficient evidence to support awake prone positioning in children with COVID-19.

Safe **prone ventilation** requires expertise and adequate human resources. Prone ventilation is one of the few interventions that have been shown to reduce mortality in mechanically ventilated patients with moderate to severe ARDS. In a large RCT of 466 patients with ARDS, prone ventilation reduced 28-day

and 90-day mortality, compared with ventilation in the supine position⁵⁹. The prone position reduces lung compression, improves lung perfusion, and reduces the ventral-dorsal transpulmonary pressure difference, resulting in improved ventilation and oxygenation⁵⁹. Prone ventilation has recently been adopted by many international guidelines as rescue management for patients with moderate to severe ARDS to reduce mortality. Adequate prone ventilation should be performed for at least 12 to 16 hours for moderate to severe PARDS cases. Usually, it is recommended to start proning in the first 48-72 hours. Prone ventilation will be insufficient later on in the disease course due to lung cell injury and fibrosis³⁸. Clinicians should recognize contraindications for prone ventilation such as spinal instability, anterior burns, unstable fractures, and active bleeding³⁸. Institutions offering prone ventilation should use a protocol for proning and should provide the necessary training.

Refractory hypoxemia

Recruitment maneuvers

Slow incremental and decremental PEEP steps (Stepwise recruitment maneuver) is preferred for hypoxic patients with severe PARDS. **Rapid** recruitment maneuvers are not recommended for those patients due to the risk of hyperinflation of healthy non-inflamed alveoli.

Inhaled Nitric Oxide (iNO)

The routine use for iNO in adults or children with COVID-19 is not currently recommended³⁸. The use of iNO in patients with ARDS may improve oxygenation temporarily but does not reduce mortality and may increase the risk of acute kidney injury (AKI). iNO may be used as rescue therapy.

High-frequency oscillatory ventilation (HFOV)

HFOV can be used in severe PARDS cases and refractory hypoxemia.

Veno-venous extra-corporeal membrane oxygenation (VV ECMO)

Extracorporeal life support (ECLS) is used in mechanically ventilated patients with refractory hypoxic respiratory failure, where all other measures and interventions fail to maintain adequate oxygenation. In the context of a pandemic, resources are valuable, and healthcare systems are under continuous strain;

therefore, the use of VV ECMO should only be reserved for patients who need it and are likely to survive or benefit if offered ECMO. In patients with COVID-19 infection with refractory hypoxemia despite optimizing ventilation, using rescue therapies, and proning, VV-ECMO is recommended if available at your center or by referring the patient to an ECMO center.

Circulatory support

COVID-19 patients may present with left ventricular failure, arrhythmia, and cardiogenic shock. Infection is triggered by the binding of SARS-CoV-2 spike protein to angiotensin-converting enzyme 2 (ACE2), which is highly expressed in the heart and lungs. The severity of the symptoms might be associated with increased expression of ACE2 in these patients compared with healthy individuals.

Using dynamic parameters is preferred over static parameters to assess fluid responsiveness in patients with COVID-19 and shock. Many critically ill patients with COVID-19 are hypovolemic and have high insensible water losses from ongoing fever. Thus, careful and frequent volume status assessment is warranted. A conservative fluid resuscitation strategy is preferred over a liberal one to avoid fluid overload. Crystalloid fluids are preferred over colloid fluids. For pediatric COVID-19 patients who develop septic shock, you can refer to the children surviving sepsis campaign guidelines.

A regular cardiac echocardiogram is recommended to track cardiac dysfunction and the evolution of coronary artery abnormalities (in the case of MIS-C). For MIS-C cases, abdominal imaging may be valuable to exclude significant abdominal pathology.

Circulatory support for MIS-C

Vasodilated 'warm' shock, relatively refractory to fluid boluses, is a common feature. Cardiac dysfunction may evolve rapidly and unexpectedly. Consider starting inotropes early via peripheral lines, for example, epinephrine infusion (Low dose infusion) and/or dopamine. Watch for extravasation. Norepinephrine, vasopressin may be needed once central access is inserted. If there is evidence of cardiac dysfunction and cardiogenic shock, epinephrine infusion should be considered early. Milrinone infusion should only be started once hypotension is improved as milrinone is a potent vasodilator and may worsen the hypotension.

Renal Replacement Therapy (RRT)

Acute kidney injury (AKI) in COVID-19 accompanies sepsis, multiorgan failure, and shock; therefore, acute tubular necrosis (ATN) appears to be the most likely cause. AKI is associated with worse outcomes in patients with COVID-19. The management of AKI in this disease is probably similar to other conditions. Start RRT if³⁸:

- Life-threatening hyperkalemia
- Severe acidosis
- Pulmonary edema
- Uremic complications are present

Early initiation of renal replacement therapy (RRT) in the absence of known indications is not recommended. Choose the modality based on availability, expertise, resources, and associated cost. Using continuous renal replacement therapy (CRRT) for a patient with hemodynamic instability or shock state is preferred over intermittent hemodialysis (IHD). It is recommended to use anticoagulation over no anticoagulation when CRRT is used for patients with COVID-19 (without coagulopathy or contraindications to anticoagulation). Choosing between regional citrate anticoagulation or unfractionated heparin will depend on the institution's local practice and procedure.

Conditions associated with critical COVID-19 infection

Cytokine Release Syndrome (CRS)

Cytokine profiles of patients with severe COVID-19 overlap with those seen in secondary hemophagocytic lymphohistiocytosis (sHLH) or macrophage activation syndrome. However, data regarding antagonists to IL-6 receptor or IL-1 receptor (tocilizumab and anakinra, respectively) for COVID-19 are limited at this time, and the efficacy of such treatments has not been determined. The current data do not support a firm course of action regarding the use of immunomodulatory agents or timing for their implementation. Thus, careful monitoring of patient clinical status and serum markers is crucial in determining the need for therapeutic intervention in exceptional cases (table 6).

First-line management of CRS is supportive, i.e., oxygen and ventilator support, fluid management, vasopressor/inotropic support, and treatment of complications. The use of dexamethasone has been proven to benefit patients on oxygen or mechanical ventilation due to acute SARS-CoV-2 infection (see dexamethasone above).

It is yet not clear if a subpopulation of CRS may benefit from IL-6 or IL-1 receptor blockers. Despite evidence of benefit in retrospective studies, preliminary analysis of phase III clinical trial on tocilizumab and sarilumab failed to demonstrate benefit in mortality or ventilator-free days⁶⁰⁻⁶³. Therefore, the use of IL-6 inhibitors should generally be avoided⁶⁴. The management of patients with CRS should be done in a multidisciplinary approach with rheumatology and infectious diseases specialists to weigh the risk-benefit of each approach.

If treatment with a biologic agent is considered as evaluated by rheumatology or infectious diseases services, it can be initiated before receiving results for these tests:

- T-spot test/QuantIFERON (Rule out latent TB).
- Hepatitis B & C serology.

Table 7. COVID-19-associated hyperinflammatory syndrome (cHIS) score⁶⁵

Variable	Score
Fever (>38°C)	1
Macrophage activation Ferritin ≥700 ug/L	1
Hematological dysfunction Neutrophil:lymphocyte ratio >10 <u>OR</u> Hb ≤ 9.2 + platelet ≤ 110	1
Coagulopathy D-dimer ≥1.5 ug/mL	1
Hepatic injury LDH ≥400 IU/L <u>OR</u> AST ≥100 U/L	1

cHIS score of 2 or more is associated with mechanical ventilation (sensitivity 95%, and specificity 59%) and in-hospital mortality (sensitivity 96%, and specificity 49%)⁶⁵. Even with a high cHIS score, alternate diagnosis for patient worsening (e.g., sepsis) should be considered.

Prothrombotic events in patients with COVID-19

In children, overall absolute venous thromboembolism (VTE) risk is much lower than adults, and the risk of thrombotic events in the context of COVID-19 in children is much less clear^{66,67}. Generally, antithrombotic therapy is not warranted in children with COVID-19. Coagulation panel (PT/INR, PTT, fibrinogen, platelet count, and D-dimer) should be considered at baseline (especially upon PICU admission) in children

with COVID-19 with projected stay > 24 hours and repeated as clinically indicated. VTE prophylaxis (pharmacological and/or mechanical) should be considered in patients with critical COVID-19 **AND** VTE risk factor^{66,68}:

- **Acute conditions:** lower extremity trauma or orthopedic surgery, spinal cord injury, burns.
- **Chronic conditions:** obesity, estrogen-containing medication, inflammatory bowel disease, nephrotic syndrome, thrombophilia
- **Historical factors:** previous DVT/PE, family history of VTE in first-degree relative <40 years

The decision of the type of VTE prophylaxis and end of prophylaxis should be made after consultation with a hematologist. Patients with limb swelling should undergo Doppler ultrasound to exclude deep vein thrombosis (DVT). CT chest Angiogram (CTA) should be requested if pulmonary embolism (PE) is suspected.

IX. Discharge of COVID-19 patients

Patients who no longer require medical attention or ongoing therapy can be discharged safely to home. However, depending on the duration of illness at the time of discharge, a further period of home isolation may be needed. For that, MOH guidelines for the discharge of hospitalized COVID-19 patients need to be followed.

Longer hospitalization and/or isolation need to be considered for a special population whose underlying condition or therapy puts them at higher risk for prolonged viral shedding (e.g., patients on steroids, immunocompromised patients, recent recipients of organ transplant). The discontinuation of transmission-based precautions should be done after discussion with infection control, or preventive medicine, or infectious diseases services (depending on the clinical situation).

Outpatient post-discharge follow-up is not needed for all COVID-19 patients. It is advised for those who develop complications or significant radiographic pneumonia to be provided with one or more follow-up visits to ensure uncomplicated recovery.

X. Out-patient follow-up

Most children with COVID-19 will not require long-term follow-up. However, some patients may

have severe disease, underlying diseases or develop COVID-19-related complications. Generally, the following patients are suggested to have post-hospitalization follow-up⁶⁹:

- Follow-up 4 weeks and three months after discharge for all admitted patients is recommended.
- The clinical encounter should review symptoms and perform a physical examination.
- COVID-19-related symptoms (cough, fever, shortness of breath, fatigue) should be reviewed at every visit.
- A repeat chest X-ray is recommended for all patients with initial abnormal radiological findings 4-6 weeks after discharge from the hospital.
- If persistent CXR changes are detected in follow-up, refer to the Pediatric Respiriology clinic for further assessment (e.g., CT chest)
- For patients who had a prolonged PICU admission with persistent hypoxemia or were discharged home on domiciliary oxygen therapy, it is recommended to do an echocardiogram looking for signs of pulmonary hypertension (PHTN).
- It is recommended for patients who develop MIS-C to have a repeat echocardiogram 4-6 weeks post-discharge (refer to the MIS-C section above for details).

XI. Special population and consideration in COVID-19

Immunocompromised children

Children who have primary immunodeficiency or are receiving immunosuppressive medication (chemotherapy, transplant patients) are at higher risk of severe and critical COVID-19. Patients and family members should strictly adhere to preventive measures.

If an immunocompromised patient is suspected or confirmed to have mild COVID-19, a close follow-up (in-person or telehealth depending on the degree of immunosuppression or disease severity) is recommended.

Patients with sickle cell disease

Patients with sickle cell disease (SCD) can present with pneumonia with or without acute chest syndrome (ACS) when infected with SARS-CoV-2⁷⁰.

Early identification and adequate management of ACS are important to prevent morbidity and manage COVID-19 pneumonia.

Neuromuscular disease patients (NMD)

Respiratory insufficiency is a major cause of mortality and significant morbidity in patients with NMD, especially in some types of NMD with respiratory muscles weakness and cardiomyopathy, which increase the risk for severe COVID-19 related complications.

Experts' opinion and special guidance for respiratory care provided to patients with NMD during active COVID-19 pandemic have suggested the following points when caring for a NMD child with Covid infection in hospital:

1. Close monitoring for increased oxygen demand, progressive CO₂ retention and acidosis in NMD patients with interstitial pneumonia.
2. Consider early initiation for ventilatory support (NIV/invasive) as they may rapidly progress to respiratory failure.
3. If noninvasive ventilation is used, a full or total face mask with a good seal is preferred. As NIMV is an aerosolizing therapy, please remember to TAKE precautions as per your hospital policy (i.e., use NIV in a negative pressure room, use a single passive circuit with two viral filters, one placed prior to the exhalation valve and the second at the circuit connection point to the PAP machine, and proper PPE)
4. Closely monitoring of the patients for signs of deterioration or no improvement on NIV. Don't delay invasive ventilation.
5. Adequate airway clearance measures are a cornerstone to expedite patient recovery. Consider mechanical insufflation- exsufflation therapy (cough assist) and chest PT with the guidance of the respirologist.
6. Caution with prone positioning in NMD patients with kyphoscoliosis as this may cause tracheobronchial compression by the vertebral bodies.
7. Tracheostomy routine care and changing the tracheostomy tube should be continued routinely and urgently in case of tube blockage during active COVID-19 infection with taking full precautions as this is an aerosol-generating procedure.

Neonates born to mothers with COVID-19

Neonatal resuscitation should be performed under airborne precautions. Breastfeeding is not contraindicated. If the mother is separated from her infant, the baby can be fed expressed breast milk. The newborn should be placed in quarantine (with or without the mother based on risk assessment) for at least 14 days after delivery. If the newborn becomes symptomatic, collect a nasopharyngeal swab for SARS-CoV-2 PCR, a full-septic workup is warranted (including a lumbar puncture), in addition to the tests mentioned under "general considerations." Initial antibiotic therapy should follow neonatal sepsis guidelines. Supportive therapy is the mainstay for COVID-19 treatment in this age group.

Breastfeeding

Based on the general consensus (WHO, AAP, CDC, NHS, and CPS), the benefit of breastfeeding outweighs any theoretical risks of viral transmission during the COVID-19 pandemic. Thus, HCWs should support and encourage breastfeeding following local infection control guidance. Those measures include wearing a facemask by the COVID-19 positive mother and adhering to hand and breast hygiene methods.

Immunization considerations

All families should be encouraged to immunize their children according to Kuwait's vaccination schedule. There is no evidence that infection with SARS-CoV-2 reduces childhood vaccine efficacy or effectiveness. However, it is not known if a period of time needs to be allowed after a child develops COVID-19. Generally, patients who are acutely infected with SARS-CoV-2 should wait until all symptoms are resolved and the child has fully recovered before receiving any vaccination.

Measles-mumps-rubella and varicella vaccines should be delayed in patients who had receive IVIG for Kawasaki disease (2 g/kg) for at least 11 months since the last immunoglobulin dose⁷¹. Also, patients actively receiving high-dose corticosteroids (≥ 2 mg/kg/day of prednisone or equivalent) for more than 14 days should avoid live vaccines (BCG, MMR, or varicella). These vaccines can be given after stopping steroids for \geq one month⁷².

Transporting COVID-19 Pediatric Patient

Transporting a patient with SARS-CoV-2 infection may be challenging as most of those patients are transported to receive advanced care in an ICU. Also, the transportation of COVID-19 patients poses an increased risk for virus transmission due to increased manipulation and proximity between the patient and HCWs during transport. Transporting children with COVID-19 infection is more challenging, as children may not adhere to wearing a face mask, and a potentially infected parent may be part of the transport. Therefore, infection control practices should be followed strictly during transport.

Safe transportation (figure 8) of critically ill patients is the goal. Efforts should be placed on staff training, pre-defined hospital transport protocols and checklists, the availability of appropriate transport equipment, and the timing of transport to ensure safe patient transfer^{73,74}. Refer to appendix 4 for more information.

XII. Acknowledgments

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XIII. List of Appendices

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- Appendix 3:** Airway Checklist for Intubation
- Appendix 4:** Treatment approach in MIS-C
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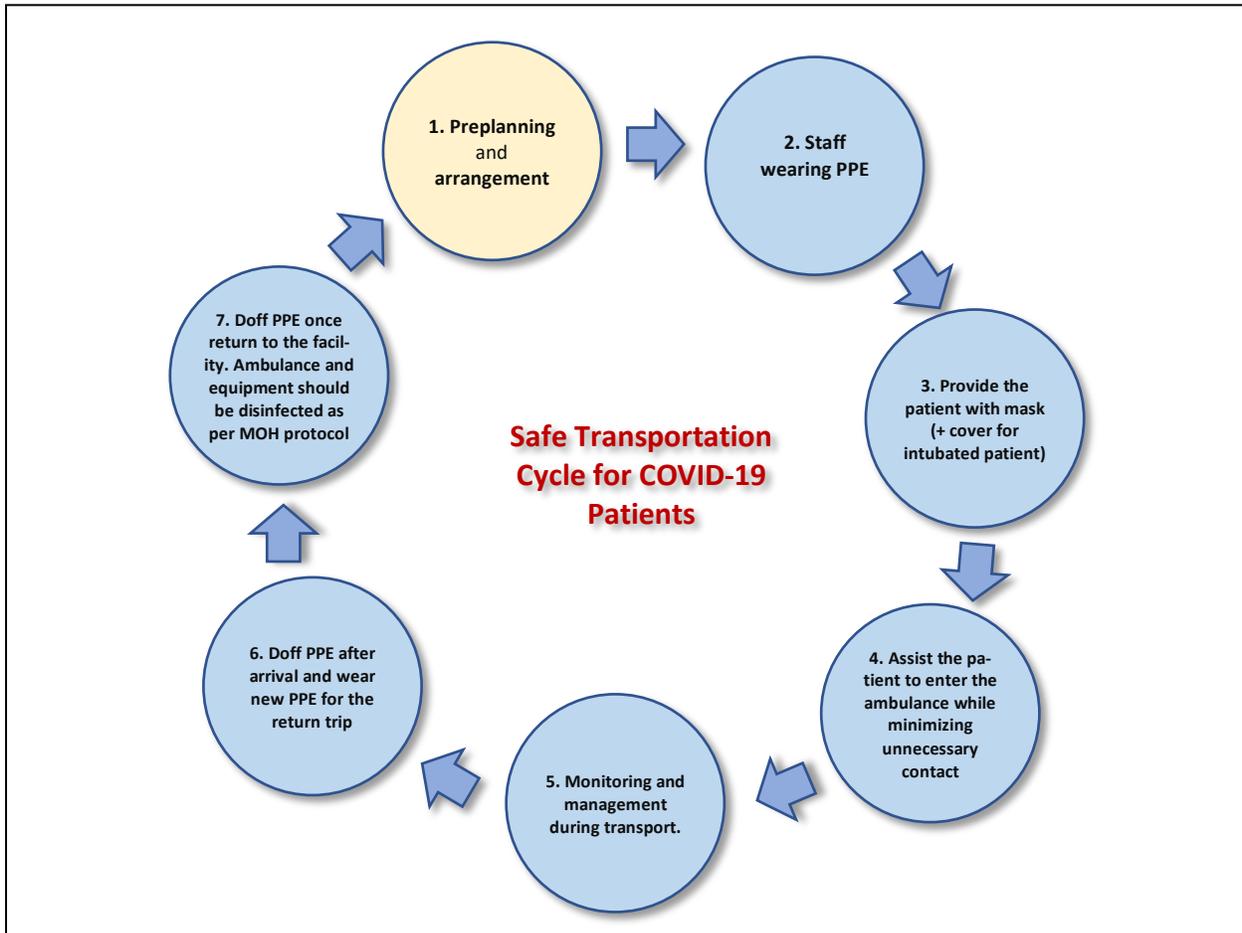


Figure 8. Safe transportation cycle for COVID-19 patients. Modified from the WHO⁵²

Version History

Version	Date	Updates
1.0	Aug 10, 2020	New Document
2.0	Nov 15, 2020	Added follow-up section Modified CRS and MIS-C sections Recommendations on the outpatient follow-up were added HFNC is no longer considered to provoke aerosol generation. Testing and management of influenza was added
3.0	Jan 1, 2022	Update in COVID-19 testing section. Update in COVID-19 & MIS-C management. Addressing the Neuro-muscular Disease (NMD) patients.

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Appendix 1: Donning and Duffing of Personal Protective Equipment (PPE)

Steps of donning PPE:

1. Perform hand hygiene using alcohol-based hand rub (ABHR) or wash hands with soap and water. ABHR is preferred when the hands are not visibly soiled.
2. Wear a long-sleeved, non-sterile, clean gown. Tie and close the gown
3. Wear a mask (medical mask or N95, depending on the type of isolation)
4. Wear goggles or face shield
5. Wear the gloves



Steps of duffing PPE:

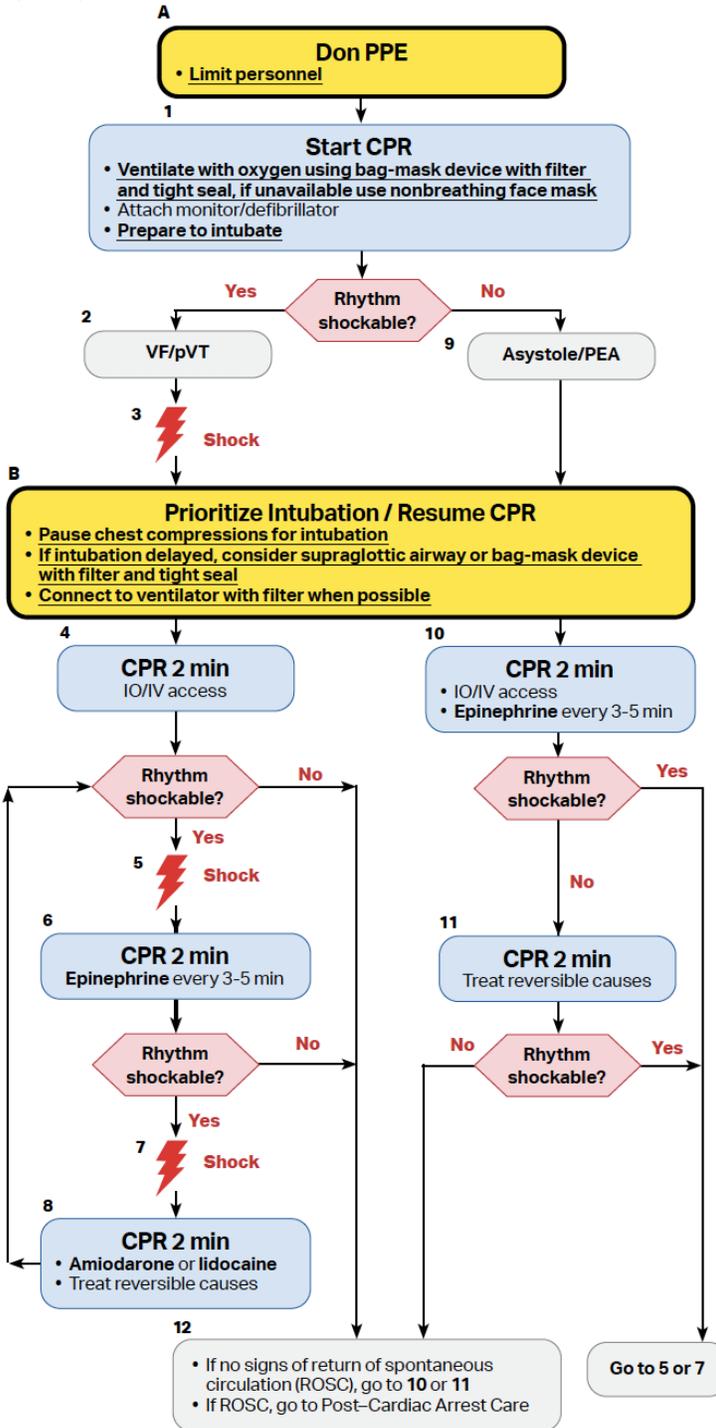
1. Remove the gloves. Gloves are removed first because they are considered heavily contaminated. The gloves should be removed by pinching the center inner aspect of the glove and turn the glove inside out while removing
2. Perform hand hygiene after removing the gloves
3. Remove the gown, starting by removing it from the back to the front. This way, the gown will be flipped inside out.
4. Perform hand hygiene
5. Remove eye protection and mask
6. Perform hand hygiene



Appendix 2. Pediatric cardiac arrest algorithm in view of COVID-19 pandemic adopted from American Heart Association²⁸

Pediatric Cardiac Arrest Algorithm for Suspected or Confirmed COVID-19 Patients

Updated April 2020



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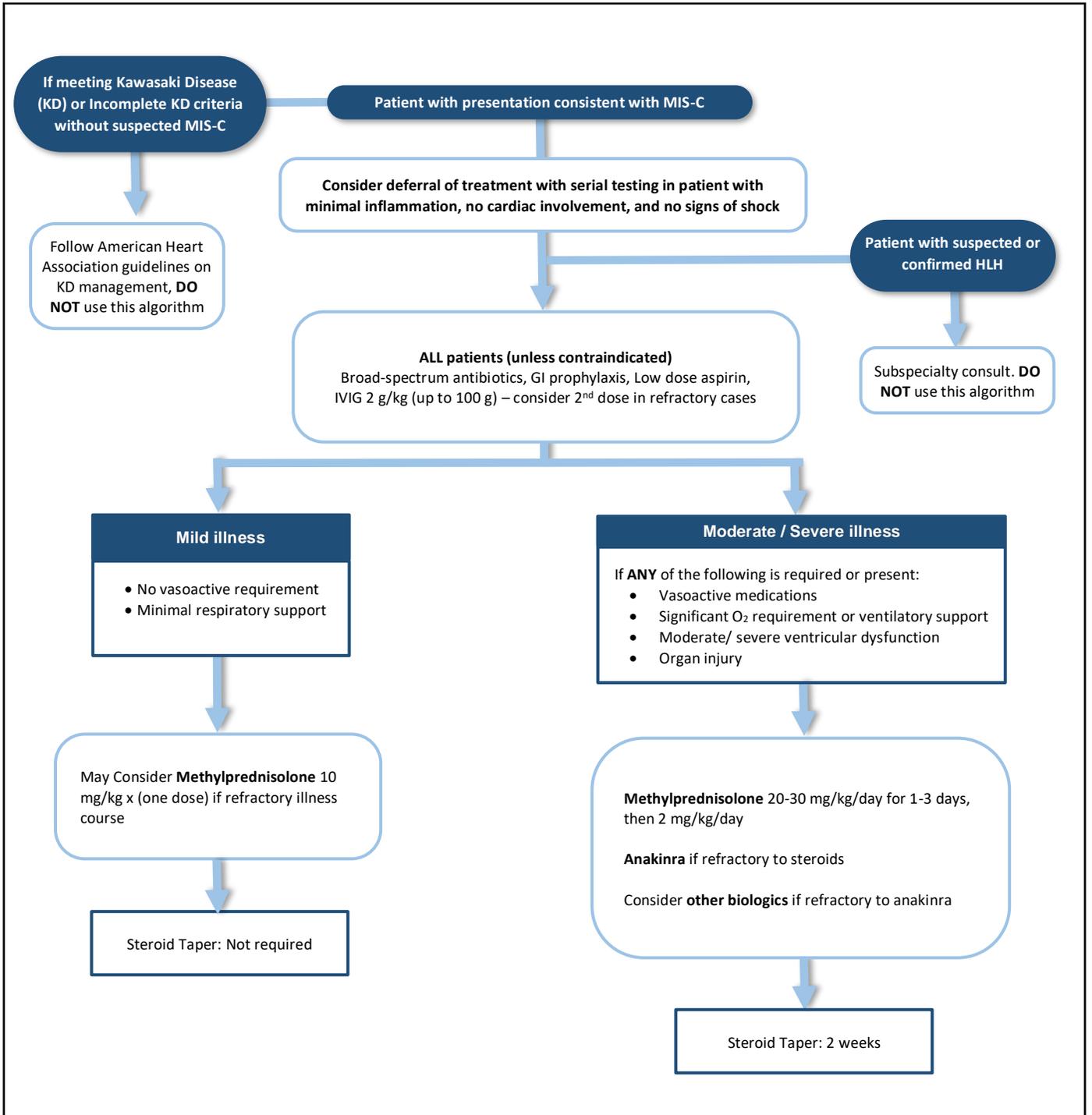
CPR Quality
<ul style="list-style-type: none"> • Push hard (≥$\frac{2}{3}$ of anteroposterior diameter of chest) and fast (100-120/min) and allow complete chest recoil. • Minimize interruptions in compressions. • Avoid excessive ventilation. • Change compressor every 2 minutes, or sooner if fatigued. • If no advanced airway, 15:2 compression-ventilation ratio.
Shock Energy for Defibrillation
<p>First shock 2 J/kg, second shock 4 J/kg, subsequent shocks ≥4 J/kg, maximum 10 J/kg or adult dose</p>
Advanced Airway
<ul style="list-style-type: none"> • Minimize closed-circuit disconnection • Use intubator with highest likelihood of first pass success • Consider video laryngoscopy • Prefer cuffed endotracheal tube if available • Endotracheal intubation or supraglottic advanced airway • Waveform capnography or capnometry to confirm and monitor ET tube placement • Once advanced airway in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions
Drug Therapy
<ul style="list-style-type: none"> • Epinephrine IO/IV dose: 0.01 mg/kg (0.1 mL/kg of the 0.1 mg/mL concentration). Repeat every 3-5 minutes. • Amiodarone IO/IV dose: 5 mg/kg bolus during cardiac arrest. May repeat up to 2 times for refractory VF/pulseless VT. or • Lidocaine IO/IV dose: Initial: 1 mg/kg loading dose. Maintenance: 20-50 mcg/kg per minute infusion (repeat bolus dose if infusion initiated >15 minutes after initial bolus therapy).
Return of Spontaneous Circulation (ROSC)
<ul style="list-style-type: none"> • Pulse and blood pressure • Spontaneous arterial pressure waves with intra-arterial monitoring
Reversible Causes
<ul style="list-style-type: none"> • Hypovolemia • Hypoxia • Hydrogen ion (acidosis) • Hypoglycemia • Hypo-/hyperkalemia • Hypothermia • Tension pneumothorax • Tamponade, cardiac • Toxins • Thrombosis, pulmonary • Thrombosis, coronary

Appendix 3. Airway Checklist for Intubation†

Checklist for intubation		
Plan ahead		
1	Make sure you have practiced donning and doffing and have a buddy. Know your PPE	
2	Assign tasks—intubator (most experienced with airways), team leader, airway assistance, a second nurse for medications. Minimize staff in the room	
3	Negative pressure room, if available	
4	Establish a clear strategy for communication	
Intubation		
1	Don PPE	
2	Establish monitoring, IV access, intubation equipment (consider video laryngoscopy, if available), filter between face-mask and bag	
3	Preoxygenate	
4	Plan for rapid sequence induction, with minimal bag mask ventilation	
5	Intubate and confirm	
6	Attach to ventilator, with inline suction	
7	Clean, relevant surfaces	
8	Disposable equipment should be disposed of via hospital protocol	
9	Ensure proper doffing, monitored by a buddy	
RSI Medications (choose one of each category)		
1	Analgesics Fentanyl (IV) 2-5 microgram/kg Morphine (IV) 0.2 mg/kg	
2	Sedatives Midazolam (IV) 0.1-0.2 mg/kg Ketamine (IV) 1-2 mg/kg	
3	Paralytics Cisatracurium (IV) 0.1 mg/kg Succinylcholine (IV) 1-2 mg/kg Rocuronium (IV) 1 mg /kg	
4	Adjuvants (if required) Atropine (IV) 0.02 mg/kg (Minimum dose 0.1 mg; Maximum dose 0.5 mg)	

†Adapted from Pediatric Intensive Care Society UK: Pediatric Critical Care Coronavirus Disease 2019 Guidance.

Appendix 4. Treatment approach of MIS-C Cases (modified from Jonat *et al.* ⁷⁵)



Appendix 5. Safe Transportation Checklist for COVID-19 Pediatric Patients[†]

Checklist for COVID-19 Transportation		
Transport equipment to be <u>pre-arranged</u>		
1	Portable ventilator connected to oxygen cylinder	
2	Extra oxygen cylinder with key	
3	Portable monitor with defibrillator	
4	Disposable or sterilizable bag-valve-mask with oxygen tubing	
5	COVID-19 Intubation, emergency medication Kit*, and Closed suction system	
6	Infusion pumps with extended tubing	
7	Transparent drape to cover the patient (such that enables easy access to the airway)	
8	Transparent protective covers for equipment	
Preparations <u>before</u> transport		
1	Coordinate the timing of transport and the final location of patient placement with the receiving Department	
2	Coordinate the transport route within the receiving and dispatching hospitals. This should be done in coordination with the transport team, with infection control and with public relation offers/hospital security. Ensure that the transport route is clear of bystanders and other hospital staff before transport	
3	Limit personnel for patient transport	
4	Ensure closed loop communication can be conducted between team members	
5	Wrap transport equipment in the transparent covers	
6	Ensure functionality of wrapped transport equipment after attaching to the patient	
7	Clearly label an emergency IV access	
<u>Transport</u> process		
1	Transport team should wear appropriate PPE outside the patient room before transport	
2	Transport team must adhere to contact/droplet precautions throughout transport	
3	Intubated patients: cover intubated patient with a plastic transparent drape and non-intubated patients should wear a surgical face mask, if possible.	
4	If a caregiver accompanies the child during transport: S/he should wear a face mask and to follow infectious control measures	
<u>After</u> arrival		
1	Ensure patient delivery to the relevant professionals in the designated COVID area	
2	Remove all protective equipment covering	
3	Doff PPE in a nearby clinical area	
4	Wear new PPE for the return journey	
5	Complete patient handover outside the patient's room	
6	Return the equipment by the same ambulance	
7	Return all the transport equipment to the area of initiation of transport for decontamination	
<u>Documentation</u>		
1	HCW identification, condition of the patient, events during transport, medication given, and duration of transport should be documented	

[†]Adopted from: Yousef et al. Intensive care medicine. 2020⁷⁴

***Content of COVID intubation and emergency medication kit:** The kit should only include single use disposable or sterilizable items. (Endotracheal tubes of different sizes, oropharyngeal airways, one tube tie, lubricant, one scalpel, one HME filter, one disposable laryngoscope, one 10-ml syringe, one plastic drape, one bougie, one disposable air-bag-valve-mask and RSI/resuscitation Medications)

Appendix 6: Summary of the dosing and medication-related information for pediatric patients with COVID-19

Medication	Dose	Notes
Anakinra (IV/SC)	The dose needs to be decided with rheumatology (typical 4mg/kg once daily) ⁵²	The dosage and duration of anakinra should be decided with rheumatology
Aspirin (PO)	Low dose: 3-5 mg/kg once daily	
Ceftriaxone (IV)	50 mg/kg/dose IV once daily (maximum daily dose, non-meningitic, 2g/dose)	
Dexamethasone (PO/NG/IV)	Severe and Critical COVID-19: 0.15 mg/kg (max 6 mg/day) once daily Mild Croup: (PO) 0.15mg/kg/dose (single dose) Moderate/Severe Croup: (PO/IV) 0.6 mg/kg/dose, to a maximum of 10 mg	Avoid high-dose steroids in patients with severe COVID-19 as may be linked to poorer outcomes
Infliximab (IV)	5 mg/kg once	
Intravenous immunoglobulin (IVIG)	MIS-C: 2 g/kg once over 12 hours. Some patients may need the second dose	Patients who receive high dose IVIG should not get MMR or varicella vaccine in the following 11 months
Ipratropium bromide (inhaled)	MDI with spacer (preferred): <20 kg = 3 puffs ≥20 kg = 6 puffs Nebulization: <20 kg = 0.25 mg ≥20 kg = 0.5 mg	- Every 20 minutes - Maximum 3 doses
Magnesium sulfate (IV)	25-50 mg/kg (maximum 2g)	- Monitor blood pressure - Bolus over 20 minutes
Methylprednisolone (IV)	1-2 mg/kg/dose (maximum 60 mg q6h) Pulse steroids: 30 mg/kg once daily	The duration of pulse steroids should be decided with rheumatology
Prednisone/prednisolone (PO)	1-2 mg/kg/day (maximum 60 mg)	
Remdesivir (IV)	Loading dose: 5 mg/kg/dose (max: 200mg) once Maintenance: (days 2-5) 2.5 mg/kg/dose (max: 100mg) once daily	Longer therapy (up to 10 days) may be considered in slow responders
Salbutamol (inhaled)	MDI with spacer (preferred): <20 kg = 5 puffs (0.1mg/puff) ≥20 kg = 10 puffs Nebulization: <20 kg = 2.5 mg ≥20 mg = 5 mg	- Every 20 minutes during the first hour - Monitor potassium serum levels in patients requiring frequent doses
Salbutamol (IV)	Loading dose: 10 mcg/kg over 10 minutes, followed by 1 mcg/kg/min Titrate upwards with increments of 1 mcg/kg/min (maximum 5mcg/kg/min)	Monitor heart rhythm and rate, glucose and electrolytes
Teicoplanin (IV)	Infants ≤2 months: 16 mg/kg/dose once, then 8 mg/kg/dose q24hr Infants >2 months and children <12 years: 10 mg/kg/dose q12hrs x 3 doses, then 6-10 mg/kg/dose q24hrs	
Tocilizumab (IV)	Weight < 30 kg: 12 mg/kg once over 1 hour (max dose 800 mg) Weight > 30 kg: 8 mg/kg once over 1 hour (max dose 800 mg)	Refer to CRS above for lab investigations and follow-up. If no improvement at 12-18 hours, consider repeat with same dose