MANAGEMENT PROTOCOL OF CHILDREN WITH COVID-19

Government of Nepal
Ministry of Health and Population

FOREWORD

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CHAPTER 1

INFECTION PREVENTION AND CONTROL (IPC) FOR COVID-19

1.1. Background

Infection prevention and control (IPC), an essential part of health care infrastructure, is the practical discipline concerned with preventing healthcare-associated infection.

The five IPC strategies required to prevent or limit transmission of COVID-19 in health care facilities include:

1. Screening and triage for early recognition of patients with suspected COVID-19, and rapid implementation of source control measures
2. Applying standard precautions for all patients
3. Implementing additional precautions
4. Implementing administrative controls
5. Implementing environmental and engineering controls

Screening and Triage for Early Recognition of Patients with Suspected COVID-19, and Rapid Implementation of Source Control Measures

To facilitate screening and triage, health-care facilities should:
Establish entrances and display information for patients with signs and symptoms of COVID-19 to report to designated area for screening
Train staffs on the signs and symptoms of COVID-19 and the most recent case definitions
Encourage health care workers (HCWs) to be alert to potential COVID-19 infection in all patients
Establish well-equipped screening and triage stations

Ensure that screening personnel maintain a distance of at least 1 meter from patients, ideally with a separation created by a glass/plastic screen. If not possible, mask and eye protection should be worn
Use a screening algorithm to promptly identify and direct patients with suspected COVID-19 to an isolation room or dedicated COVID-19 waiting area; all suspected COVID-19 patients should wear masks for source control purposes and be positioned at least 1 meter apart from each other in a designated, well-ventilated, waiting area

For Isolation or designated waiting area:
Health-care facilities without enough single isolation rooms in emergency departments should designate a separate, well-ventilated area (with benches/chairs placed at least 1 meter apart) where suspected COVID-19 patients can wait
The area should have toilets, hand hygiene stations, and trash bins with lid for disposal of paper tissues and display graphic information on how to perform hand and respiratory hygiene

1.1. Applying standard precautions for all patients

Standard precautions represent the basic level of infection control precautions that should be used at all times in the care of all patients. Standard precautions include, but are not limited to, hand and respiratory hygiene, the use of appropriate personal protective equipment (PPE) according to risk assessment, environmental cleaning, and safe waste management.

1.1.1 Hand hygiene is one the most effective measures to prevent the spread of COVID-19 and other pathogens. For optimal hand hygiene performance, following principles should be applied:
• perform hand hygiene according to the WHO's My 5 Moments for Hand Hygiene (Figure 1) approach in the following five situations: before touching a patient, before performing any clean or aseptic procedure, after exposure to body fluid, after touching a patient, and after touching a patient's surroundings
• hand hygiene includes either cleansing hands with an alcohol-based hand rub (ABHR) containing at least 70% alcohol (for 20-30 seconds), or with soap, water and disposable towels (for 40-60 seconds)

• alcohol-based hand rub products are preferred if hands are not visibly soiled
• wash hands with soap and water (Figure 2) when they are visibly soiled

1.2.2 Respiratory hygiene (Figure 3) measures to be ensured are:
• display graphic information on the need to cover nose and mouth with a tissue or bent elbow when coughing or sneezing
• perform hand hygiene after contact with respiratory secretions or objects that may be potentially contaminated with respiratory secretions
• give patients with suspected COVID-19 a medical mask to wear
Children aged up to five years should not wear masks for source control. The rationale includes consideration of the fact that by the age of five years, children usually achieve significant developmental milestones, including the manual dexterity and fine motor coordination movements needed to appropriately use a mask with minimal assistance.

1.2.3. Use of personal protective equipment (PPE):

The rational and correct use of PPE (Table 1) reduces exposure to pathogens. The effectiveness of PPE strongly depends on:

• Staff training on putting on and removing PPE;
•Prompt access to sufficient supplies;
• Appropriate hand hygiene;
• Health worker compliance;
• Regular monitoring and feedback by IPC personnel.

Steps to put on (don) and remove (doff) PPE are included in Figure 4

and 5 Table 1. Recommended type of PPE to be used in the context of COVID-19 disease, according to the setting, personnel and type of activity

Targeted peronnel	Activity	Medical Mask	Gown		Eye Protection	Respirator (N95/ FFP2)			Remarks
Healthcare facilities (Inpatient facilities): Patient room									
Healthcare workers	Providing direct care to COVID patients	✔	✔	✔	✔	✖	✖	✖	
	Aerosol-generating procedures	✔	✔	✔	✔	✔	✔		
Cleaners	Entering the room of COVID-19 patients	✔	✔	✔ (heavy duty)	✔	✖	✖	✔	eye protection if risk of splash from organic material or chemicals
Visitors[b]	Entering the room of a COVID patient	✔	✔	✔	✖	✖	✖	✖	
Inpatient facilities: Other areas of patient transit (e.g., wards, corridors)									
All staffs & HCWs	Any activity that does not involve contact with COVID-19 patients COVID-19 patients	✖	✖	✖	✖	✖	✖	✖	No PPE required
Inpatient and Outpatient facilities: Triage									
HCWs	Preliminary screening not involving direct contact[c]	✖	✖	✖	✖	✖	✖	✖	No PPE required[d] Maintain spatial distance of at least 1 m
Patients with respiratory symptoms	Any	✔	✖	✖	✖	✖	✖	✖	Maintain spatial distance of at least 1 m. Provide medical mask if tolerated by patient

Patients without respiratory symptoms	Any	✗	✗	✗	✗	✗	✗	✗	No PPE required
Inpatient facilities: Laboratory									
Lab Technician	Manipulation of respiratory samples	✓	✓	✓	✓	✗	✗	✗	Eye protection if risk of splash
Healthcare facilities (Outpatient facilities): Consultation room									
Healthcare workers	Examination of patients with respiratory symptoms	✓	✓	✓	✓	✗	✗	✗	
HCWs	Examination of patients without respiratory symptoms								PPE as per standard precau-tions &risk assess-ment
Patients with respiratory symptoms	Any	✓							Provide medical mask if tolerated
without respiratory symptoms	Any								No PPE required
Cleaners	After and between consulta-tions with patients with respiratory symptoms	✓	✓	✓ **(heavy duty)**	✓			✓	Eye protection if splash risk from organic mate-rial or chemicals
Outpatient facilities: Waiting room									
Patients with respiratory symptoms	Any	Provide medical mask if tolerated; Immediately move the patient to an isolation room; if not feasible, ensure spatial distance of at least 1 m from other patients							
Patients without respiratory symptoms	Any								No PPE required
Administrative areas									
All staff, including HCWs	Administra-tive tasks								No PPE required

Ambulance or transfer vehicle									
Healthcare workers	Transporting suspected COVID-19 patients to the referral healthcare facility	✔	✔	✔	✔				
Driver	Involved only in driving the suspected patient and the com-partment separated								No PPE required; Maintain spatial distance of at least 1 m.
	Assisting with loading/ unloading of suspected patient	✔	✔	✔	✔				
	No direct contact with patient but no separa-tion between compart-ment	✔							
Patient with suspected COVID-19	Transport to the referral healthcare facility	✔							Medical mask if tolerated
Cleaners	Cleaning after and between transport of patients with suspected COVID-19 disease to the referral healthcare facility	✔	✔	✔	✔			✔	

[a] In addition to using appropriate PPE, frequent hand hygiene & respiratory hygiene should always be performed. PPE should be discarded in an appropriate waste container after use, and hand hygiene performed before putting on (donning) and after taking off PPE (doffing).

[b] Number of visitors should be restricted. If visitors must enter a COVID-19 patient's room, they should be provided with clear instructions on: donning &doffing perform hand hygiene before donning & doffing; supervised by a healthcare worker.

[c] This category includes the use of no-touch thermometers, thermal imaging cameras, and limited observation and questioning, all while maintaining a spatial distance of at least 1 m.

[d] All rapid response team members must be trained in performing hand hygiene, donning & doffing to avoid self-contamination.

1.2.4. Environmental cleaning (Table 2)

- Clean surfaces thoroughly with water and detergent;
- Apply a disinfectant solution, either 0.1% (1000ppm) sodium hypochlorite or 70-90% ethanol. However, if there are large spills of blood or body fluids, a concentration of 0.5% (5000ppm) sodium hypochlorite should be used;
- Contact time of a minimum of 1 minute is recommended for ethanol, chlorine-based products and hydrogen peroxide ≥0.5%;
- After appropriate contact time, disinfectant residue may be rinsed off with clean water if required.
- Medical devices and equipment, laundry, food service utensils and medical waste should be managed in accordance with safe routine procedures.

Table 2. Health-care setting: Recommended frequency of cleaning of environmental surfaces, according to the patient areas with suspected or confirmed COVID-19 patients.

Patient area	Frequency a	Additional guidance
Screening/triage area	At least twice daily	Focus on high-touch surfaces, then floors (last).
Inpatient rooms / cohort- occupied	At least twice daily, preferably three times daily, in particular for high-touch surfaces	Focus on high-touch surfaces, starting with shared/common surfaces, then move to each patient bed; use new cloth for each bed if possible; then floors (last).
Inpatient rooms- unoccupied (terminal cleaning)	Upon discharge/ transfer	Low-touch surfaces, high-touch surfaces, floors (in that order); waste and linens removed, bed thoroughly cleaned and disinfected.

Outpatient / ambulatory care rooms	After each patient visit (in particular for high-touch surfaces) and at least once daily terminal clean	After each patient visit (in particular for high-touch surfaces) and at least once daily terminal clean
Hallways/corridors	At least twice daily [b]	High-touched surfaces including railings and equipment in hallways, then floors (last).
Patient bathrooms/ toilets	Private patient room toilet: at least twice daily Shared toilets: at least three times daily	High-touch surfaces, including door handles, light switches, counters, faucets, sink bowls, then toilets and finally floor (in that order). Avoid sharing toilets between staff and patients.

[a]Environmental surfaces should also be cleaned and disinfected whenever visibly soiled or if contaminated by body fluid (e.g., blood); bFrequency can be once a day if hallways are not frequently used.

1.2.5. Waste Management

Health-care waste produced during the care of patients with suspected or confirmed COVID-19 is considered to be infectious and should be collected safely in clearly marked lined containers and sharp safe boxes.

To safely manage health-care waste, facilities should:
• assign responsibility and adequate human and material resources to segregate and dispose of waste
• treat waste preferably on-site, and then safely dispose them. If waste is moved off-site, it is critical to understand where and how it will be treated and disposed
• use appropriate PPE (boots, long-sleeved gown, heavy-duty gloves,] mask, and goggles or a face shield) while managing infectious waste and perform hand hygiene after doffing
• prepare for increases in the volume of infectious waste during the COVID-19 outbreak, especially through the use of PPE.

1.3. Implementing additional precautions

Transmission of the COVID-19 virus may occur by direct contact with infected people (respiratory droplets and contact routes) and indirect contact with surfaces in the immediate environment or with objects used on the infected person (e.g. stethoscope or thermometer). Airborne transmission of the COVID-19 virus is possible under circumstances and settings where aerosol generating procedures (AGPs) are performed.

Apart from standard precautions, additional precautions that can be implemented for COVID-19:

Isolation and cohorting of patients with suspected or confirmed COVID-19 in single rooms or, if unavailable, cohorting them in the same room with the following principles:
designate a team of health workers, where possible, for care of patients with suspected or confirmed COVID-19 to reduce the risk of transmission
restrict the number of health workers in contact with each COVID-19 patient
patients should be placed in well ventilated single rooms if feasible
when single rooms are not available, suspected, probable or confirmed COVID-19 patients should be grouped together (cohorted) in adequately ventilated areas with beds placed at least 1 meter apart (e.g. suspected with suspected)
avoid moving and transporting patients out of their room or area unless medically necessary. Use designated portable X-ray equipment and/or other designated diagnostic equipment
If transport is required, use predetermined transport routes to minimize exposure for staff, other patients and visitors, and give the patient a medical mask to wear if tolerated
ensure that HCWs who are transporting patients perform hand hygiene and wear appropriate PPE
equipment should be either single-use and disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers). If equipment needs to be shared between patients, clean and disinfect after each use
maintain a record of all staff entering the patient's room

Contact and droplet precautions in addition to standard precautions should be followed, with the following principles:
perform hand hygiene before donning and after doffing; use appropriate PPE
HCWs and caregivers working in clinical areas (in areas with community transmission COVID-19 should continuously wear a medical mask during all routine activities throughout the entire shift
It is not necessary for HCWs and caregivers to wear boots, coverall and apron during routine care
extended use of medical mask, gown and eye protection can be applied during the care of COVID-19 patients during PPE shortages
For a COVID-19 patient who is infected with a multi-drug resistant organism (e.g. Clostridioides difficile), a new set of gown and gloves are needed after caring for such patients
HCWs should refrain from touching their eyes, nose or mouth with potentially contaminated gloved or bare hands
notify the area receiving the patient of any necessary precautions before the patient's arrival
frequently clean and disinfect surfaces with which the patient is in contact
Some AGPs have been associated with an increased risk of transmission of coronaviruses (SARS-CoV-1, SARS-CoV-2 and MERS-CoV). The current WHO list of these AGPs is: tracheal intubation, non-invasive ventilation (e.g. BiPAP, CPAP), tracheotomy, cardiopulmonary resuscitation, manual ventilation before intubation, bronchoscopy, sputum induction induced by using nebulized hypertonic saline, and autopsy procedures. It remains unclear whether aerosols generated by nebulizer therapy or high-flow oxygen delivery are infectious.
perform procedures in an adequately ventilated room
use appropriate PPE: wear a particulate respirator at least as protective as a US National Institute for Occupational Safety and Health (NIOSH)-certified N95, European Union (EU) standard FFP2, or equivalent
Although initial fit testing is needed prior to the use of a particulate respirator, many countries and health-care facilities do not have a respiratory fit testing programme. Therefore, it is critical that when health workers put on a disposable particulate respirator, they should always perform the required seal check to ensure there is no leakage

Other PPE items include eye protection (i.e. goggles or a face shield), long-sleeved gown and gloves. If gowns are not fluid resistant, HCWs performing AGPs should use a waterproof apron if the procedure is expected to produce a large volume of fluid that might penetrate the gown
in the intensive care units, where AGPs are frequently performed, the HCW may choose to wear a particulate respirator throughout his or her shift, in areas of community transmission; keep the number of persons present in the room to the absolute minimum required for the patient's care.

1.4. Implementing administrative controls:

Administrative controls and policies for the prevention and control of transmission of COVID-19 within the health-care facility include:
• Establishing sustainable IPC infrastructures and activities
• Educating patients' caregivers
• Developing policies for early recognition of patients with suspected COVID-19
• Ensuring access to laboratory testing for COVID-19 detection
• Preventing overcrowding, especially in the emergency department
• Providing dedicated waiting areas for symptomatic patients
• Planning for (e.g. repurposing of other wards) and isolating COVID-19 patients
• Ensuring adequate supplies of PPE
• Ensuring adherence to IPC policies and procedures in all aspects of health care

1.5. Implementing environmental and engineering controls

Environmental and engineering controls, an integral part of IPC, aim to reduce the concentration of infectious respiratory aerosols (i.e. droplet nuclei) in the air and the contamination of surfaces and inanimate objects. They include standards for adequate ventilation according to specific areas in health-care facilities, adapted structural design, spatial separation, as well as adequate environmental cleaning.

1.1.1 Collecting and handling laboratory specimens from patients with suspected COVID-19:

All specimens collected for laboratory investigations should be regarded as potentially infectious. Health workers who collect, handle or transport any clinical specimens should adhere to the following measures and biosafety practices to minimize the possibility of exposure to pathogens:

Ensure that HCWs who collect specimens, including nasopharyngeal and oropharyngeal swabs, use appropriate PPE (i.e. eye protection, a medical mask, a long-sleeved gown and gloves). If the specimen is collected with an AGP (e.g. sputum induction), personnel conducting the procedure should wear a particulate respirator at least as protective as a NIOSH-certified N95, an EU standard FFP2, or equivalent
Ensure that all personnel who transport specimens are trained in safe handling practices and spill decontamination procedures
Place specimens for transport in leak-proof specimen bags (i.e. secondary containers) that have a separate sealable pocket for the specimen (i.e. a plastic biohazard specimen bag), with the patient's label on the specimen container (i.e. the primary container), and a clearly written laboratory request form
Ensure that laboratories adhere to appropriate biosafety practices and transport requirements based on WHO's interim Laboratory biosafety guidance related to COVID-19
Deliver all specimens by hand whenever possible. Do not use pneumatic-tube systems to transport specimens
Document clearly patient's full name, date of birth and clinical diagnosis of the suspected case of COVID-19 on the laboratory request form. Notify the relevant laboratory as soon as possible that the specimen is being transported

1.2 Considerations for surgical procedures:

In the context of the COVID-19 pandemic, every surgical procedure may entail risk for both health workers and patients. Any decision on whether to operate on a patient should not be based on the patient's COVID-19 status, but on need (e.g. trauma or emergency), the risks and benefits of surgery (e.g. life-threatening outcomes of patient harm if surgery is delayed), and patient clinical conditions. Recent data point to a high proportion of post-operative pulmonary complications associated with increased mortality in patients with COVID-19.

1.3 IPC measures recommended for outpatient care:

• Apply the basic principles of IPC and standard precautions in all health-care facilities, including outpatient settings and primary care
• consider alternatives to face-to-face outpatient visits using telemedicine (e.g. telephone consultations or cell phone videoconference) to provide clinical support without direct contact with the patient
• screening, early recognition and isolation of patients with suspected COVID-19
• emphasis on hand hygiene, respiratory hygiene and medical masks to be used by patients with respiratory symptoms
• appropriate use of contact and droplet precautions when performing clinical exam on patients with suspected COVID-19
• when symptomatic patients are required to wait, ensure they have a separate waiting area where patients can sit at least 1-meter apart and provide them with masks

1.4 Dead body management:

Health workers should do a preliminary evaluation and risk assessment before undertaking any activity related to the management of suspected or confirmed COVID-19 fatality and follow WHO's IPC guidance for safe management of dead bodies in the context of COVID-19.

Health workers should:
• perform hand hygiene before and after handling the body
• use appropriate PPE based on the level of interaction with the body and risk assessment (e.g. use of eye protection and medical masks in addition to gloves and fluid-resistant gown or apron, if there is a risk of body fluids splashes while handling the body)
• ensure that any body fluids leaking from orifices are contained and cover body in cloth to transfer to mortuary area
• not be engaged in any other activity during body handling or preparation
• disinfect any non-disposable equipment used during handling of the body as per WHO guidance
• correctly remove and dispose of PPE when finished
Body bags are not necessary for COVID-19, although they may be used for other reasons such as excessive body fluid leakage or absence of re-frigerated morgue, especially in countries with a warm climate. If more than 24 hours has passed since the person died, or if burial/cremation is not foreseen within the next 24-48 hours, a second body bag may be used.

CHAPTER 2

SUSPICION, TESTING AND MANAGEMENT OF COVID-19 IN CHILDREN

2.1. When to suspect COVID 19 infection in children?

If the **children** are having signs/symptoms like:

Most common symptoms:

- Fever
- Dry cough
- Tiredness

Less common symptoms:

- Aches and pains
- Sore throat
- Diarrhea
- Conjunctivitis
- Headache
- Loss of taste or smell
- A rash on skin, or discoloration of fingers or toes

Serious symptoms:

- Difficult breathing or shortness of breath
- Chest pain or pressure
- Loss of speech or movement

Infants may have following additional symptoms:

- Diarrhea
- Vomiting
- Decreased feeding

2.2. Diagnosis of suspected children with COVID 19 symptoms

Indications for testing:

- A child with acute respiratory illness (fever and cough or fever and shortness of breath) AND new loss of smell OR taste.
- A child with acute respiratory illness (fever and cough or fever and shortness of breath) AND any two of these (chills, muscle pain, diarrhea, sore throat).
- A child with acute respiratory illness (fever and cough or fever and shortness of breath) in the absence of an alternative diagnosis that fully explains the clinical presentation.
- Fever (>3 days) AND two of the following:

(i) Rash, non-purulent conjunctivitis or muco-cutaneous inflammation;

(ii) Hypotension or shock;

(iii) New cardiac abnormalities;

(iv) New bleeding disorder; and

(v) Diarrhea, vomiting or abdominal pain.

- A child with acute respiratory illness (fever and cough or fever and shortness of breath) with underlying chronic conditions, immunocompro mised conditions.
- Presentation with severe illness (e.g. new requirement for supplemental oxygen or increased requirement from baseline, new or increased need for ventilation [invasive or noninvasive] or clinical manifestations of multisystem inflammatory syndrome in children.
- **Children who were in close contact** (contact of at least 15 minutes over a 24-hour period within a distance of less than 6 feet) **with a person with confirmed or probable SARS-CoV-2 infection, and developed ANY of the symptoms described above.**
- Children who require screening, i.e. prior to a medical procedure such as elective surgery or as a school or workplace requirement.
- Infant born to a mother with suspected or confirmed COVID-19.
- If the treating clinician suspects COVID 19.

2.2.1 Testing Modalities

a. Nucleic Acid Amplification Tests (NAATs):

b. Antigen Testing for SARS-CoV-2

c. Antibody testing

It is useful for diagnosis of prior infection (or infection of at least 3 to 4 weeks' duration). The specimen used is blood.

Possible Indications of Antibody testing

1. In case of suspected post-infectious syndrome
   (e.g., Multisystem Inflammatory Syndrome in Children; MIS-C).
   (For details, please refer to the chapter on Multisystem Inflammatory Syndrome in Children; MIS-C).
2. In surveillance and epidemiologic studies.

2.3. Clinical spectrum of COVID 19

WHO has classified COVID 19 disease in the following three categories:

1. Critical COVID-19– Defined by the criteria for acute respiratory distress syndrome (ARDS), sepsis, septic shock, or other conditions that would normally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy.

2. Severe COVID-19– Defined by any of:

- Oxygen saturation < 90% on room air*;
- Respiratory rate > 30 breaths/min in children > 5 years old; ≥ 60 breaths/min in children < 2 months old; ≥ 50 in children 2–11 months old; and ≥ 40 in children 1–5 years old;
- Signs of severe respiratory distress (accessory muscle use, inability to complete full sentences, and, in children, very severe chest wall in drawing, grunting, central cyanosis, or presence of any other general danger signs).

3. Non-severe COVID-19– Defined as absence of any criteria for severe or critical COVID-19.

*Saturation measurement in children is very difficult and unreliable, clinical judgment is very essential to treat a child with SpO_2 monitoring. So, in a clinical setting SpO_2 <92% should be meticulously monitored and if needed aggressive treatment as severe COVID-19 should be done.

***Acute respiratory distress syndrome**

- Respiratory symptoms of hypoxemia and radiological change within 1 week of disease onset due to SARS-CoV-2 not explained by acute left ventricular failure or volume overload.
- The radiological findings of new infiltrates consistent with acute pulmonary parenchymal disease
- Partial pressure of oxygen (PaO_2) to fraction of inspired oxygen (FiO_2) ratio to be used as measure of oxygenation for noninvasive ventilation and a oxygenation index for invasive mechanical ventilation.
- Wherever partial pressure of oxygen (PaO_2) measurement facility is not available oxygen saturation to fraction of inspired oxygen (FiO_2) ratio to be used for the noninvasive ventilation and oxygenation saturation index (OSI) for invasive ventilation.

Oxygenation	Non-Invasive mechanical Ventilation	Invasive mechanical ventilation		
	No severity stratification	Mild	Moderate	Severe
	Face mask bi-level ventilation or AP CPAP ≥5 cm H2O PF≤300 SF ratio≤264	4 ≤OI* <8 5 ≤ OSI#<	8 ≤OI <16 7.5≤OSI	OI ≥ 16 OSI ≥ 12.3

- The Severity of ARDS is given in the table below.

*OI = (FiO2 × mean airway pressure × 100)/PaO2
*OSI = (FiO2 × mean airway pressure × 100)/SpO2
*Rapid respiration (age based): <2 months ≥60/min;
2-12 months ≥50/min;
1-5 years ≥40/min;
>5 years ≥30/min

2.4 Management of children with COVID 19 infection

2.4.1 Outpatient management of Children with COVID 19

The parents should be counseled regarding isolation, monitoring for clinical deterioration, and supportive care. They must be informed about the chances of clinical deterioration, which may occur suddenly after one week of symptoms.

The symptoms of clinical deterioration include:

- Severe respiratory distress,
- Difficulty breathing (for infants: grunting, central cyanosis, inability to breastfeed),
- Chest pain or pressure,
- Blue lips or face,
- Findings associated with shock (e.g. cold, clammy, mottled skin; new confusion; difficulty arousing; substantially reduced urine output), etc.

Use of telephone and digital media like video call can be used for the purpose of counseling and monitoring.

2.4.2 Duration of home isolation:

At 10 days after illness onset, recovery of replication-competent virus in viral culture is decreased and approaches zero.

For persons recovered from COVID-19 illness, the CDC recommends that isolation be maintained for **at least 10 days after illness onset and at least 3 days (72 hours) after recovery.** Illness onset is defined as the date symptoms begin. Recovery is defined as resolution of fever without the use of fever-reducing medications with progressive improvement or resolution of other symptoms.

A. Non-severe disease

- Children to remain in home isolation under parental supervision.
- These children should be given symptomatic treatment such as antipyretics for fever and pain, adequate nutrition and appropriate rehydration.
- Antibiotic therapy or prophylaxis should not be used in these children.
- COVID appropriate behavior including face masks (for more than 2 year of age, hand hygiene and physical distancing advised.
- Any routine medications, which the child is taking, should be continued.
- Caregivers of children with COVID-19 should also monitor their patients for any signs and symptoms of clinical deterioration requiring an urgent re-evaluation. These include difficulty breathing/fast or shallow breathing, blue lips or face, chest pain or pressure, new confusion as well as an inability to wake up, interact when awake, drink or keep liquids down. For infants these include grunting and an inability to breastfeed.
- Home pulse oximetry measurements should be done regularly to look for any deterioration or desaturation so that they bring their child to the hospital if saturation drops below 90%.

2.5 Indication for hospital admission:

1. Children with severe or critical COVID-19
2. Children with mild to moderate COVID-19 may require hospital admission if they are at risk for severe disease due to underlying conditions (e.g. immune compromised).

2.5.1 Indications for admission to the hospital for non-severe disease

- Presence of certain co-morbid conditions that lead to rapid clinical deterioration in a child with non-severe disease require hospital admission which include:
- Diabetes
- Congenital heart disease
- Chronic lung disease
- Cerebrovascular disease
- Chronic kidney disease
- Nephrotic syndrome
- Immunosuppression
- Obesity
- Malignancy

Other patients can be managed in home under telemedicine guidance of the Health Care provider. Oral antimicrobials to be used on a case by case basis, especially for children with high risk of disease progression (immunocompromised, congenital heart disease, malignancy, etc.) and also in those cases suspicion of bacterial co-infection (after sending blood culture) as per the hospital antibiotic policy. Oral Paracetamol and other symptomatic treatment to be done as explained above. Corticosteroids may be needed in moderate infection if there is a need for supplemental oxygen. Intravenous fluids are to be started in those patients with poor oral intake. Rest to be done as per treatment of mild infection.

2.5.2 Indication for Referral to Tertiary centers:

1. Children with COVID-19 worsening severe or critical disease
2. Children with mild to moderate COVID-19 who are at risk for severe disease due to underlying conditions (e.g. immune compromised) may be referred.

2.6 Investigations to be sent in COVID 19 patients

Although not all children infected with COVID 19 require investigations, they are mandatory for all children with severe and critical disease.

A. For those children with non-severe disease on case to case basis:

- Complete blood count
- Serum electrolytes (sodium, potassium), blood glucose,
- Erythrocyte Sedimentation rate (ESR),
- Blood culture (if secondary infection is suspected),
- Chest X-ray

B. Severe Cases

- Complete Blood Count,
- Serum electrolytes (sodium, potassium),
- Blood glucose,
- Erythrocyte Sedimentation rate (ESR),
- C-Reactive Protein,
- Liver Function Test,
- Renal Function Test (serum urea, creatinine),
- Liver Function test,
- Inflammatory markers: Serum ferritin, D-dimer, serum Lactate dehydrogenase (LDH),
- Coagulation profile: aPTT, PT/INR,
- Arterial Blood Gas (ABG),
- Blood culture and sensitivity (to rule out bacterial sepsis/coinfection),
- Chest- X ray
- CRP, D-dimer, ferritin, and LDH needs to be done two or three times per week to monitor for cytokine storm

2.7 Management of COVID-19 in Severe and Critical infection:

To be admitted in COVID High Dependency Unit (HDU) or Pediatric Intensive Care Unit (PICU). The treatment strategies involve use of

- Supplemental oxygen,
- Fluid and electrolyte balance,
- Use of corticosteroids (as indicated),
- Low molecular heparin (as indicated),
- Management of ARDS,
- Sepsis, shock,
- Renal replacement Therapy (as per the standard guidelines) nutrition,
- Avoidance of unproven drugs.

2.7.1 Supplemental Oxygen

Indications for supplemental oxygen: Children with Oxygen Saturation less than 94% in room air, Obstructed or absent breathing, severe respiratory distress, Central cyanosis, Shock, Coma or convulsions. While interpreting the oxygen saturation level we should take into consideration about the child's previous disease condition and baseline SPO2 e.g. a child with chronic lung disease or congenital heart disease might have a baseline of SpO2 of 90%, which can be considered normal for that child. So, a cutoff of 94% can be used in previously healthy children without underlying disease conditions.

Modes of giving oxygen therapy:

Non-Invasive: Face mask, nasal cannula, hood box, non-rebreathing mask, HFNC (High-Flow Nasal Cannula), NIPPV (Noninvasive Positive Pressure Ventilation),

Invasive: Intubation and Invasive Mechanical Ventilation, HFOV and Extracorporeal Membrane Oxygenation (ECMO).

A. Heated Humidified HFNC (High-Flow Nasal Cannula):

Indicated in children with COVID-19 who persist to have increased work of breathing and hypoxemia on supplemental oxygen

- Flow rate for HFNC therapy is same for all children regardless of disease conditions.

  - o < 12 kg: 2 L/kg/min
  - o >12 kg: 2 L/kg/min + 0.5 L/kg/min for each kg thereafter (max flow 50 L/min)
  - o Increase flow to the prescribed rate over a few minutes as tolerated.
  - o When supplemental oxygen is required, titrate FiO2 to maintain the \ target SPO2.

- Airborne precautions to be followed with adequate PPE. HFNC should be tried for a maximum of 1-2 hours.
- Signs of improvement are decrease in heart rate and respiratory rate by 10-20%, decrease in FiO2 requirement to less than 50% and improvement in oxygen saturations.
- Patients with progressive respiratory distress despite HFNC, or where HFNC is unavailable, can be escalated to NIV, bCPAP, or bi-level positive airway pressure (BiPAP). Patients with worsening hypercapnia, acidemia, respiratory fatigue, hemodynamic instability or those with altered mental status should be considered for early invasive mechanical ventilation.

B. Non-Invasive Ventilation:

- Routine use of NIV is not recommended in COVID-19. It should be used only in selected patients with hypoxemic respiratory failure **(mild cases of ARDS without hemodynamic instability but needs close monitoring for escalation of treatment.**
- Ideally, negative pressure single rooms are preferable for patients on NIV; in lack of such rooms keeping a distance of at least two meters between two beds should be considered.
- Conventional ventilators with NIV option having double lumen tubing is a safer option than NIV ventilator with single lumen tubing requiring exhalation port to washout the CO2.
- Antiviral/Antibacterial filters should be attached to the exhalation limb of the circuit to reduce environmental contamination. Preferred interfaces are helmet (hood), total face mask and oro-nasal non-vented masks.

  -PaO2/FiO2 is a sensitive and accurate indicator of oxygenation function on NIV and can be used to define the severity of ARDS once the patient has been on a PEEP of 5 cm for a minimum of 30 minutes.

  - Invasive ventilation must be considered if PaO2/FiO2 ratio is below 300.

- NIV might reduce intubation and mortality in mild ARDS, it is associated with higher mortality in moderate-to-severe ARDS

C. Bubble CPAP:

- In resource limited settings, bubble CPAP should be considered for respiratory support in children with hypoxemia, severe pneumonia and/or ARDS where both non-invasive and invasive mechanical ventilation are not available.
- Bubble nasal CPAP (commercial or indigenous) may be used for new borns and children with severe hypoxemia as these are readily available alternatives in resource-limited settings.
- For minimization of environmental contamination, the infant could be placed in an oxygen hood to reduce droplets.
- These patients should be on continuous monitoring and in case the patient acutely deteriorates or does not improve after a short trial (about 2 hours) the patient needs to be intubated.

D. Endotracheal Intubation and mechanical ventilation:

Indications for invasive mechanical ventilation:

- Moderate/severe ARDS with PaO2/FiO2 ratio below 200,
- Hemodynamic instability
- Multi-organ failure
- Abnormal mental status
- Patients with worsening hypoxia and work of breathing

2.7.2 Corticosteroids:

Indications for using glucocorticoids:

1. Children with severe or critical COVID-19 who require mechanical ventilation or those who require supplemental oxygen and have risk factors for disease progression or those with rapid disease progression or those who develop septic shock.

2. Steroids should be continued in children with an underlying condition requiring chronic steroid treatment

3. Cases of comorbid conditions where steroid therapy is indicated like NS.

Steroids are to be used only after, first 3-5 days of illness, as it may prolong viral clearance, if used earlier. Low-dose glucocorticoid regimens include one of:

- **Dexamethasone** 0.15 mg/kg orally, IV, or through nasogastric tube (NG tube) once daily (maximum dose 6 mg) OR
- **Prednisolone** 1 mg/kg orally or NG once daily (maximum dose 40 mg) OR
- **Methylprednisolone** 0.8 mg/kg IV once daily (maximum dose 32 mg) OR
- **Hydrocortisone**
  - For neonates (<1 month of age): 0.5 mg/kg IV every 12 hours for 7 days followed by 0.5 mg/kg IV once daily for 3 days;
  - For children ≥1 month: 1.3 mg/kg IV every 8 hours (maximum dose 50 mg; maximum total daily dose 150 mg).

The duration of therapy is 5-7 days and tapered up to 14 days.

2.7.3 Low Molecular Weight Heparin:

LMW heparin is known to reduce the risk of Venous Thromboembolism (VTE) and may have anti-inflammatory properties. Unlike adults, the decision to start venous thromboembolism (VTE) prophylaxis in children is individualized.

2.7.3.1 Indications for starting prophylactic Low Molecular Weight Heparin in children:

1. Strong personal or family history of VTE
2. Indwelling central venous line and two or more additional risk factors
3. Four or more risk factors

Risk factors for thrombosis to consider:
• Personal history of thrombophilia or VTE
• First degree relative with VTE

- Presence of central venous line
- Congenital Heart Disease
- Post pubertal age
- Prematurity
- Antiphospholipid syndrome
- Decreased mobility from baseline
- Burns
- Active malignancy
- Indications of venous stasis or cardiac low flow state
- Estrogen therapy
- Active systemic infection
- Flare of inflammatory disease
- Obesity
- Severe dehydration
- Recent surgery or trauma

An assessment of bleeding risks (intracranial hemorrhage, active bleeding, coagulopathy, neurosurgical procedure within 24 hour, etc.) versus benefit should be compared on each pediatric patient. Alternative methods of prophylaxis, such as early ambulation or mechanical prophylaxis should be considered in contraindicated patients and all COVID-19 pediatric patients, if applicable.

2.7.3.2 Dose and route of prophylactic Enoxaparin:

0.5 mg/kg (maximum dose 40 mg) given twice a day subcutaneously. It can be administered alternatively between the left and right anterolateral and left and right posterolateral abdominal wall. To avoid bruising, the injection site should not be rubbed.

Monitoring of patients on Enoxaparin: If facilities are available in the center, anti-factor Xa levels after 4 hour of subcutaneous dose completing the third consecutive dose can be done to obtain a level of 0.20-0.49 anti-Xa U/mL.

2.3 Indication of full dose anticoagulation:

- Documented or strongly suspected venous thromboembolism (VTE)
- Clotting of vascular access devices.
- Patients receiving anticoagulation therapy prior to admission.

For such children injection enoxaparin is given at the dose of 1 mg/kg subcutaneously every 12 hourly with an anti-Xa factor target of 0.5–1 IU/ml.

Individuals who have suffered from venous thromboembolism require three months of anticoagulation after they get discharged.

2.8 Management of COVID 19 with ARDS (CARDS)

A. Mild ARDS: High flow nasal oxygen or non-invasive ventilation (BiPAP or CPAP) may be given with close monitoring for increase in severity of illness.

B. Moderate to Severe ARDS: The following lung protective ventilation strategy to follow:

Parameter	Strategy
Low Tidal Volume	4-8 ml/kg of Predicted body weight
Plateau Pressure	< 28 cm H2O
Mean Airway Pressure	<18-20 cm H2O
Driving pressure	<15 cm H2O
Positive End Expiratory pressure (PEEP)	Moderate ARDS < 10 cm H2O Severe ARDS 10-15 cm H2O
FiO2	<60%
Sedation with or without neuromuscular block-ade	Adequate

ET tube	Cuffed
Suctioning	Inline suctioning preferred to open suctioning (to avoid disconnections)
Nutrition	Enteral nutrition within 24 hour
Position	Prone (ideally 12-16 hours per day, only if feasible in severe ARDS)
Fluids	Restrictive fluid strategy, 2/3rd of total maintenance fluid
Weaning	Daily assessment for weaning, early weaning.
Weaning	If oxygenation and hemodynamically stable, threshold Hb <7; if hypoxemia or shock, threshold Hb<10.

High-frequency oscillatory ventilation (HFOV) (for refractory respiratory failure), Extracorporeal Membrane Oxygenation (ECMO) may be considered in patients with continued severe hypoxemia despite maximal support if facilities is available.

2.9 Management of shock

- Give Intravenous fluid bolus **10–20 ml/kg per bolus up to 40–60 ml/kg,** over the first hour of resuscitation.
- The initial fluid of choice should be **crystalloids**. In children with COVID-19 and shock, age-appropriate mean arterial pressure (MAP) should be targeted. In settings where accurate MAPs cannot be easily obtained, systolic blood pressure is an acceptable option. For inotropic support, **epinephrine** should be chosen as the first-line vasoactive infusion. **Epinephrine should be considered as the first-line agent in patients with shock and if not improved other inontropes can be\ added. For further management NEPAS guidelines for Shock can be referred to.**
- If there is no improvement with one inotrope another one can be added accordingly. Vasopressin should be considered in children who need high doses of catecholamines. Inodilators such as milrinone, dobutamine or

levosimendan could be used when there are signs of tissue hypoperfusion and cardiac dysfunction, despite high doses of catecholamines.

• Hydrocortisone should be added if there is fluid refractory catecholamine resistant shock (avoid if already on dexamethasone or methylprednisolone).

• Once stabilized, restrict IV fluids to avoid fluid overload. Enteral nutrition to be initiated as early as possible if there is no contraindication. Empirical antibiotics to be instituted within the first hour after sending the R blood culture, as per the hospital policy.

2.10 Empiric antibiotics:

For patients with suspected or confirmed asymptomatic COVID-19, antibiotic therapy or prophylaxis is not warranted. For those patients with non-severe COVID-19, antibiotics should not be prescribed unless there is clinical suspicion of a bacterial infection. For patients with suspected or confirmed severe COVID-19, the use of empiric antimicrobials to treat all likely pathogens is recommended, based on clinical judgment, patient host factors and local epidemiology, and this should be done as soon as possible (within 1 hour of initial assessment if possible), ideally with blood cultures obtained first. Antimicrobial therapy should be assessed daily for de-escalation. Duration of empiric antibiotic treatment should be as short as possible; generally 5–7 days.

2.11 Antiviral therapy for select patients:

Given the lack of data from controlled trials supporting the efficacy of antiviral agents for the treatment of COVID-19 in children, we agree with recommendations from the multicenter interim guidance on the use of antiviral agents for children with COVID-19 and other experts that antiviral therapy should be considered on a case-by-case basis and preferably occur in the context of a clinical trial, if a clinical trial is available.

Antiviral therapy for COVID-19 should be reserved for children with documented severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections if testing is available.

Potential indications– Decisions to use antiviral therapy should be individualized according to disease severity, clinical trajectory, existing evidence of effectiveness, and underlying conditions that may increase the risk for progression.

Despite the unproven benefits, we suggest antiviral therapy for children with documented severe or critical COVID-19. Antiviral therapy also may be warranted for children with non-severe disease and an underlying condition that increases or may increase the risk of severe disease (e.g., medical complexity, congenital heart disease, among others).

Choice of agent/regimen

Remdesivir– When a decision is made to use antiviral therapy in a child who cannot be enrolled in a clinical trial, we suggest remdesivir rather than other antiviral agents, in agreement with the multicenter panel. Remdesivir is dosed according to weight as follows:

- ≥3.5 to <40 kg: 5 mg/kg intravenous (IV) loading dose on day 1, followed by 2.5 mg/kg IV every 24 hours
- ≥40 kg: 200 mg IV loading dose on day 1, followed by 100 mg IV every 24 hours

The usual duration of therapy is up to 5 days for children with severe disease; for children with critical disease who are not improving after 5 days, the duration may be extended to up to 10 days.

Remdesivir should not be administered with hydroxychloroquine or chloroquine, because co-administration may decrease Remdesivir's antiviral activity. Reported adverse effects of Remdesivir include nausea, vomiting, and transaminase elevations.

2.12 Renal Replacement therapy:

Whenever it is indicated

2.13 Avoidance of unproven medicines:

There is Favipiravir, Hydroxychloroquine, Chloroquine, Ivermectin, Azithromycin, Lopinavir/ ritonavir, Convalescent plasma, toclizumab/ anakinra in the management or prophylaxis of COVID 19 in children.

2.14 When to discontinue isolation in admitted children?

- For asymptomatic persons: 10 days after testing positive.
- For most children with COVID-19 illness, isolation and precautions can be discontinued 10 days after symptom onset* and after resolution of fever for at least 24 hours, without the use of fever-reducing medications, and with improvement of other symptoms.
- Some children with severe illness may produce replication-competent virus beyond 10 days that may warrant extending duration of isolation and precautions for up to 20 days after symptom onset; severely immunocompromised patients** may produce replication-competent virus beyond 20 days and require additional testing and consultation with infectious diseases specialists and infection control experts.
- For children who are severely ill or severely immunocompromised, a test-based strategy should be considered in consultation with infectious diseases experts.
- For all others, who are not severely ill or severely immunocompromised, a test-based strategy is not recommended, and isolation and precautions should be maintained for at least 10 days as outlined above.

CHAPTER 3

NEONATES WITH COVID-19

The immature immune system, passive transfer of maternal IgG antibodies, and lower ACE-2 expression may result in less inflammation, milder illness, and hastened recovery in infants and children compared to adults.

3.1 Early-onset neonatal COVID-19:

This manifests between 2 and 7 days after birth. Most neonates are asymptomatic or have:

- Mild symptoms such as rhinorrhea and cough and fever
- Moderate to severe symptoms such as respiratory distress, poor feeding, lethargy, vomiting and diarrhea and clinical evidence of multi-organ failure have been observed as well.

Laboratory finding

There might be leukocytosis, lymphopenia, thrombocytopenia, and non-specific findings of elevated inflammatory markers.

Management:

The management is supportive.

3.2 Late-onset neonatal COVID-19:

This manifests beyond 5 to 7 days after birth. This might have been acquired from respiratory secretions of mother, caregivers, or household contacts. Many affected neonates have negative initial RT-PCR test results (at 24 and 48 hours after birth) before initial discharge from the hospital

Clinical Features:

- Hyperthermia
- Coryza
- Mild respiratory symptoms

- Apnea
- Poor feeding or vomiting
- Lethargy

Age less than 1 month has been associated with a 3-fold higher risk of critical care admission.

Management:

Management includes supplemental oxygen, respiratory support, fluid resuscitation, and temperature control. Antiviral medications and steroids in neonatal COVID-19 are lacking. However use of Remdesivir, dexamethasone has been reported.

3.3 Multisystem inflammatory syndrome in neonates (MIS-N):

Neonatal MIS (MIS-N) has rarely been reported. Neonates are usually asymptomatic or they have mild illness but some of them may develop severe symptoms. This entity in neonates may be under reported as these babies might present with signs of sepsis. Hence, MIS-N diagnosis should be considered on babies presenting with multisystem involvement and evaluated accordingly.

3.4 Prevention of transmission from infected mother to newborns

3.4.1 Key points in neonatal resuscitation

The following points must be noted:

- Use of appropriate PPE by the caregivers.
- Initial steps are unlikely to be aerosol generating; they include drying, tactile stimulation, placement into a plastic bag or wrap, assessment of heart rate, and placement of pulse oximetry and ECG leads.
- Suction should not be performed unless indicated.
- Endotracheal medications should be avoided.
- Intravenous epinephrine via a low-lying umbilical venous catheter is preferred.
- Closed incubators should be used.

3.4.2. Testing in neonates

- Testing for SARS-CoV-2 RNA by RT-PCR should be done for all neonates born to COVID positive mothers even in the absence of signs of infection in the neonate.
- Obtain either a single swab of the nasopharynx or a single swab of the throat followed by the nasopharynx or two separate swabs from each of these sites for RT-PCR test.
- Testing for both symptomatic and asymptomatic neonates born to suspected or confirmed COVID-19 should be done first at approximately 24 hours of age and if initial test results are negative, or not available, testing should be repeated at 48 hours of age.
- If it is planned that a healthy newborn will be discharged prior to 48 hours of age, clinicians may choose to order a single test at 24-48 hours of age.
- For infants who require ongoing hospital care, caregivers should continue to use appropriate PPE until discharge, or until the infant has two consecutive negative tests collected ≥24 hours apart

3.4.3 Mother-baby contact

- Babies born to suspected or confirmed COVID-19 should be enabled to remain together and practice skin-to-skin contact.
- Breastfeeding should be established early and mothers should be encouraged to continue breastfeeding.
- The newborn's risk for acquiring SARS-CoV-2 from the mother is low, and data suggest no difference in risk of neonatal SARS-CoV-2 infection whether the neonate is cared for in a separate room or remains in the mother's room.
- Rooming-in helps establish breastfeeding, facilitates bonding and parental education, and promotes family-centered care.
- As there is a potential risk of SARS-CoV-2 transmission to the neonate via contact with infectious respiratory secretions from mother or caregivers, all caregivers should practice infection prevention and control measures while caring for a neonate.

- If separation is necessary for mothers who are too sick to care for their sick babies or who need high levels of care, expressed breast milk should be given to babies.
- If a baby's RT-PCR is positive for COVID-19, separation of mother with suspected or confirmed COVID from baby in order to reduce the risk of transmission of disease is not required.
- Measures to reduce the risk of transmission:
    - Mothers or caregivers should wear a mask and practice hand hygiene during contact with neonates.
    - Masks and face shields are not recommended for neonates or children < 2 years of age.
    - Maintain a physical distance of >6 feet between mother and neonate in other times if feasible

3.5 Discontinuation of isolation and precaution guidelines for confirmed COVID mothers

- At least 10 days have passed since symptoms first appeared (up to 20 days if they have more severe to critical illness or are severely immuno compromised).
- At least 72 hours have passed since their last fever without the use of antipyretics.
- Other symptoms have improved.
- For asymptomatic mothers, after at least 10 days of positive test results.

3.6. Breastfeeding:

- The risk of SARS-CoV-2 transmission from ingestion of breast milk is minimal.
- Mothers with suspected or confirmed COVID-19, should be encouraged to continue breastfeeding and she should be counselled for the benefits of breastfeeding, which outweigh the potential risks of transmission.
- A breastfeeding mother who is not fully vaccinated against COVID-19 should take precautions to protect themselves and the breastfed child when either member of the family has suspected or confirmed COVID-19.
- Mothers and caregivers should follow these precautions during their recommended period of isolation:
    - Wash hands with soap and water before touching the baby or expressing breast milk.
    - Use of hand sanitizer if soap and water are not available.
    - Wear mask
- If a mother is not able to breastfeed her baby due to her severe illness, she should be encouraged to express milk for her baby following appro priate IPC measures.
- If a mother is very sick to breastfeed or express breast milk, we need to discuss with mother and parents regarding donor human milk based on the local culture and practice.
- If this is also not possible, consider wet nursing (defined as another woman breastfeeds the child) or appropriate breast milk substitutes, informed by feasibility, safety, sustainability, cultural context, acceptability to mother and service availability.

3.7 Antiviral drug safety in lactating mothers

For mothers who are receiving remdesivir, their infants are not likely to absorb clinically important amounts of the drug from breast milk.

3.8 SARS-CoV-2 vaccines safety in lactating mothers

Lactating mothers should receive a vaccine against SARS-CoV-2. COVID-19 antibodies present in breast milk may have protective effects in infants.

Refer to Flowchart 1, 2, and 3 for an approach to neonates born to suspected and positive mothers in Appendices.

CHAPTER 4

MULTI-SYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)

4.1 Background

Multisystem Inflammatory Syndrome in Children (MIS-C) also known as pediatric hyper-inflammatory syndrome, pediatric multisystem inflammatory syndrome (PIMS) or pediatric hyper-inflammatory shock. MIS-C is a condition that is temporally associated with SAR-CoV-2 and is characterized by fever, inflammation and multi-organ dysfunction, which manifests several weeks after the infection of SARS-CoV-2. This condition should be differentiated from other pediatric inflammatory conditions like Kawasaki disease, bacterial sepsis, staphylococcal and streptococcal toxic shock syndromes and macrophage activation syndromes as these conditions have features similar to that of MIS-C.

4.2 When to suspect MIS-C?

Any children who fulfil the case definition criteria given by CDC3 or WHO4 should be evaluated for MIS-C.

WHO case Definition of MIS-C

• Children and adolescents (0-19 years) with fever ≥ 3days

AND: Clinical sign of multisystem involvement (at least 2 of the following):

1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
2. Hypotension or shock
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-pro BNP)
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers)
5. Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)

AND

• Elevated ESR, C-reactive protein, or procalcitonin

AND

• No other obvious 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

Diagnostic evaluation of MIS-C

A child suspected for MIS-C should also be evaluated for other common clinical disease conditions like infectious and non-infectious causes that justify the patient's clinical manifestation.

Outpatient evaluation for MIS-C may be appropriate for assessing well-appearing children with stable vital signs and for ensuring that physical examinations provide close clinical follow-up.

Patients presenting with shock, significant respiratory distress, neurologic changes (altered mental status, encephalopathy, focal neurologic deficits, meningismus, and papilledema), dehydration, or features of KD should be admitted for further evaluation, regardless of MIS-C status, in accordance with standard of care.
Refer to Appendix 3 I for clinical manifestations and details of investigations that can be done for MIS-C
Refer to Appendix 3 II for distinctions between MIS-C and Kawasaki disease
Refer to Appendix 3 III for definition of organ system involvement
Refer to Appendix 2 flow diagram 4 and 5 for the evaluation and management of MIS-C

4.3 Indications for hospitalization

- Features of Kawasaki disease (KD)
- Severe abdominal pain or vomiting, especially if unable to tolerate oral feeds
- Clinical or laboratory evidence of dehydration
- Marked elevations of inflammatory markers (CRP >10 mg/dl)

4.4 Indications for PICU/HDU admission (if facilities available)

- Abnormal vital signs (tachycardia, tachypnea)
- Respiratory distress of any severity
- Abnormal EKG findings
- Hemodynamic instability (shock, arrhythmia)
- Significant respiratory compromise/ Severe respiratory distress/ respiratory failure
- Evidence of cardiac involvement (myocarditis, elevated troponin or brain natriuretic peptide, depressed ventricular function or coronary artery abnormality on echocardiogram, abnormal echocardiogram)

- Neurologic changes (e.g., depressed mental status, abnormal neurologic examination, seizures)
- Evidence of acute kidney injury, acute hepatic injury, or coagulopathy
- Underlying medical condition that may place the child at increased risk for complications (e.g., immunodeficiency, cardiac or pulmonary conditions)

4.5 Approach to a child with suspected MIS-C

Refer to Flow chart 4 in the appendices

4.6 Management of MIS-C

Refer to Flow chart 5 in the appendices

4.7 Treatment protocols can be grouped under 4 major categories

1. Supportive care
2. Antibiotics
3. Cardiac management
4. Immunomodulatory treatment
5. Antiplatelet and anticoagulation therapy

1. Supportive care

- Primary Assessment Pentagon (ABCDE).
- The ABCDE approach consists of stabilization of airway, breathing, circulation and neurological status.
- If the patient is in shock, vasoplegic or cardiogenic, manage with fluids, Vasopressors or inotropes as per the protocol.

2. Antibiotics

- Empirical first dose of broad-spectrum antibiotics of ceftriaxone and van comycin/ cloxacillin preferably within the first hour of presentation after blood culture is obtained.
- Clindamycin is added if there are features consistent with toxin-mediated illness (e.g., erythroderma). Antibiotics should be discontinued once bacterial infection has been excluded if the child's clinical status has stabilized.

3. Cardiac management

- BNP and/or troponin T at diagnosis should be trended over time until they normalize.
- EKGs every 48 hours and during follow up visits for detecting conduction abnormalities.
- Echocardiograms at diagnosis and follow up for ventricular/valvular function, pericardial effusion, coronary artery (CA) dimensions using z-scores.
- Echocardiograms repeated at a minimum of 7-14 days and 4-6 weeks after initial presentation. Echo should be repeated 1 year after MIS-C diagnosis in children with cardiac involvement during acute phase of illness. Children with LV dysfunction and coronary artery aneurysms (CAAs) will require more frequent echocardiography.
- Cardiac MRI at 2-6 months post-acute illness may be considered in children with moderate to severe LV dysfunction to evaluate for myocardial fibrosis and scarring.

4. Immunomodulatory treatment

- Patients with mild symptoms and without organ dysfunction may only require close monitoring and supportive treatment without immunomodulatory treatment
- Stepwise progression of immunomodulatory therapies to be used with IVIG as 1st line of therapy
- IVIG should be given to MIS-C patients who are hospitalized and or fulfill KD criteria.

- High-dose IVIG (typically 2 gm/kg, based on ideal body weight) should be used for treatment of MIS-C.
- Before starting IVIG, cardiac function and fluid status should be assessed. Children with depressed cardiac function will require close monitoring and diuretics while IVIG administration.
- In some patients with cardiac dysfunction, IVIG may be given in divided doses (1 gm/kg daily over 2 days).
- IV Methylprednisolone (MP) @ 1–2mg/kg/day should be given with IVIG as adjunctive therapy for patients with shock and/or organ dysfunction
- In patients who do not respond to IVIG + MP and requires high dose or multiple inotropes and/or vasopressors, high-dose, IV pulse Methylprednisolone (10–30 mg/kg/day) may be considered
- In patients with refractory MIS-C despite a single dose of IVIG, a second dose of IVIG is not recommended, given the risk of volume overload and hemolytic anemia associated with large doses of IVIG.
- IV MP (1–2 mg/kg/day) may also be considered with milder forms of MIS-C who are persistently febrile and symptomatic despite a single dose of IVIG.
- Anakinra (>4 mg/kg/day IV or SC) may be considered in patients with features of macrophage activation syndrome, when long-term use of glucocorticoids is contraindicated, or treatment of MIS-C is refractory to IVIG and glucocorticoids
- If IVIG in not available, MP (2mg/kg/day in 2 divided doses) should be given
- After defervescence and clinical improvement, steroids can be changed to an equivalent oral dose of Prednisolone at discharge and tapered off over 3-4 weeks
- Other immunomodulation: Anakinra, Tocilizumab, Infliximab

5. Antiplatelet and anticoagulation therapy

Low dose aspirin (3-5mg/kg/day; max 81mg/day)

Indications

- All cases with diagnosis of MIS-C
- MIS-C with CAAs and a maximal z-score of 2.5-10.0

Contraindications

- Active bleeding
- Significant bleeding risk
- Platelet count ≤80,000/μL

Duration: until normalization of platelet count and confirmed normal coronary arteries at ≥4 weeks after diagnosis

Enoxaparin: subcutaneous dose

- < 2months:1.5 mg/kg/dose every 12 hours (therapeutic), 0.75 mg/kg/dose every 12 hours (prophylactic)
- >2months: 1 mg/kg/dose every 12 hours (therapeutic), 0.5 mg/kg/dose every 12 hours (prophylactic)
- MIS-C with CAA z score ≥10.0 should be treated with low dose aspirin and enoxaparin (factor Xa level 0.5-1.0) or warfarin

- Longer outpatient enoxaparin dosing
- CAAs with z-score of >10.0 (indefinite treatment)
- Documented thrombosis (treatment for >3months pending thrombus resolution)
- Ongoing moderate to severe LV dysfunction

CHAPTER 5

CRISIS RESPONSES AND PSYCHO-SOCIAL MANAGEMENT FOR CHILDREN AND ADOLESCENTS DURING COVID-19 PANDEMIC

5.1 When to seek help?

There are 3 ways in which stress can affect everybody including the C&A. Sometimes these problems can make doing day-to-day life very difficult. This could be because of:

- Problems with feelings (Emotional symptoms): e.g. feeling sad, angry, irritated, crying, fearful and anxious.
- Problems in the body (Physical symptoms): e.g. headaches, abdominal pain, body aches, fainting like episodes, trembling, weakness of limbs, etc.
- Problems in our behavior/action (Behavioral symptoms): e.g. Irritation, clinginess to parents, excessive crying, aggression, demanding behaviors, substance use, school refusal, etc.
- There can be problems in sleep and appetite (Eating habits)
- The caregivers should seek help if the C&A present with the above-mentioned symptoms that are well in excess than normal and haven't responded to normal intervention. Symptoms are severe enough to cause disruption of daily functioning (even after applying coping techniques as mentioned in 10.2, then the child should be referred for further evaluation to a mental health professional.
- Pharmacotherapy for symptoms secondary to stress resulting in impairment in functioning and not improving after coping techniques:

I. For children below 6 years of age

- Pharmacotherapy is not the first choice
- If needed refer to a specialist (C&A Psychiatrist or Psychiatrist)

II. For children 6 to 12 years of age:

- Tablet SERTRALINE 25 mg ½ tablets PO in the morning after food.
- Can be increased tablet SERTRALINE 25 mg 1 tablet PO in the morning after food if needed.

III. For children more than 12 years of age:

- Tablet SERTRALINE 25 mg PO in the morning after food.
- Tablet CLONAZEPAM 0.25 mg PO HS (not more than 15 days)
- To follow up weekly for first 2 weeks then
- Follow up once fortnightly then
- Follow up monthly

•Note Medication not to be used for more than 6 months. If need arises to continue medication for more than 6 months, then refer to Child & Adolescent clinic or Psychiatrist.**

•For Assistance contact: 9808522410- CAP KCH Helpline and 16600110666 CAP KCH Hotline.

APPENDICES

APPENDIX 1: FIGURES

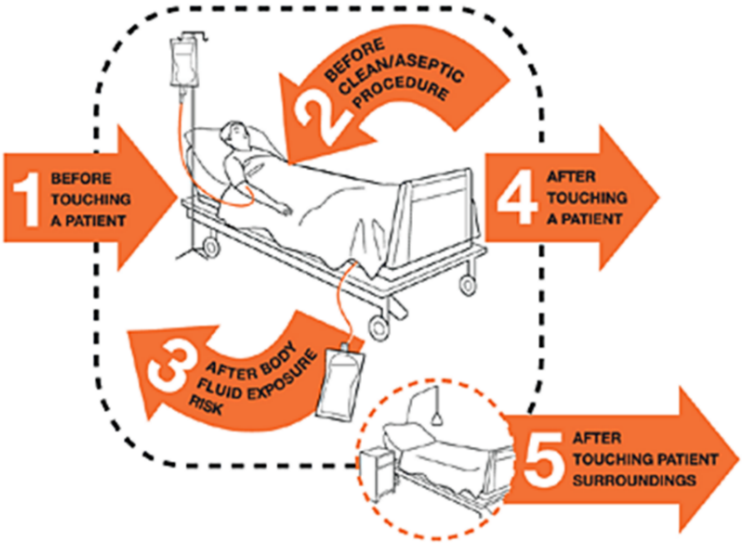


Figure 1: WHO's My 5 Moments for Hand Hygiene

Appendix 1: Figures

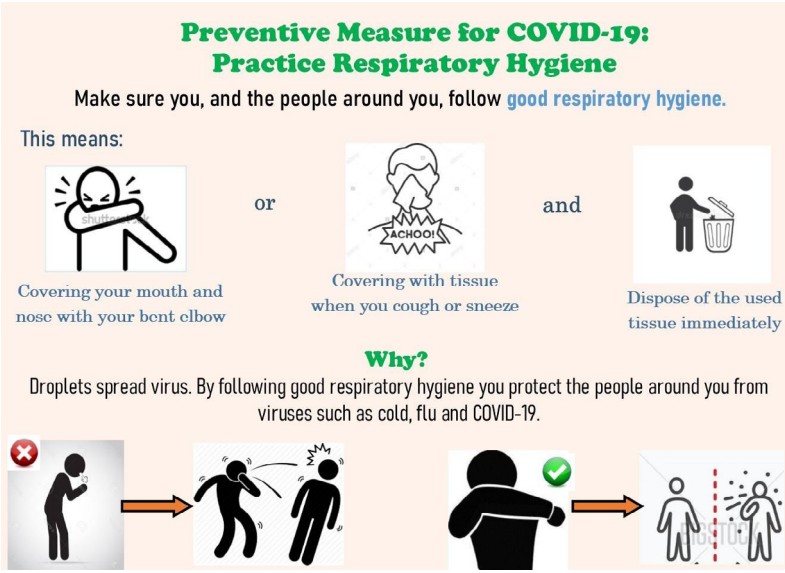


Figure 2: Respiratory Hygiene

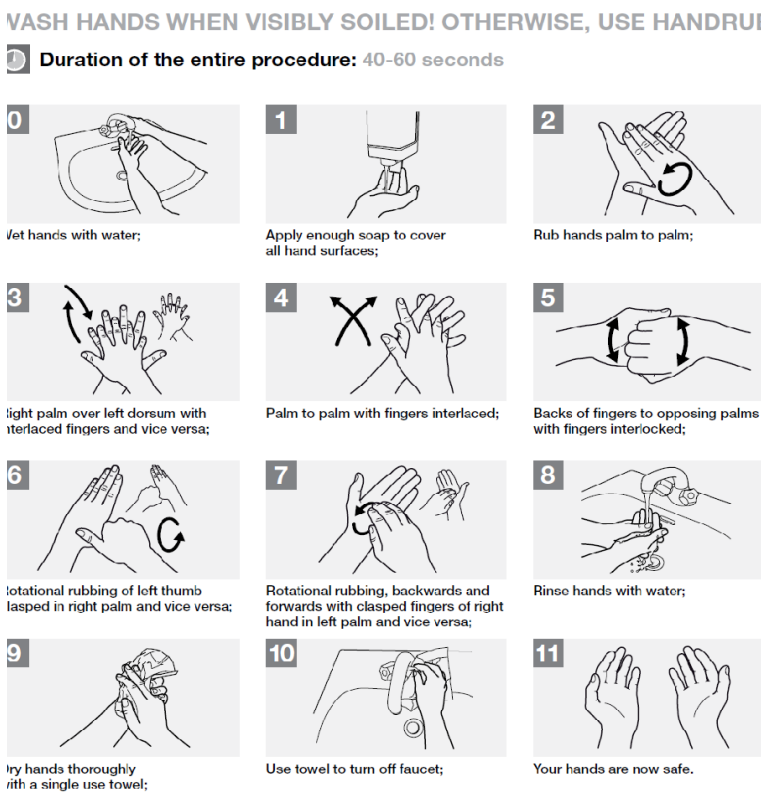


Figure 3: How to Handwash?

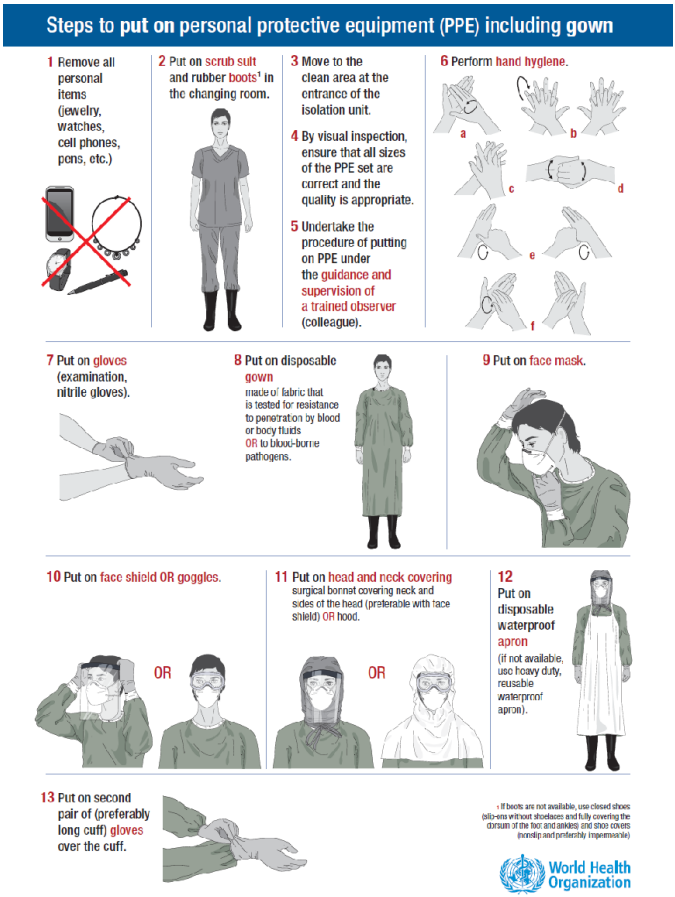


Figure 4: Steps to put on PPE (donning)

Figure 5: Steps to Remove PPE (doffing)

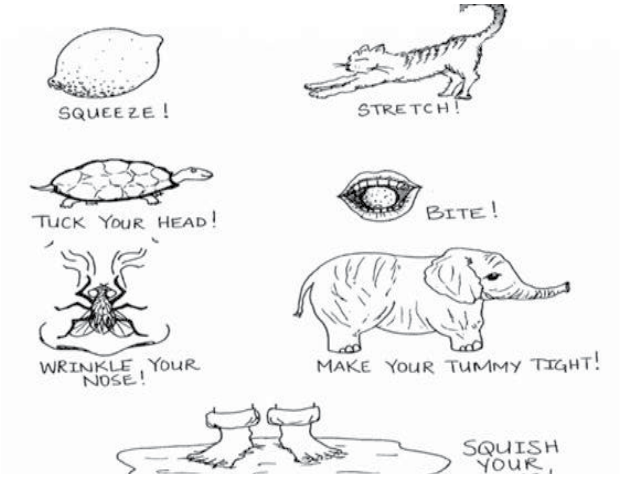


Figure 6. Relaxation Activities for Child and Adolescent (C&A)

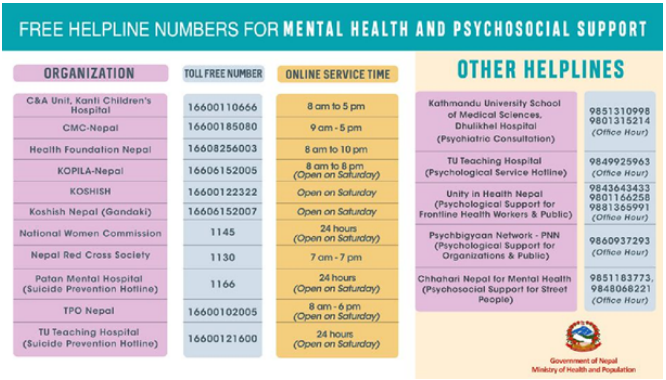
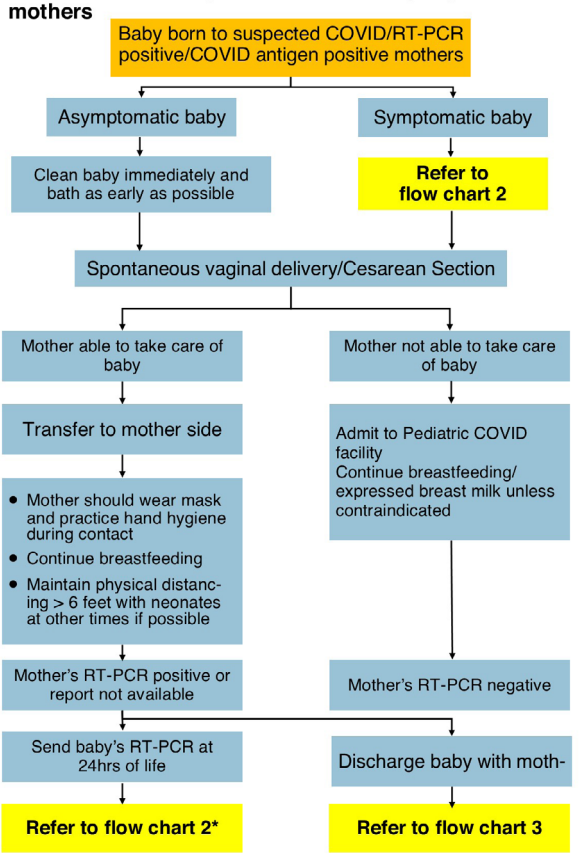


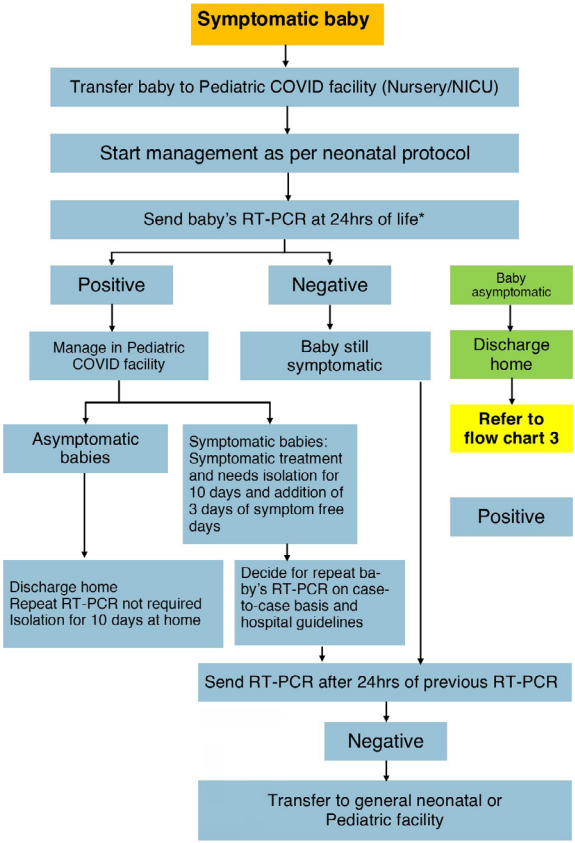
Figure 7. Provide Service Related Information

APPENDIX 2: FLOW CHARTS

Flow chart 1:
Approach to baby born to suspected/RT-PCR positive/COVID antigen positive mothers

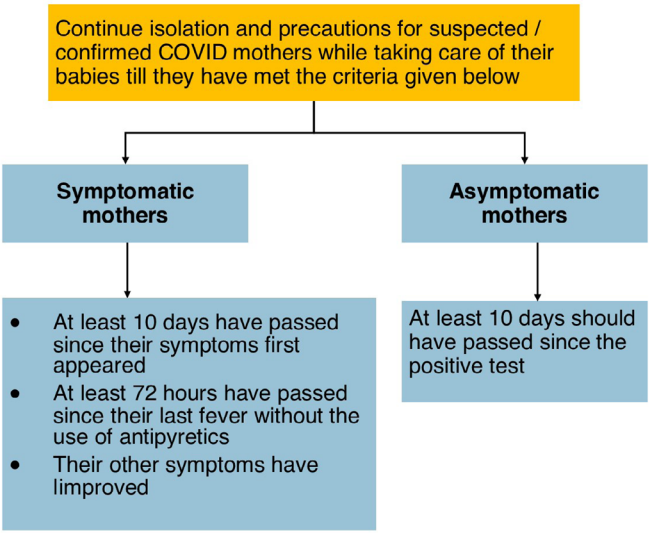


Flow chart 2:
Approach to a symptomatic baby born to suspected/RT-PCR positive/COVID antigen positive mothers



Flow chart 3:

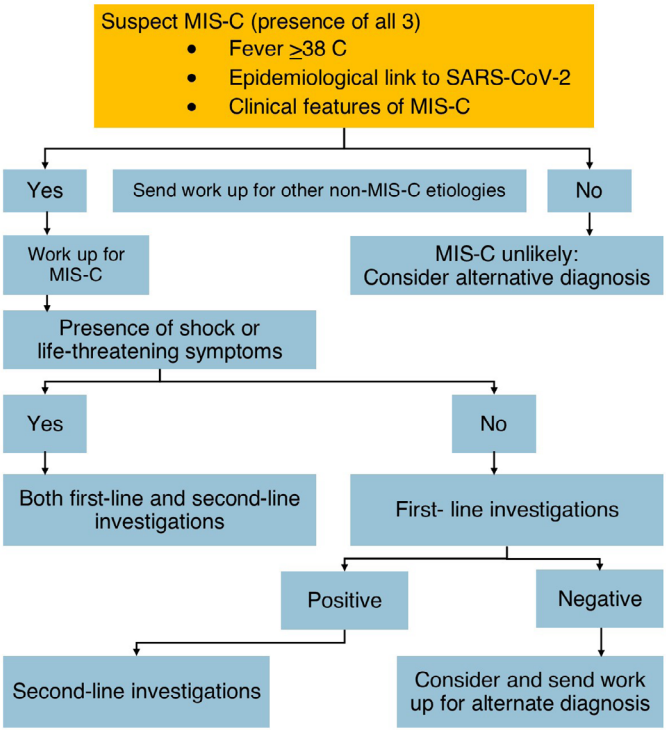
Discontinuing isolation and precautions guidelines for suspected or confirmed COVID mothers



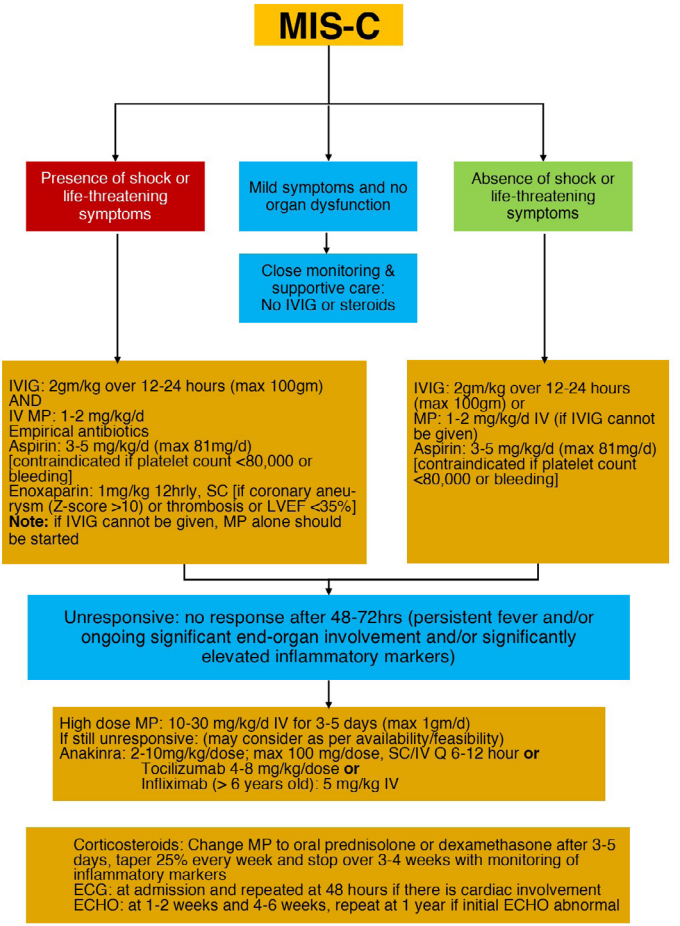
Recommendations for breastfeeding and breast milk feeds in the context of COVID-19

- Breastfeeding should be encouraged and continued. If direct breastfeeding is not possible, expressed breast milk should be given to baby unless contraindicated
- Mother should wash their hands using soap and water before touching their child or expressing breast milk. If soap and water are not available, use hand sanitizer with at least 60% alcohol.
- Mother should wear a mask when they are less than 6 feet from the child (including when feeding at the breast or feeding from a bottle) and when expressing breast milk
- If mother is very sick to breastfeed or express breast milk, donor human milk, wet nursing or appropriate breast milk substitutes should be considered based on feasibility, safety, sustainability, cultural context, acceptability to mother and service availability.

Flow Chart 4:
Diagnostic algorithm for the evaluation of patient with suspected MIS-C



Flow Chart 5:
Algorithm for the management of MIS-C



APPENDIX 3: DIFFERENT TABLES ABOUT MISC

I. Clinical manifestations of MIS-C

Symptoms	Signs
• Fever • Gastrointestinal: abdominal pain, vomiting, diarrhea • Rash • Conjunctivitis • Mucous membrane involvement • Neurological: headache, lethargy, confusion • Respiratory: tachypnea, labored • breathing • Sore throat • Myalgias • Swollen hands/feet • Lymphadenopathy	• Shock • Features of Kawasaki disease • Myocardial dysfunction (by echo cardiogram or elevated troponin/ BNP) • Arrhythmia • Acute respiratory failure requiring noninvasive or invasive ventilation • Acute kidney injury • Serositis (small pleural, pericardial, and ascitic effusions) • Hepatitis or hepatomegaly • Encephalopathy, seizures, coma, or meningo-encephalitis
Laboratory Investigations Abnormal blood cell counts • Lymphocytopenia • Neutrophilia • Mild anemia • Thrombocytopenia • Elevated inflammatory markers • C-reactive protein • Erythrocyte sedimentation rate • D-dimer (if available)	**Radiology** Echocardiogram • Depressed LV function • Coronary artery dilation/ aneurysm • Other findings can include mitral regurgitation and pericardial effusion

• Erythrocyte sedimentation rate • D-dimer (if available) • Fibrinogen (if available) • Ferritin • Procalcitonin (if available) **Elevated cardiac markers** • Troponin • BNP (if available) • Hypoalbuminemia • Mildly elevated liver enzymes • Elevated lactate dehydrogenase • Hypertriglyceridemia	**Chest radiograph** • Normal in many patients • Abnormal findings: small pleural effusions, patchy consolidations, focal consolidation and atelectasis **Chest CT** • Findings generally similar to those on chest radiograph • A few patients had nodular ground-glass opacification **Abdominal imaging (ultrasound and/or CT)** • Ascites • Bowel and mesenteric inflammation • Terminal ileitis • Mesenteric adenopathy/adenitis • Pericholecystic edema

II. Distinction features between MIS-C and Kawasaki disease (KD)

	MIS-C	KD
Age	Older children & adolescents	Infants & young children
Ethnicity	Increased incidence in African, Afro-Caribbean and Hispanic descent	Common in East Asian children
Gastrointestinal symptoms	More common	Less prominent
Shock	More common	Less common
Myocardial dysfunction (arrhythmias & ventricular dysfunction)	More common	Less common

Neurological symptoms	More common	Less common
Inflammatory markers	Markedly elevated	Elevated
Platelet count	Thrombocytopenia	Thrombocytosis
Coronary artery involvement	Risk present	Risk present

III. Definition of organ system involvement

Gastrointestinal: nausea/vomiting, diarrhea, abdominal pain, appendicitis, pancreatitis, hepatitis, gallbladder hydrops or edema
Cardiovascular: hypotension or shock, cardiac dysrhythmia or arrhythmia, ejection fraction <55%, pulmonary edema due to left heart failure, coronary artery z score ≥2.5, pericarditis or pericardial effusion or valvulitis, B-type natriuretic peptide (BNP) >400 pg/mL, elevated troponin, receipt of vasopressor or vasoactive support, receipt of cardiopulmonary resuscitation (CPR)
Hematologic: Total white blood cell <4,000, anemia for age, platelet count <150,000 /μL, deep vein thrombosis, pulmonary embolism, hemolysis, bleeding or prolonged PT/aPTT, ischemia of an extremity
Mucocutaneous: bilateral conjunctival injection, oral mucosal changes, rash or skin ulcers, 'COVID' toes, swollen red cracked lips, erythema of palms or soles, edema of hands or feet, periungual (nails) desquamation
Respiratory: receipt of mechanical ventilation or any type of supplemental oxygen (or· increased support for patients receiving respiratory support at baseline), severe bronchospasm requiring continuous bronchodilators or pulmonary infiltrates on chest radiograph, lower respiratory infection, pleural effusion, pneumothorax or other signs of barotrauma, pulmonary hemorrhage, chest-tube or drainage required
Musculoskeletal 23% (more frequent in teens): arthritis or arthralgia, myositis or myalgia
Renal: acute kidney injury with or without dialysis
Neurologic: stroke or acute intracranial hemorrhage, seizures, encephalitis, aseptic meningitis, or demyelinating disorder, altered mental status, suspected meningitis with negative culture

IV. Differentiating features between MISC and Severe COVID in children

Features	MIS C	Severe Covid-19
Age group (years)	6-12	0-5
Severe pulmonary involvement	Less common	Common
Multi organ dysfunction (MODS) • Cardiovascular • Gastrointestinal • Mucocutaneous	Common	Less common
• Laboratory parameters • Thrombocytopenia (150×103/μL) • Elevated CRP (>100 mg/dl) • Hypoalbuminemia • Neutrophil lymphocyte ratio (>5)	Common	Less common

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