Protocol for Management of Covid - 19 in the Pediatric Age Group

Based on guidelines issued by MoHFW, Government of India 20.04.2021

Background and Epidemiology

- WHO declared covid 19 caused by SARS cov-2 as a public health emergency of international concern on 30th January 2020 and subsequently declared it to be a pandemic on 11th March 2020.
- Children are less commonly affected, majority of them are asymptomatic or mildly symptomatic.

A small proportion (<10%- 20%) of symptomatic children may need hospitalization and 1% to 3% of symptomatic children may have severe illness requiring intensive care admission.

Transmission –

Close Contact – mainly respiratory droplet, surface contamination

- Median incubation period is 5.1 days (range 2 to 14 days)
- As per current evidence, the period of infectivity starts 2 days prior to onset of symptoms and lasts up-to 8 days

Patho-physiology

- Most patients with covid-19 predominantly have respiratory tract infection
- Some may progress to severe and systematic disease characterized by
 - ARDS,
 - sepsis and septic shock,
 - multiorgan failure including acute kidney injury, acute cardiac injury.
- Autopsy findings in adults in China, European countries
 - endothelial damage of pulmonary vasculature,
 - microvascular thrombosis and hemorrhage linked to extensive alveolar and interstitial inflammation ultimately resulting in pulmonary intravascular coagulopathy,
 - hypercoagulability impaired ventilation perfusion, acute respiratory distress syndrome.

(Limited data are available for children)

Case definition (As per WHO surveillance guidelines)

Suspect case:

A patient with acute respiratory illness (fever and at least one sign/ symptom of respiratory disease, e.g. Cough, shortness of breath), AND a history of travel to or residence in a location reporting community transmission of covid – 19 disease during the 14 days prior to symptom onset.

Or

A patient with any acute respiratory illness AND having been in contact with a confirmed or probable covid – 19 case in the last 14 days prior to symptom onset

Or

A patient with severe acute respiratory illness (fever and at least one sign/ symptom of respiratory disease, e.g.; Cough, shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation

Case definition (As per WHO surveillance guidelines)

Probable case:

A suspect case for whom RT-PCR testing for covid – 19 virus is inconclusive.

Or

A suspect case for whom RT – PCR test could not be performed for any reason.

Confirmed case:

A person/ child with laboratory confirmation of covid – 19 infection irrespective of clinical signs and symptoms

Clinical Features

- Majority of children with covid infection may be asymptomatic or mildly symptomatic.
- · Common symptoms include
 - fever,
 - cough,
 - breathlessness/ shortness of breath,
 - fatigue, myalgia, rhinorrhea,
 - sore throat,
 - diarrhea,
 - loss of smell, loss of taste etc.
 - Few children may present with gastrointestinal symptoms and atypical symptoms.

Multi system inflammatory syndrome (MIS –C) has been described in children. Characterized by: unremitting fever > 38°c, epidemiological linkage with SARS cov – 2 and clinical features suggestive of multi system inflammatory syndrome

Management of COVID-19 in children (from 2 months to 18 years) (Interim Protocol)

Child with COVID-19

Mild illness

Sore throat, rhinorrhea, cough. No fast breathing

Home isolation, supportive care, Rest, adequate hydration, paracetamol 10-15 mg/kg/dose for fever, report for danger signs

Evaluate all admitted children with CBC, LFT, RFT, Coagulogram, CRP, D-dimer, Fibrinogen, Chest X-ray, blood culture.

If home monitoring not possible, admit children with mild illness with co-morbidities: chronic lung disease, symptomatic heart disease, chronic kidney disease, neurological disorder

Avoid nebulization; Use MDI and spacer if inhaled medications

Moderate illness Pneumonia

Fast breathing (age based):

- ≥60/min for <2months,
- \geq 50/min for 2-12 months,
- \geq 40/min for 1-5 years,
- ≥ 30/min for >5years

No signs of severe pneumonia/illness

Admit

Monitor for progress

Feeds / fluids: avoid dehydration and

overhydration

Antipyretic: Paracetamol Amoxycillin if

suspicion of bacterial infection

If SpO2<94%, start oxygen. Add steroids only if

very rapid

Severe illness

Severe pneumonia, ARDS Sepsis, Septic Shock, MODS Pneumonia with cyanosis, SPO2 <94%, Increased respiratory efforts(grunting, retraction), Lethargy, somnolence, seizure

Admit, preferably in ICU/ HDU those with ARDS/ Sepsis/ Septic shock/

MODS: Evaluate for thrombosis, hemophagocytic lympho- histiocytosis. organ failure Steroids ± Remdesivir Empiric antimicrobials Oxygen therapy: nasal prong, face mask, HFNC and NIV SpO2 target > 94% during Resuscitation (once stable > 90%) Consider Awake Prone positioning (in older children) Restrictive fluid therapy, organ support

Steroids: Dexamethasone 0.15 mg/kg per dose (max. 6 mg) twice a day for 5-14 days (duration depending on clinical response) is preferred. Equivalent dose of methylprednisolone/ prednisolone may be used, Remdesivir - >40 kg: 200 mg on d1, then 100 mg once daily3.5-40 kg: 5 mg/kg on d1, then 2.5 mg/kg once daily for 5 days

ARDS

Mild ARDS: HFNO/NIV trial Severe ARDS:

Mechanical ventilation: Low tidal volume (6ml/kg), high PEEP, cuffed endotracheal tube Fluid restriction Sedation If poor response: may try prone ventilation

Shock

Septic shock/ Myocardial dysfunction Crystalloid bolus 10-20 ml/kg over 30-60 min, fast if hypotensive; careful administration/ avoid if myocardial dysfunction suspected Early inotrope support Monitor for fluid overload

Children with covid 19 infection may be asymptomatic, mildly symptomatic, moderately sick or severe illness.

- Asymptomatic. Such children do not require any treatment except monitoring for development of symptoms and subsequent treatment according to assessed severity.
- Mild disease: children with mild disease may present with sore throat, rhinorrhea, cough with no
 breathing difficulty. Few children may have gastrointestinal symptoms also. Such children do not need
 any investigations. These children can be managed at home with home isolation and symptomatic
 treatment.

For home isolation it is important to assess whether -

- 1. There is requisite facility for isolation at his/her residence and also for quarantining the family contacts
- ii. Parents or other care taker who can monitor and take care of child
- iii. If available, arogya setu app should be downloaded
- iv. The parents/care giver has agreed to monitor health of the child and regularly inform his/her health status to the surveillance officer/doctor
- v. The parents/ care giver has filled an undertaking on self-isolation and shall follow home isolation/quarantine guidelines

Children with underlying comorbid condition including:

- congenital heart disease,
- chronic lung diseases,
- chronic organ dysfunction,
- obesity (bmi> 2sd)

may also be managed at home - if they have features of mild disease and there is easy access to health facility in case of any deterioration.

In case there is lack of proper arrangement to manage these children at home/ access to health facility is difficult, such children may be admitted.

Treatment of mild illness in home isolation (symptomatic)

- For fever: paracetamol 10-15 mg/kg/dose repeat every 4-6 hours
- For cough: warm saline gargling

Older children and adolescents: ensure oral fluids to maintain hydration, and nutritious diet

- Antibiotics: not indicated
- There is no role of hydroxychloroquine, favipiravir, ivermectin, lopinavir/ritonavir, remdesivir, umifenovir, immunomodulators including tocilizumab, interferon b 1 a, convalescent plasma infusion or dexamethasone.
- Monitoring at home: explain parents/ care taker to maintain a monitoring chart including
 - counting of respiratory rates 2-3 times a day when child is not crying,
 - looking for chest indrawing,
 - bluish discoloration of body, cold extremities, urine output, oxygen saturation monitoring (hand held pulse oximeter) if feasible, fluid intake, activity level
- Regular communication with doctor or health care worker.
- Parents/ caregiver should be explained whom to contact in case of emergency.

Mild illness Sore throat. rhinorrhea, cough. No fast breathing Home isolation Supportive care Rest Adequate hydration and feeding Paracetamol 10-15 mg/kg/dose for fever Report if worsening of danger signs.

Evaluate all admitted children with CBC, LFT, RFT, Coagulogram, CRP, D-dimer, Fibrinogen, Chest X-ray, blood culture.

If home monitoring not possible, admit children with mild illness with co-morbidities: chronic lung disease, symptomatic heart disease, chronic kidney disease, neurological disorder.

Avoid nebulization; Use MDI and spacer if inhaled medications indicated

Management of children with Moderate Covid – 19 disease

Rapid respiration

- < 2 months: respiratory rate >60/ min
- 2 to 12 months: respiratory rate ≥50/min
- 1 to 5 years: respiratory rate \geq 40/min, age:
- >5 years: respiratory rate >30/min. And oxygen saturations above 90%.

Children with moderate covid – 19 disease may be suffering from pneumonia (clinically not apparent)

Investigations: no lab tests required routinely unless indicated by associated co-morbid conditions.

Treatment: Should be admitted to healthcare facility and monitored for clinical progress.

Maintain fluid and electrolyte balance.

Encourage oral feeds (breast feeds in infants);

if oral intake poor, intravenous fluid therapy should be initiated.

Moderate illness Pneumonia

Fast breathing (age based):

- ≥60/min for <2months,
- ≥ 50/min for 2-12 months.
- ≥ 40/min for 1-5 years,
- ≥ 30/min for >5years.

No signs of severe pneumonia/illness

Admit

Monitor for progress

Feeds / fluids: avoid dehydration

and overhydration

Antipyretic: Paracetamol

Amoxycillin if suspicion of bacterial

infection.

If SpO₂<94%, start oxygen. Add steroids only if very rapid progression

Management of children with Moderate Covid – 19 disease

- > For fever Paracetamol 10-15 mg/kg/dose. May be repeated every 4-6 hourly. (Temperature > 38°c, i.E. 100.4°f).
- Amoxycillin to be administered, if there is evidence/ strong suspicion of bacterial infection.
- For Spo2 below 94%, Oxygen supplementation is required.
- Corticosteroids may be administered in rapidly progressive disease. It is not required in all children with moderate illness, specifically during first few days of illness.
- > Supportive care for comorbid conditions

Management of children with Severe Covid-19 disease

- Children with spo2 level less than 90% are categorized as having severe degree of covid-19 infection.
- Such children may have severe pneumonia, acute respiratory distress syndrome, septic shock, multi-organ dysfunction syndrome (MODS), or pneumonia with cyanosis.
- Clinically presentation
 - Grunting,
 - Severe retraction of chest,
 - · Lethargy,
 - Somnolence,
 - Seizure.
- Should be admitted in dedicated covid hospital/ secondary/ tertiary level healthcare facility. May require care
 in HDU/ICU areas of these facilities.
- Assess for: thrombosis, haemophagocytic lympho histiocytosis (HLH), and organ failure.

Investigations:

Complete blood counts, liver and renal function tests, chest x-ray

Treatment

Intravenous fluid therapy

Corticosteroids - dexamethasone 0.15 mg/kg per dose (max 6 mg) twice a day is preferred. Equivalent dose of methylprednisolone may be used for 5 to 14 days depending on continuous clinical assessment.

Anti-viral agents:

Remdesivir is antiviral agent.

(There is lack of sufficient safety and efficacy data in children below 19 years of age and randomized controlled trials of this drug in patients has not shown significant survival benefits in this age).

Dose -

- □ body weight > 40 kg: 200 mg on 1stday then 100 mg once daily for 4 days.
- □ body weight is between 3.5 kg to 40 kg: 5mg/kg on 1st day, 2.5 mg/kg once daily for 4 days.

There is no role of hydroxychloroquine, favipiravir, ivermectin, lopinavir/ritonavir, umifenovir.

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Management of ARDS:

- Mild: High flow nasal oxygenation, non-invasive ventilation may be given.
- > Severe: mechanical ventilation may be given with low tidal volume (<6 ml/kg and high positive end expiratory pressure).
- If the child does not improve clinically even then, may consider (if available) high frequency oscillatory ventilation, extracorporeal membrane oxygenation (ECMO).
- Awake prone position may be considered in older hypoxemic children if they tolerate.

Management of shock:

if the child develops septic shock or myocardial dysfunction then he/ she may require:

- Crystalloid bolus administration: 10 to 20 ml/kg over 30 to 60 minutes (caution for cardiac dysfunction)
- Early inotrope support with monitoring of fluid overload like any other cause of shock

ARDS

Mild ARDS: HFNO/NIV trial

Severe ARDS:

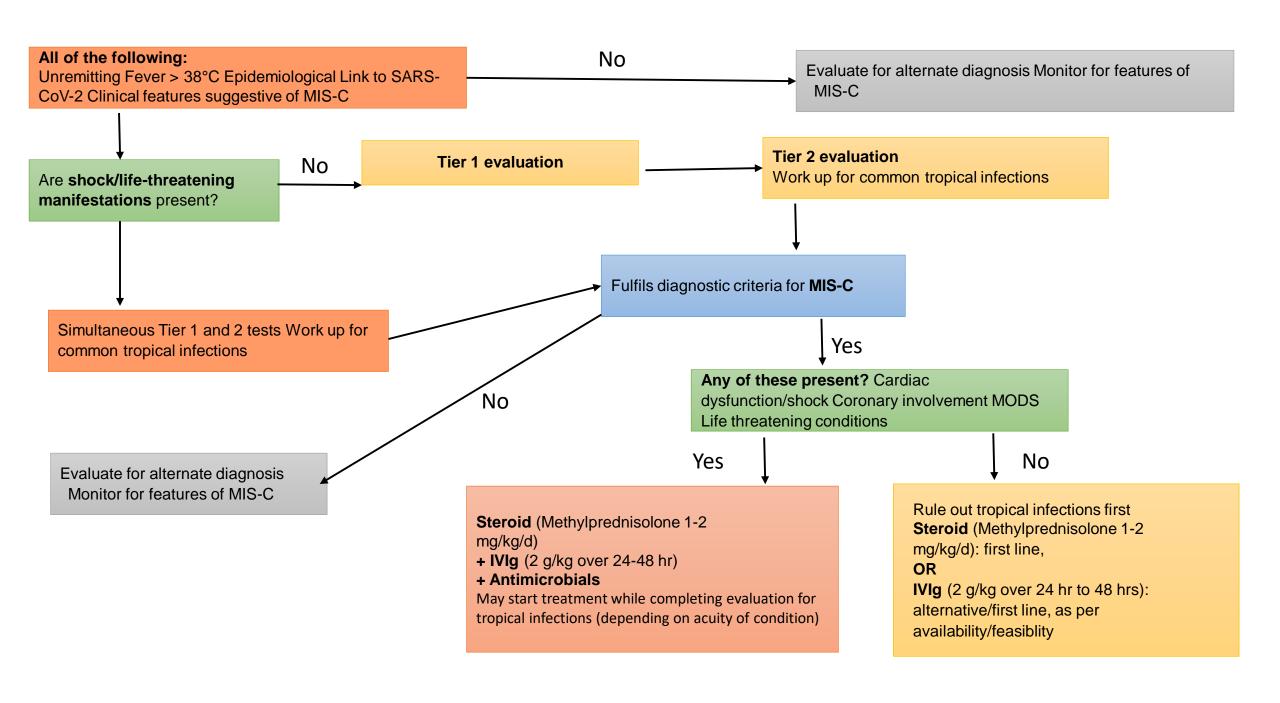
Mechanical ventilation: Low tidal volume (6ml/kg), high PEEP, cuffed endotracheal tube Fluid restriction
Sedation

If poor response: may try prone ventilation, HFOV

Shock

dysfunction
Crystalloid bolus 10-20 ml/kg
over 30-60 min, fast if
hypotensive; careful
administration/ avoid if
myocardial dysfunction
suspected
Early inotrope support
Monitor for fluid overload

Management of Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19 (MIS-C)



Diagnostic Criteria for MIS-C

Children and adolescents 0–19 years of age with fever \geq 3 days

AND two of these:

- -Rash or bilateral non-purulent conjunctivitis or muco-cutaneous 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-pro BNP),
- -Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).

Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain). AND Elevated markers of inflammation such as 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

If no improvement or worsening of symptoms, options include

- Repeat IVIg and/ or High dose steroid (Methylprednisolone 10-30 mg/kg/d for 3-5 days)
- If unresponsive to above, may consider high dose Anakinra; 2-10 mg/kg/dose (max 100 mg/dose) SQ/IV q6-12h

Aspirin (indications: Thrombocytosis, or Coronary aneurysm Z-score ≥ 2.5)

➤ Dosage: 3 - 5 mg/kg/day; max 81 mg/day

Enoxaparin (indications: Coronary aneurysm (Z-score > 10) or Thrombosis or LVEF < 35%)

- ➤ Dosage: 1 mg/kg twice daily SC
- > Preferably monitor with factor Xa level 0.5-1
- □ Taper steroids over 2-3 weeks while monitoring inflammatory markers
- For Children with cardiac involvement
 - > Repeat ECG 48 hourly, Repeat ECHO at 7-14 days and between 4 to 6 weeks (and after 1 year, if initial ECHO was abnormal)

Tier 1 Investigations (may be done at Covid Care Centre, Dedicated Covid Health Centre): CBC, Complete metabolic profile (LFT/RFT/blood gas/glucose), CRP and/or ESR, SARS-CoV-2 Serology and/or PCR, Blood culture

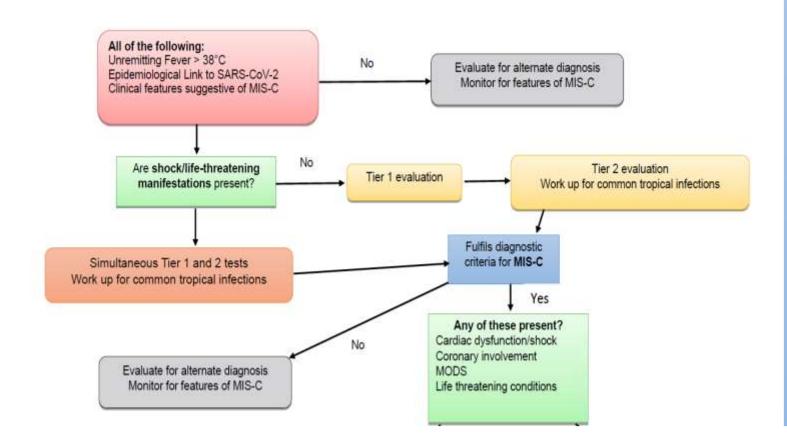
Positive Tier 1 screen (both of these should be present): 1. CRP> 5 mg/dL and/or ESR > 40 mm per hour; 2. At least one of these: ALC < $1000/\mu$ L, Platelet < $150,000/\mu$ L, Na < 135 mEq/L, Neutrophilia, Hypoalbuminemia

Tier 2 Investigations (may be done at Dedicated Covid Hospital): Cardiac (ECG, Echocardiogram, BNP, Troponin T); Inflammatory markers (Procalcitonin, Ferritin, PT, PTT, D-dimer, Fibrinogen, LDH, Triglyceride, Cytokine panel); Blood Smear; SARS-CoV-2 serology.

Common tropical infections include: Malaria, Dengue, Enteric fever, Rickettsial illness (scrub typhus), etc

MISC characterized by: unremitting fever > 38° C, epidemiological linkage with SARS cov – 2 and clinical features suggestive of multi system inflammatory syndrome.

Diagnostic criteria of MISC in children (WHO criteria): a constellation of clinical and laboratory parameters has been suggested for diagnosis (as shown in fig)



Diagnostic Criteria for MIS-C

■ Children and adolescents 0–19 years of age with fever > 3 days

AND two of these:

- Rash or bilateral non-purulent conjunctivitis or muco-cutaneous 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-pro BNP).
- Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
- Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND

Elevated markers of inflammation such as ESR,
 C-reactive protein, or procalcitonin.

AND

 No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

AND

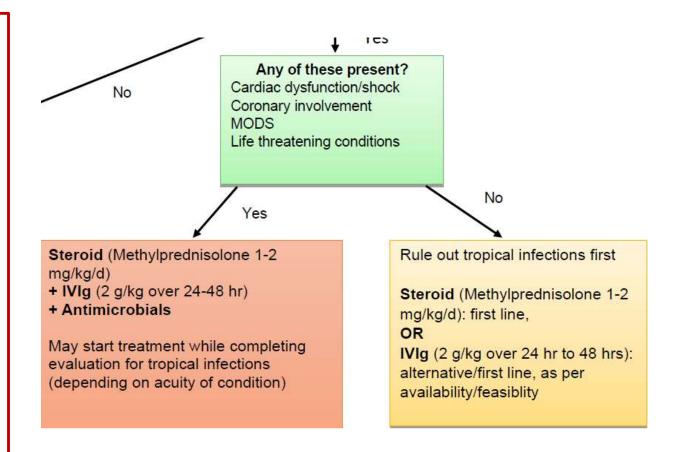
 Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

Treatment of MIS-C

- i. **Steroids:** methylprednisolone 1 to 2 mg/kg per day.
- ii. Intravenous immunoglobulin 2 g/kg over 24 to 48 hours.
- iii. Antimicrobials

The child needs appropriate supportive care, preferably in ICU.

In absence of cardiac dysfunction, shock, coronary involvement, multi organs dysfunction, one may use steroids or IVIG (for details, see algorithm)



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If the child does not improve with the above treatment or deteriorates, options include:

- Repeat Ivig
- High dose corticosteroid (methylprednisolone 10 to 30 mg/kg/day for 3 to 5 days)
- Aspirin: 3 mg/kg/day to 5 mg/kg/day max 81 mg/day (if thromobosis or coronary aneurysm score is ≥ 2.5)
- Low molecular weight heparin: enoxaparin: 1 mg/kg twice daily subcutaneously. Clotting factor xa should be between 0.5 to 1 (if patient has thrombosis/ coronary aneurysm score > 10 or LVEF < 30%)

Steroids have to be tapered over 2 to 3 weeks while monitoring inflammatory markers. For children with cardiac involvement, repeat ECG 48 hourly, repeat ECHO at 7 to 14 days and between 4 to 6 weeks and at 1 year if initial ECHO was abnormal.