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Complications of COVID in Children

Mary Anbarasi Johnson

Professor and Head Pediatric Nursing Department CMC Vellore Department of College of Nursing, Dr.MGR Medical University / College of Nursing CMC Vellore, India

***Corresponding author:** Dr. Mary Anbarasi Johnson, Professor and Head Pediatric Nursing Department CMC Vellore, Department of College of Nursing, Dr.MGR Medical University /College of Nursing CMC Vellore, India

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Abstract

Covid 19 has caused detrimental effects both on adults and children.Since December 2019, Covid-19 has become a challenge for doctors around the world, including pediatricians. In most infected children, the disease manifests itself in a mild or is char- acterized by a subclinical course. At the same time, in some cases, a severe clinical picture of the so-called late Covid disease may develop, in the form of a multisystem syndrome and other complications.The common complications due to Covid are

- *Multi system Inflammatory syndrome in children(MIS-C)*
- *Acute Respiratory distress syndrome*
- *Mucormycosis*

Keywords: Misc, Phenotype, ARDS, Mucor mycosis

Multi system inflammatory syndrome in children (MIS-C)

Introduction

Multisystem inflammatory syndrome in children (MIS-C) is a serious condition that appears to be linked to coronavirus disease 2019 (COVID-19). Most children who become infected with the COVID-19 virus have only a mild illness. But in children who go on to develop MIS-C, some organs and tissues — such as the heart, lungs, blood vessels, kidneys, digestive system, brain, skin or eyes — become severely inflamed. Signs and symptoms depend on which areas of the body are affected.

The condition has been termed multisystem inflammatory syndrome in children (MIS-C; also referred to as pediatric multisystem inflammatory syndrome [PMIS], pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 [PIMS-TS], pediatric hyperinflammatory syndrome, or pediatric hyperinflammatory shock).

Results from an abnormal immune response to the virus, mimics Kawasaki disease therefore called Kawa covid

- Occurs post covid-Peak 4-6 weeks
- Total MISC in CMC-43

DEFINITION OF MIS-C (WHO)

Children and adolescents 0–19 years of age with fever > 3 days AND two 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-proBNP),
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

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

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

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

Other criteria

- Involvement of other systems(renal,respiratory,neurological,dermatologic or hematological)
- Neutrophilic leukocytosis
- Thrombocytopenia,hypoalbuminemia,hyponatremia

MIS-C-PHENOTYPES

3 Phenotypes:

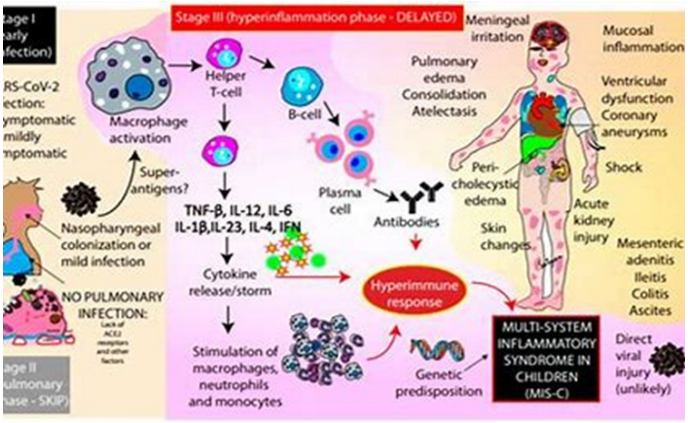
• Febrile inflammatory state:
Persistent fever, mild symptomslike headache and fever

• KD like illness: Features of Kawasaki illness(rash,conjunctivitis,strawberry tongue,cervical lymphadenopathy) but no signs of shock

• Severe MIS-C: Cardiac involvement,shock Markedly elevated inflammatory markers

Pathophysiology

The pathophysiology of MIS-C is not well understood. It is thought to result from an abnormal immune response to the virus, with some clinical similarities to KD, macrophage activation syndrome (MAS), and cytokine release syndrome. However, MIS-C appears to have an immunophenotype that is distinct from KD and MAS. Most affected children have positive serology for SARS-CoV-2 with negative polymerase chain reaction (PCR), a finding that further supports the hypothesis that MIS-C is related to immune dysregulation occurring after acute infection has passed. However, some children do have positive PCR testing



Clinical Manifestations

- Fever that lasts 24 hours or longer
- Vomiting
- Diarrhea
- Pain in the stomach
- Skin rash
- Feeling unusually tired
- Fast heartbeat
- Rapid breathing
- Red eyes
- Redness or swelling of the lips and tongue
- Redness or swelling of the hands or feet
- Headache, dizziness or lightheadedness
- Enlarged lymph nodes

Emergency warning signs of MIS-C

1. Severe stomach pain
2. Difficulty breathing
3. Pale, gray or blue-colored skin, lips or nail beds - depending on skin tone
4. New confusion
5. Inability to wake up or stay awake

Diagnosis

Step 1 screening

CBC, CRP, ESR, LFT, electrolytes, creatinine, blood culture, Widal, Weil Felix, Urine routine

Positive screen: CRP or ESR elevated
ALC,Platelets,Sodium,neutrophilia
Cardiac:ECG/ECHO/roponin

Inflammatory markers:
Procalcitonin, PT, PTT, D dimer, Fibrinogen, LDH, Triglyceris=de, SARS COV -2 serology

Management

Setting of care and management:

The appropriate setting of care is determined by the severity of illness, risk of complications, and adequacy of follow-up. Most children with MIS-C are managed in the inpatient setting.

● **Inpatient management –** Children with moderate to severe manifestations of MIS-C and those at risk for complications should be admitted to the hospital. This includes any of the following

- Abnormal vital signs (tachycardia, tachypnea)
- Shock
- Respiratory distress
- Evidence of cardiac involvement (eg, elevated troponin or brain natriuretic peptide, depressed ventricular function or coronary artery [CA] abnormality on echocardiogram, abnormal electrocardiogram)
- Features of Kawasaki disease (KD)
- Neurologic changes (eg, depressed mental status, abnormal neurologic examination, seizures)
- Severe abdominal pain or vomiting, especially if unable to tolerate oral feeding
- Clinical or laboratory evidence of dehydration
- Laboratory evidence of acute kidney injury, acute hepatic injury, or coagulopathy
- Underlying medical condition that may place the child at increased risk for complications (eg, immunodeficiency, cardiac or pulmonary conditions)
- Inability to return for follow-up

In addition, we generally hospitalize children with clinical findings that strongly suggest a diagnosis of MIS-C, even if their symptoms are relatively mild initially. This is because children with MIS-C often have worsening of their clinical status as the illness progresses.

The level of care (ward versus pediatric intensive care unit [PICU]) is determined by the severity of illness.

Admission to a PICU is appropriate for children with hemodynamic instability (shock, arrhythmia), significant respiratory compromise, or other potentially life-threatening complications.

● **Outpatient management –** It may be reasonable to manage select patients with mild symptoms in the outpatient setting, provided that the child is well-appearing and close clinical follow-up can be assured.

For children who are managed in the outpatient setting, it is critical to provide instructions for when to seek care and to ensure appropriate follow-up

Treatment guidelines:

- Remdesvir-no role
- Antibiotics-as per protocol(Cefotaxim/Merpenam/Teicoplanin/Azithromycin)
- If child in shock:
- IVIG-2gm/kg and
- Inj.Methyl prednisolone 1-2 mg/kg/day
- If no shock:IVIG-2gm/kg
-

And refractory with no improvement:

Inj.Methylprednisolone:30mg/kg

Antiplatelets: If thrombocytosis or coronary artery aneurysm

- Low dose Aspirin 3-5mg/kg/day
- Z score-2.5-10
- Anticoagulation: Enoxaparin/Clexane
- <2 mon-0.5mg/kg SC Q12 H
- >2 mon-1mg/kg SC Q12 H
- Z score>10
- Severe LV dysfunction EJ <35%/thrombosis

Prevention

- Keep hands clean Avoid people who are sick
- Practice social distancing at least 6 feet (2 meters) from other people
- Wear cloth face masks in public settings
- Avoid touching your nose, eyes and mouth
- Cover your mouth with a tissue or your elbow when you sneeze or cough
- Clean and disinfect high-touch surfaces every day Wash clothing and other items as needed

Covid related Pneumonia with Acute Respiratory Distress Syndrome:

Introduction:

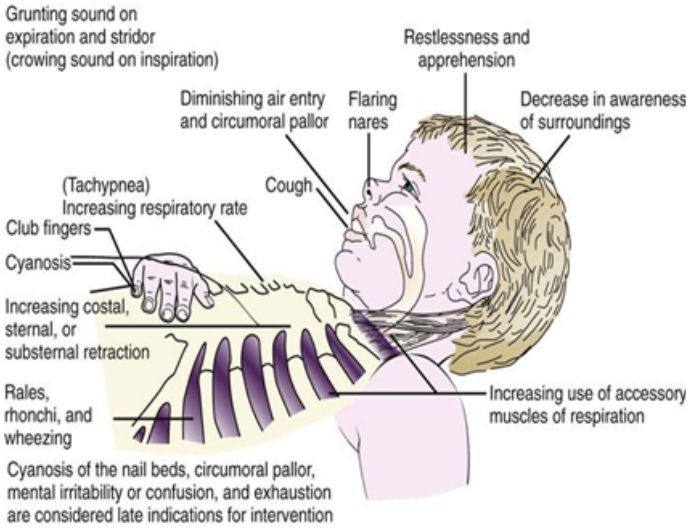
COVID-19 is less serious in children than in adults. However, respiratory management dominates the clinical picture of hospitalized COVID-19 even in children. In some case series, deterioration of the clinical picture wherein dyspnea, cyanosis, and the onset of acute respiratory distress syndrome (ARDS) emerged ~8-10 days after the onset of SARS-CoV-2 infection, which could rapidly progress to multiple organ failure and death

The clinical spectrum of COVID-19 is wide, varying from completely asymptomatic forms to those characterized by severe respiratory distress requiring intensive care. Respiratory management dominates the clinical picture of hospitalized COVID-19 patients. In some case series, deterioration of the clinical picture wherein dyspnea, cyanosis, and the onset of acute respiratory distress syndrome (ARDS) emerged approximately 8–10 days after the onset of SARS-CoV-2 infection, which could rapidly progress to multiple organ failure and death

Pathophysiology:

The immune response induced by SARS-CoV-2 infection is characterized by two phases: an initial immunoprotective phase and an activation phase of the cytokine storm, which yields a more severe clinical manifestation. In the first phase, a robust adaptive response can control the virus and block inflammatory progression. If the immune system fails to control this phase, cell damage in organs with high concentrations of ACE2, especially pneumocytes, progresses by the release of cytokines and chemokines (IL-6, IL-10, and interferon) and the recruitment of inflammatory cells, which mediate lung damage and progression toward ARDS with evidence of diffuse alveolar damage with desquamation of pneumocytes, hyaline membrane formation, and the presence of fibromyxoid cells with interstitial lymphocyte infiltration . SARS-CoV-2 causes interstitial pneumonia.

Clinical manifestations of child with Respiratory distress syndrome:



Investigations:

CBC, RFT, LFT, CRP, ECG, ABG, CXR, LDH, Ferritin and ECHO, Chest Xray, CT Thorax

General Support

Hospitalized children must have their vitals monitored and have adequate intake of fluids and calories aimed at maintaining a hydro-electrolytic homeostasis. Additionally, bed rest and maintenance of cleared upper airways are recommended

Oxygen Therapy

In case of hypoxia (SpO_2 <95%) without signs of respiratory distress, the administration of oxygen via nasal cannulae or mask is sufficient, while constant monitoring of vital parameters and attending to changes in the acid-base balance may be indicative of clinical worsening

Ventilatory Support

In case of respiratory distress associated with hypoxemia, simple oxygen administration is insufficient. In these cases, high-flow nasal oxygen (HFNO) or non-invasive ventilation, such as continuous positive airway pressure (CPAP), should be used . The World Health Organization (WHO) recommends that HFNO be used in single or negative pressure rooms “whenever possible.” A valid alternative to HFNO is CPAP—preferably helmet CPAP—with positive end-expiration pressure (PEEP) ranging from 5 to 10 cmH_20 .In any case, the critically ill child should be transferred to a pediatric intensive care unit and, in the event of

non-response to non-invasive ventilation or of onset of pediatric acute respiratory distress syndrome (PARDS), initiation of invasive mechanical ventilation should be considered and, ultimately, extracorporeal membrane oxygenation (ECMO).

Pharmacological Treatment

There is little reliable evidence for the utility of drugs in treating COVID-19 pneumonia in pediatric populations.

No specific anti-SARS-CoV-2 drug has yet been proven effective. Antiviral drug therapy seems to be effective if initiated before clinical deterioration. possible pharmacological interventions include:

- Lopinavir/Ritonavir: effective in reducing viral replication as long as it is administered in the very early stages of the disease. Common side-effects include diarrhea and nausea, and it is contraindicated in cases of hepatic impairment

- Ribavirin: A drug used in combination with interferon-alpha or Lopinavir/Ritonavir. Hemolytic anemia is a possible side-effect
- Remdesevir: A new-generation antiviral that has a potent antireplicative action against SARS-CoV-2
- Hydroxychloroquine

Antiviral drugs used in Pediatrics:

Antiviral	Route of administration	Pediatric dose	Duration of treatment
Interferon-α*	Inhalation	200,000–400,000 IU/kg in 2 mL of sterile water, twice daily	5–7 days
Lopinavir/Ritonavir	Oral	12 mg/3 mg/kg if weight 7–15 kg, 10 mg/2.5 mg/kg if weight 15–40 kg, 400 mg/100 mg (adult dose) if weight > 40 twice daily	1–2 weeks
Ribavirin	Intravenous	10 mg/kg/dose, 2 or 3 times daily	Max 5 days
Remdesevir	Intravenous	5 mg/kg loading dose, then 2.5 mg/kg once daily	10 days
Hydroxychloroquine sulfate	Intravenous	3–5 mg/kg/day (max dose 400 mg), twice daily	5 days

Most commonly used.

- Antibiotics: Their use is discouraged unless there are signs of bacterial co-infection. The usefulness of macrolides, especially azithromycin, for their anti-inflammatory properties is also questionable

- Corticosteroids: Their routine use is discouraged; however, they should be considered in cases of PARDS. In these cases, the administration of methylpredisolone at a dose of 1–2 mg/kg/day for a maximum of 4–5 days is recommended

- Gamma globulins: Their effectiveness is not clear. They can be attempted in particularly severe forms of COVID-19 and in those with symptoms similar to Kawasaki disease at the dose of 2 g/kg/day for one day, 1 g/kg/day for two days or 400 mg/kg/day for five days

- Tocilizumab: This human anti-IL-6 monoclonal antibody appeared to be effective in the treatment in adults with extensive and bilateral lung involvement .It should be used cautiously in children: 12 mg/kg in children weighing <30 kg, 8 mg/kg (max: 800 mg) in children >30 kg, to repeat once after 12 h if no improvement

Shock- adequate istonic fluid boluses (10-20 ml/kg over 30-60 min,).

Ionotropic agents for fluid refractory shock.Adrenalin Infusion for cold shock and Nor adrenalin infusion for warm shock.

Conclusion

• Nurses play an important role.Early recognition of deterioration and timely management improves outcomes. Interdisciplinary team approach is the key to successful management.

MUCORMYCOSIS

Introduction:

Mucormycosis is an infection caused by fungi that belong to the order Mucorales. Mucoraceae represent the third most common cause of invasive fungal infection. Mucormycosis is caused by a common mould which is normally all around us and affects the sinuses, lungs, skin, and brain. The infection of the oral cavity or brain is the most common form of Mucormycosis, the fungus can also infect other areas of the body such as the gastrointestinal tract, skin, and other organ systems.

Risk Factors:

- Hematological malignancy
- Post Covid due to treatment with steroids
- Poorly controlled Diabetes Mellitus
- Rheumatologic/autoimmune disorders
- Prematurity
- Burns and traumatic wounds-cutaneous mucormycosis
- Immunosuppression
- Misuse/overuse of steroids, cancer
- Organ/stem cell transplantation
- Those under prolonged ICU treatment

Clinical Manifestations:

- One sided facial pain, numbness or swelling
- Blackish discoloration over bridge of nose/palate
- Toothache, loosening of teeth, jaw involvement
- Blurred or double vision with pain; fever, skin lesion; thrombosis & necrosis (eschar)
- Chest pain, pleural effusion, haemoptysis, worsening of respiratory symptoms

Treatment:

- Surgical debridement and antifungal therapy
- Recommendations for dosing L Amphotericin B(LAmB)-3-5 mg/kg per day, and a higher dosage (10 mg/kg per day) is favored for CNS infection
- Isavuconazole or Posaconazole to continue for 4 -6 weeks
- 7-12 mg/kg/dose IV twice on the first day and maintenance dose - 7-12 mg/kg IV once a day, starting on the second day

Nursing Management

1. Pain management:

- Assess pain score-administer pain medication
- Ice application over cheeks and periorbital region
- Oral hygiene
- Preparation for emergency surgery
- Fever management:Antipyretics

2. Endoscopic debridement:

- Maxillectomy/Orbital eventeration
- Pack removal at 2nd or 3rd day
- Nasal douching
- Use of nasal sprays q^2 hourly

3. Antifungal therapy:

- LIPOSOMAL AMPHOTERICIN B-prolonged infusion over 3-4 hours through a central venous catheter or PICC and closely monitoring KFT and electrolytes(Potassium and Mg). Check for thrombophlebitis.W/F oliguria and I&O
- Inj.Avil and Paracetamol given ½ hour before drug administration
- Reconstitute in water for injection, and dilute in 5 per cent dextrose (do not use normal saline/Ringer's lactate)
- Conventional Amphotericin 1mg/kg
- Pre and post hydration
- KCL supplemented if hypokalemia

4. Nutrition:

- Nasogastric tube feeds in early stages
- Later:Pharyngeal feeds
- Liquids---semisolids----solids

5. Psychological support:

- Reassurance
- Call bells and prevention of injury

Conclusion

Even though COVID-19 is known to be a less severe in the paediatric population, the complications of the virus have caused a great deal of stress to the paediatric patients' parents and Health care workers worldwide, and hence, emphasis should be given to the management of coronavirus complications in paediatrics.

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