INDIAN MEDICAL ASSOCIATION
HOSPITAL BOARD OF INDIA

COVID 19 IN CHILDREN

Coordinator	Contributors	
Dr Ravi Wankhedkar	Dr Ashok Rai	Dr Digant Shastri
	Dr Bhaskar Shenoy	Dr Mangesh Pate

Children of all ages can get infected with Covid-19. Approximately 4-6% children were infected in first wave, though many were asymptomatic. Second wave of the pandemic has shown more paediatric patients (approx. 10-15%, though exact data is not available of India) from all age groups. Though serious illness is not seen commonly in children, the trend of increasing paediatric cases & few more requiring hospitalisations adds to the worry. As the estimates speak, we may face flooding of the paediatric patients in coming future.

Children with comorbidities, such as congenital heart diseases, liver ailments, obesity, diabetes and asthma or other underlying conditions like genetic diseases, may be at high risk of getting moderate to severe disease.

Different Response of Paediatric Population to Covid-19

Though scientifically not clear as yet, there appears a different response from paediatric age groups to the corona virus. Various reasons are being thought over & same will lead the way forward for the expected surge in children.

Coryza is the most common viral infection in children. And usually, it is most commonly caused by infection with rhinoviruses, coronaviruses, influenza & parainfluenza viruses, respiratory syncytial virus (RSV), enteroviruses and adenovirus, Mycoplasma pneumoniae which typically causes sore throat and cough in children. These infections are far common in Paediatric Population as compared to adults. This

can be a major factor for the immune system in children which may already been primed against the corona virus infections.

Immune response to corona virus also may play an important role. As seen in adults. those with hyper-reacting immune responses have shown serious illness in Covid 19. Already primed & so controlled immune response in children to corona viruses must be protecting them from moderate or serious covid illness. Children have shown a distinct immune response to the Covid 19 infection as compared to adults. It was also noted that children who had contracted Covid 19 infection produced lower levels of neutralizing antibodies and fewer types of antibodies.

This can be an important reason that even the symptoms like fever and cough are common in children with covid 19 infection, the lesions typically seen in the adult lungs with Covid 19 are rare. This does not mean that children are immune to the Covid 19 infection. Covid 19 related multi-system inflammatory syndrome (MIS) in children has been identified recently in few countries & stands as a cause of concern.

The adult patients with the serious symptoms of ARDS [Acute Respiratory Distress Syndrome] have shown the high levels of antibodies while children with mostly milder symptoms have lower antibody responses. This does not mean that children have weaker immune response. It is also thought that adults produce more types of antibodies than children because they have a higher viral load than that in children.

Cellular immunity has been shown to play an important role along with the antibody related immune response. T-cell response is said to be a better indicator of prognosis in patients with Covid 19. In this view, the cellular immune response in paediatric age group may be playing the key role in giving the different response to the Covid 19.

Quantitative analysis of the antibody response & cellular immune response in children, with and without moderate to severe Covid 19 infection, will play the most important role in understanding the response to disease & will prove to be helpful in channelizing the treatment strategies.

Transmission of Covid 19 in Children

A family member with Covid 19can be the commonest cause of transmission in children while others can get it due to exposure to a suspected case outside home. On many occasions there is no clear source of transmission detected. Family cluster transmissions are found to be common during the second wave. Paediatric population is more thought to be infective to adults as compared to they getting infected from adults. This was truer during the first wave. Second wave has seen more adults getting infected & setting a cluster family transmission as a trend. Mother infected with the coronavirus can in rare cases pass the disease to her baby. New-borns can also become infected after birth. Transmission in schools, classes, educational or child care settings are very much possible owing to infectivity rate of coronavirus & likely lack of safety protocols in these places.

The public health policy must consider the transmission modes in children during policymaking for schools and classes. Masks, Social Distancing, Hand & General Hygiene are most important & should be routinely taught to children. Good air ventilation at home is important for prevention of spread.

CLINICAL COURSE

The incubation period for COVID-19 is thought to extend to 14 days, with a median time of 4-5 days from exposure to symptoms onset. The signs and symptoms of COVID-19 present at illness onset vary, but over the course of the disease, most children with COVID-19 will experience the following:

- **Fever**
- **Cough**
- **Fatigue**
- **Anorexia**
- **Shortness of breath**
- **Myalgia**

Atypical presentation is seen in children with medical comorbidities and may have delayed presentation of fever and respiratory symptoms. Headache, confusion, rhinorrhoea, sore throat, haemoptysis, vomiting, and diarrhoea have been reported but are less common (<10%). Some persons with COVID-19 have experienced gastrointestinal symptoms such as diarrhoea and nausea prior to developing fever and lower respiratory tract features.

Illness Severity

- **Mild to moderate (mild symptoms up to mild pneumonia): 81%**
- **Severe (dyspnoea, hypoxia, or >50% lung involvement on imaging): 14%**
- **Critical (respiratory failure, shock, or multi organ system dysfunction): 5%**

Children with no reported underlying medical conditions had lower case fatality rate, but case fatality was higher for children with comorbidities like cardiovascular disease, chronic respiratory disease, chronic kidney disease, immunocompromised states, etc. Among children who developed severe disease, the medium time to develop dyspnoea ranged from 5 to 8 days, the median time to acute respiratory distress syndrome (ARDS) ranged from 8 to 12 days, and the median time to ICU admission ranged from 10 to 12 days. Clinicians should be aware of the potential for some children to rapidly deteriorate within one week after the onset of illness. The median length of hospitalization among survivors was 10 to 13 days.

Children may play a role in the spread of SARS-CoV-2 in the community as viral RNA was detected in respiratory specimens up to 22 days after symptoms began and in stool up to 30 days after symptoms began according to some studies. Although transmission of SARSCoV-2 from asymptomatic or pre-symptomatic persons has been reported, risk of transmission is thought to be greatest when children are symptomatic. Viral RNA shedding, measured indirectly by RT-PCR cycle threshold values, is greatest at the time of symptom onset and declines over the course of several days to weeks.

Clinical recovery has been correlated with the detection of IgM and IgG antibodies which signal the development of immunity. However, overall control of pandemic depends of development of herd immunity either by infection or mass

immunization (under research process). There are no data concerning the possibility of re infection with SARS-CoV-2 after recovery from COVID-19.

Moderate disease
• Mild pneumonia • Symptoms such as fever, cough, fatigue, headache and myalgia • No complications and manifestations related to severe infections
Severe disease
• Mild or moderate clinical features plus any manifestations that suggests disease progression • Tachypnea as per age. (<2months- >60; 2-12 months - >50; 1-5 yrs - >40; >5 yrs - >30) • Hypoxia • Loss of consciousness, Depression, coma, convulsions • Dehydration, difficulty feeding, gastrointestinal dysfunction • Myocardial injury • Elevated liver enzymes • Coagulation dysfunction, rhabdomyolysis and any other manifestations suggesting injuries to vital organs
Critical illness
Rapid disease progression plus any other conditions • Respiratory failure with need for mechanical ventilation (e.g., ARDS, persistent hypoxia that cannot be alleviated by inhalation through nasal catheters or through mask) • Septic shock • Organ failure that needs monitoring in ICU

Diagnosis of Covid 19 in Children

Testing recommendations in Neonates

Testing is recommended for all neonates born to mothers with suspected or confirmed COVID-19 regardless of whether there are signs of infection in the neonate. Diagnosis in neonates should be confirmed by testing for SARS-CoV-2 RNA by Reverse Transcription Polymerase Chain Reaction (RT-PCR). For Rt-PCR, swabs can be collected from nasopharynx, oropharynx or nasal mucosa.

When to test in Neonates

Neonates born to mothers with suspected or confirmed COVID-19 should undergo swab test at approximately 24 hours of age. If initial test is negative, RT-PCR should be repeated at 48 hours of age.

Testing in Infants & older children

- **Infants, older children should be tested as they develop symptoms. RT-PCR, Rapid Antigen Test or TrueNAT.**

- **Rapid antigen test**
  - **Sensitivity 30%, done from nasopharyngeal swab. RTPCR alwaysrecommended in RAT negative covid suspects.**
  - **Detect viral spike protein in a nasal swab.**
  - **Quick results (20 minutes).**
  - **Rapid point of care test; optimal in ER setting, early in course of disease ▪**
  - **Negative test does not rule out infection .**

- **RTPCR**
  - **Sensitivity 38 - 72%; high specificity.**
  - **Molecular test of choice for the etiologic diagnosis.**
  - **Most accurate, less prone to contamination.**

- **Truenat**
  - **Chip based, portable RTPCR mechanism.**
  - **Detect an enzyme Rd Rp found in the RNA of SARS cov-2.**

- **Anti body test**
  - **Done to find out whether an individual has been infected with covid-19.**

- **Used to know estimates of the rate of infection. Not to be done for initial diagnosis**

Other Investigations in Covid 19 in children

Lymphopenia is a good predictor of disease severity in COVID-19 infection. CRP and procalcitonin can to be mildly elevated particularly in children with features of pneumonia. Liver enzymes are increased in few children. D-Dimer is more likely to be elevated in symptomatic children infected by SARS-CoV-2. Elevated C-reactive protein (CRP), Elevated serum ferritin, Elevated lactate dehydrogenase are seen in few patients. Raised ESR is a good acute phase reactant with CRP. Leucocytosis with lymphopenia may be seen. Elevated inflammatory markers and lymphocytopenia may indicate multisystem inflammatory syndrome in children.

WHO Definition for Multisystem Inflammatory Syndrome in Children All 6 Criteria must meet		
1	Age	0 to 19 years
2	Fever	For ≥3 days
3	Clinical signs of multisystem involvement (at least 2 of the following)	
		Rash, bilateral nonpurulent conjunctivitis, or mucocutaneous inflammation signs (oral, hands, or feet)
		Hypotension or shock
		Cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities (including echocardiographic findings or elevated troponin/BNP)
		Evidence of coagulopathy (prolonged PT or PTT; elevated D-dimer)
		Acute gastrointestinal symptoms (diarrhoea, vomiting, or abdominal pain)
4	Elevated markers of inflammation	(e.g., ESR, CRP, or procalcitonin)
5	No other obvious microbial cause of inflammation, including bacterial sepsis and staphylococcal/streptococcal toxic shock syndromes	
6	Evidence of SARS-CoV-2 infection	Any of the following: • Positive SARS-CoV-2 RT-PCR

		• Positive serology • Positive antigen test • Contact with an individual with COVID-19

Reference: World Health Organization. Multisystem inflammatory syndrome in children and adolescents with COVID-19: Scientific Brief. 2020. Available at: https://www.who.int/publications-detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19

CRP, Procalcitonin, Interleukin 6, Ferritin, D-dimer are the potential markers of severe disease. The clinical features of MIS-C may be similar to those of Kawasaki disease, Kawasaki disease shock syndrome, and toxic shock syndrome. They include persistent fever, hypotension, gastrointestinal symptoms, rash, myocarditis and laboratory findings associated with increased inflammation.

HRCT scan has been used extensively in adults. In paediatric age group however, the typical ground glass opacities may be seen rarely, that too in moderate to severe cases. Ground-glass opacity, local and bilateral patchy shadowing are found in few symptomatic children. Unlike adults, RT-PCR negative children may not show CT changes as an early diagnostic tool. Findings typical of other viral respiratory infections (e.g., hyperinflation, bronchial markings) are not reported. Pleural effusions are reported in rare cases. HRCT should be performed as indicated to evaluate clinical findings suggestive of respiratory involvement, risk factors for disease progression, potential complications or worsening respiratory status.

How to Protect Children from Covid 19

Avoiding children from coming in contact with outsiders or even family members with symptoms is the most important. Carelessness by family members while having some symptoms of viral infection may result in infecting others in the family.

Maintain physical distancing outside & at home. The more people your kids come in contact with higher is the risk of infection with the Covid 19. Children should stay at least 6 feet away from others while they go out. Limit playing with other children and be sure the children wear masks properly even while playing. Household maids or workers are the commonest cause of transmission. Avoid contact with those visiting your home from outside.

Wear a mask. When any of the family members are out in public, both adults and children should wear a mask that covers both nose and mouth. Strictly avoid

the places outside the home where physical distancing is not possible. Help & teach your children practice wearing masks.

General & Hand hygiene. Teach children to wash their hands after using the bathroom, sneezing, coughing or blowing their nose, before eating and immediately after coming from playing outdoors. Parents should teach kids to wash their hands regularly with soap and water. Also teach them to use hand sanitizer containing at least 60% alcohol.

Cough and sneeze with due care. Everyone in the family should make it a habit cough and sneeze into their elbow instead of their hands. Use tissues or separate handkerchiefs. Throw tissues immediately or keep the handkerchiefs away from rest in the family.

Keep hands off faces. Parents should remind children to avoid touching their face as much as possible.

Keep things clean. Wipe the toys, floors and surfaces your child touches regularly. Using good disinfectants specifically for surface cleaning is must.

Management of Paediatric Covid

A) MILD DISEASE

- **Home isolation**
- **Supportive care; monitoring at home**
- **Feeding as per age**
- **Adequate hydration and feeding**
- **Paracetamol 10-15 mg/kg/dose for fever (every 6 hourly)**
- **Avoid Ibuprofen.**
- **Nasal saline drops for nasal block**
- **Zinc, Vitamin C & Multivitamin as per recommendation**
- **Explain danger signs**
- **To report to health facility if any worsening**

- **Zinc: plays an important role in immune function, wound healing & regulation of gene expression. Currently indirect evidence suggests that zinc may potentially reduce the risk, duration & severity of SARS-COV2 infection. Using**

a high dose (1mg per kg of zinc as a supplement can improve frequent viral & bacterial infections.)

- **Vitamin-C is a water-soluble vitamin having multiple pharmacological characteristics as antiviral, antioxidant, anti-inflammatory & immunomodulatory effects. It improves epithelial barrier integrity, natural killer cell activity & phagocytosis. Insufficient data available to recommend either for or against the use of vitamin-C in non-critically ill patients.**

Duration of home isolation -

- **10 days after symptom onset and no fever for 3 days. [This is followed by further 7 days of home isolation and self-monitoring]**
- **Documentation of negative RT-PCR no longer recommended**

B) Mild illness with Co-morbidities

Co-morbidities

- **Chronic lung disease**
- **Uncorrected heart disease (heart failure or cyanotic heart disease)**
- **Chronic renal disease**
- **Neurological disability (cerebral palsy, muscular dystrophy)**
- **Immune-compromised state**

Management

- **Treat as mild illness with home care if Parents are capable of home monitoring and health access if danger signs appear**
- **Otherwise, admit for monitoring and treat as mild illness**

Indications for hospital admission

- **Respiratory distress**
- **SpO2 < 94% on room air**
- **Shock/ poor peripheral perfusion**
- **Poor oral intake, especially in infants and young children**
- **Lethargic, especially in infants and young children**
- **Seizures/ encephalopathy**

- **Children with high risk for severe disease with mild symptoms:**
    - **Congenital or acquired heart disease,**
    - **Chronic lung, liver, kidney or neurological disease,**
    - **Immunosuppressive drugs,**
    - **Congenital or acquired immunodeficiency**

Indications for PICU admission

- **Moderate to severe ARDS requiring mechanical ventilation**
- **Shock requiring vasopressor support**
- **Worsening mental status**
- **Multi-organ dysfunction syndrome**
- **MIS-C**

C) MODERATE DISEASE

- **Admission in covid facility**
- **Watch for Pneumonia & Fast breathing**
- **Investigation as per protocol.**
- **Monitor for progress**
- **Feeds / fluids: avoid dehydration and overhydration**
- **Antipyretic: Paracetamol**
- **Amoxycillin if suspicion of bacterial infection.**
- **If SpO2 <94%, start oxygen and give steroids**
- **Steroids should be used in moderate to severe covid-19 disease. Glucocorticoids may modulate inflammation mediated lung injury and thereby reduce progression to respiratory failure. Safety & effectiveness of dexamethasone or other corticosteroids have not been sufficiently evaluated in paediatric patients.**
- **Dexamethasone is used in dosage of 0.15 mg/kg/dose (max. dose 6mg) once daily for up to 10 days. (equivalent dose of methylprednisolone may be used).**

- **Remdesivir – no proven role, only shortens duration of stay. High spectrum efficacy against different corona virus has been demonstrated invitro studies. Emergency use authorisation has been given to be used in restricted manner within 3 days of onset of symptoms in adults &**

children >12 yrs. It is advised for hospitalized children >12 yrs. who have risk factors for severe disease.

- **Dosage of Remdesivir- 5mg/ kg iv (in 30 min.) on first day followed by 2.5 mg/kg iv (in 30 min.) for another 9 days. Though limited data is available in children.**
- **No role of hydroxychloroquine, favipiravir, ivermectin, lopinavir/ ritonavir.**

D) SEVERE PNEUMONIA

Watch for Severe pneumonia with any of the following -

- **Cyanosis (SpO2 < 90%)**
- **Increased respiratory efforts (grunting, severe retraction)**
- **Lethargy, somnolence,**
- **Seizure**

- **Admit in PICU**
- **Investigations as per protocol.**
- **Steroids**
- **Empiric antimicrobials**
- **Oxygen therapy: nasal prong, face mask, HFNC**
- **CPAP, invasive & non-invasive ventilation as per requirements.**
- **SpO2 target > 94% during resuscitation**
- **Consider Awake Prone ventilation (in older children)**
- **Restrictive fluid therapy**
- **Anti-coagulants (Enoxaparin). Suggested treatment is with subcutaneous Enoxaparin 100-200 U /kg/day, that can be increased to 150-300 U/kg/day in neonates.**
- **Antibiotics.**
- **Remdesivir as per recommendation.**
- **Tocilizumab: recombinant humanized monoclonal antibody belonging to G1 immunoglobulin class. Studies suggests that alveolar damage due to cytokine storm (including IL-6) improve with the use of tocilizumab.**
- **Tocilizumab Dose –**

- ***The first infusion 10-12 mg/kg (<30 kg) & 8 mg/kg (>30 kg) (max. dosage 800mg) in 60 min.***
- ***Second infusion should be given 12 hours after the first infusion (in case of no response).***
- ***It should be used in critical or serious cases, high levels of IL-6 (more than 40 pg/ml); high levels of D-dimer, & /or CRP & /or ferritin & /or fibrinogen increasing progressively.***
- ***It should not be used when transaminases level is above 5 times normal level & neutrophil value lower than 500 cells/ml; though limited data are available in children.***

E) CRITICALLY DISEASE – ARDS, SHOCK, MIS

Admit in PICU -

- **Preferably negative pressure room**
- **Steroids**
- **Empiric antimicrobials**
- **Evaluate for hemophagocytic lymphohistiocytosis**
- **Organ support – renal replacement.**

Management of Shock -

- **Crystalloid bolus 10-20 ml/kg over 30-60 min, fast if hypotensive**
- **Early inotrope support**
- **Monitor for fluid overload**

Management of ARDS (Acute Respiratory Distress Syndrome)

- **HFNO/NIV trial for mild ARDS**
- **Mechanical ventilation: Low tidal volume (6ml/kg), high PEEP, Cuffed endotracheal tube**
- **Fluid restriction**
- **Sedation**
- **If poor response: may need**

- **prone ventilation, HFOV, ECMO**

- **In mild ARDS, high flow nasal oxygenation and non-invasive ventilation should be used whereas mechanical ventilation with low tidal volume may be used for severe ARDS. High frequency oscillatory ventilation and extracorporeal membrane oxygenation (ECMO) may be tried if patient does not respond to mechanical ventilation.**

Multisystem Inflammatory Syndrome (MIS)

- **Recently diagnosed during covid-19 pandemic.**
- **Children and adolescents with fever more than 3 days and two of the following:**
    - **Skin rash or bilateral non purulent conjunctivitis are mucocutaneous inflammation signs (oral, hands or feet)**
    - **Hypotension or shock**
    - **Signs of myocardial dysfunction (including echocardiographic findings or elevated troponin/ NT-proBNP)**
    - **Evidence of coagulopathy**
    - **Acute gastrointestinal problems (Diarrhoea, vomiting or abdominal pain**

      AND
    - **Elevated inflammatory markers such as ESR, CRP or procalcitonin**

      AND
    - **No other obvious microbial cause of inflammation including bacterial sepsis, Staphylococcal or Streptococcal shock syndrome**
    - **Treated with steroids (methylprednisolone 1-2 mg/kg/day):**
    - **Intravenous immunoglobulin (2mg/kg over 24-48 hrs); Antimicrobials, Inotropes.**
    - **If the child does not improve with this treatment, then repeat IV Ig, high dose corticosteroid (methylprednisolone 10-30 mg/kg/day for 3-5 days), low molecular weight heparin (Enoxaparin) (1mg/kg twice daily subcutaneously).**