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THE EXCHANGE

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A Knowledge Sharing Initiative by Medanta

COVID-19: Clinical Manifestations and Management in Children

COVID-19 affects children of all ages; however, young children and adolescents usually have milder symptoms of SARS-CoV-2 than adults and are less likely to progress to severe COVID-19. [1] Of age-disaggregated cases reported to the WHO between 30th December, 2019 and 13th September, 2021, children below five years of age represented 1.8% of global cases and 0.1% of global deaths. Older children and younger adolescents (5 to 14 years) were responsible for 6.3% of global cases and 0.1% of global deaths, while older adolescents and young adults (15 to 24 years) contributed to 14.5% of global cases and 0.4% of global deaths. [2] The actual incidence of infection may be far higher as milder symptoms may have led to less testing resulting in fewer identified cases of SARS-CoV-2 infection in children and adolescents. Similar to the world data, evidence from India also suggests that the incidence of COVID-19 infection is higher in children above 10 years of age compared to the 0-10 years age group. [3,4]

Clinical manifestations: There is some evidence that older children have higher rates of asymptomatic disease than infants, however majority of such children do not appear to be silent spreaders of infection. [2]

Clinical findings in children with COVID-19 are diverse and can be categorized broadly into the following phenotypes:

a) **Respiratory presentation -** Mild fever, cold and cough

b) **Febrile inflammatory state -** High-grade fever, body ache and tiredness

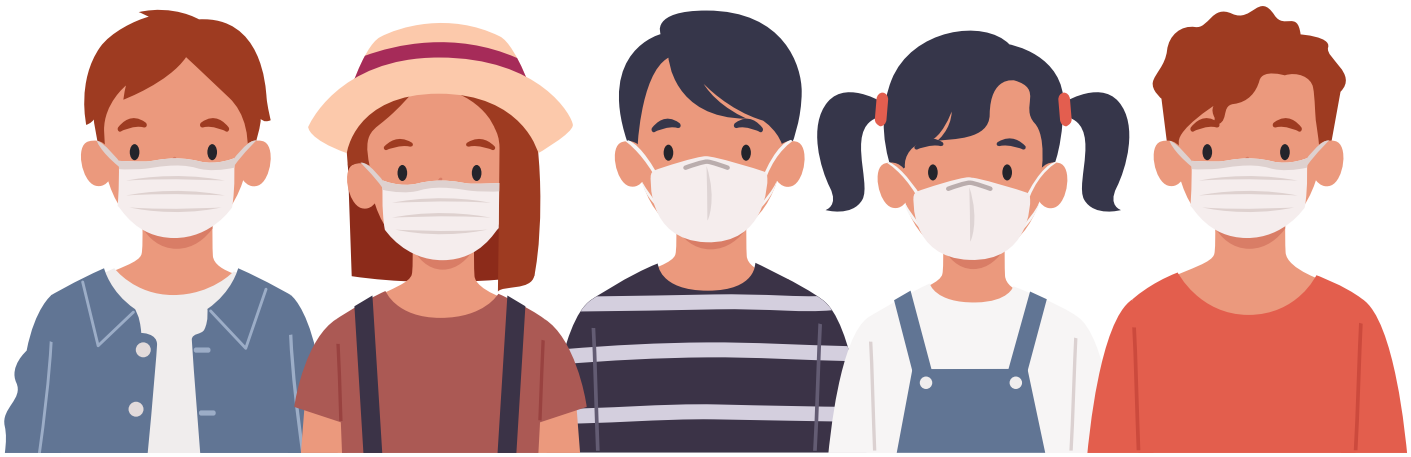
c) **Gastrointestinal presentation -** Vomiting, diarrhoea, abdominal pain

d) **Atypical/ Severe presentation**

Most children recover within 3 to 7 days of disease onset.

COVID test: In suspected symptomatic cases, COVID testing by nasopharyngeal RT-PCR is preferable. Rapid antigen test can be done as an alternative, but is less sensitive. An asymptomatic contact need not be tested unless the child belongs to a high risk category.

Treatment: In the initial stages of the pandemic in 2020, a lot of drugs were studied for their efficacy against COVID-19. These included: antibacterials (azithromycin, doxycycline), anti-parasitic (ivermectin), anti-inflammatory

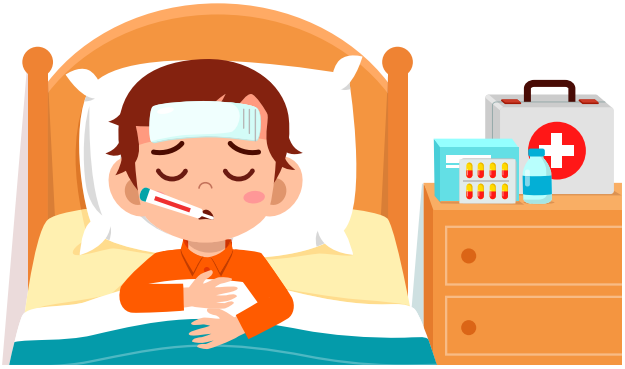


(hydroxychloroquine) and antivirals (ribavirin, lopinavir/ ritonavir, and oseltamivir). Now with better understanding and new evidence, the treatment recommendations have been updated. It is important to be aware of the ever-changing situation and closely follow updates in Indian and international guidelines for COVID-19 treatment. As per the present protocol, here's a treatment overview:

For mild illness i.e. children who are feeling well, have no respiratory difficulty, and have SpO2 > 92% in room air

- Home isolation and tele-consultation to monitor progress of the patient is recommended.
- Control of fever (>100F) by using paracetamol (10–15 mg/kg/ dose SOS/ q 4–6 hourly, if required) and sponging if fever >102F.
- Antibiotics are not indicated unless one suspects a co-infection with bacteria.
- For cough, throat soothing agents can be given. Older children may use warm saline gargles.
- Nebulization can be done in children with asthma. Nasal drops in infants can be given for nasal block.
- Counsel parents about danger signs such as drowsiness, SpO2 < 94%, persistent vomiting, fast breathing.
- Ensure adequate hydration.
- Nutritional supplements have no major role in acute illness.
- No role of medications like molnupiravir or favipiravir, in children below 18 years of age.

Duration of isolation for mild cases: Afebrile patients should isolate for three successive days and at least seven days if tested positive. There is no need for testing prior to discharge from home isolation. Post-discharge, they should continue wearing masks.



Laboratory testing: For mild and asymptomatic cases, no blood or radiological testing is recommended. For moderate cases with fast breathing, breathing difficulty or hypoxemia SpO2 < 94% - CBC with ESR, chest radiograph and blood glucose is advised. For severe cases - CBC with ESR, blood glucose, CRP, LFT, KFT, serum ferritin, D-Dimer, VBG, and chest radiograph, or HRCT chest is advised. Also consider endemic tropical infections (like dengue, malaria, scrub typhus, typhoid, etc) as a differential diagnosis and evaluate as necessary.

Severe disease: Although extremely rare, severe disease can present as worsening pneumonia, ARDS, septic shock, MIS-C and MODS. It is important to recognize severe disease early and initiate appropriate management in a hospital setting. Underlying morbidities may increase the risk of severe disease in children such as chronic neurological conditions, metabolic conditions, congenital heart disease/cardiovascular disease, obesity, diabetes mellitus, asthma or other chronic pulmonary diseases, sickle cell disease, immunosuppression, and other chronic medical conditions.

Indications for hospitalization: Anyone with respiratory distress, SpO2 < 92% on room air, shock/ poor peripheral perfusion, poor oral intake (especially in infants), lethargy (especially in infants), seizures/ encephalopathy should be hospitalized.

Treating severe cases: In addition to symptomatic management, medications like steroids, anti-coagulants, and remdesivir can be used in ICU settings, with specific indications. Remdesivir (an emergency use authorization drug) is not recommended in children, but exceptions can be made in certain situations. For MIS-C: steroids, IVIG, aspirin, and biological agents can be used.

Multisystem inflammatory syndrome (MIS-C): Multisystem inflammatory syndrome in which various body systems including the heart, lungs, kidneys, brain, skin, eyes, blood, or gastrointestinal organs get affected/inflamed, can occur in anyone under 21 years of age. MIS-C usually occurs after a child has recovered from a recent symptomatic/ asymptomatic COVID-19 infection. It is important to be aware of this condition and suspect it in children with high-grade fever for more than three days, especially in the coming months following the third wave. Rarely, it can be seen during an active COVID-19 infection too.

Long COVID: Long COVID in children is a newly recognised condition, and data is scant. It is defined as signs and symptoms consistent with COVID-19 lasting for more than 12 weeks, that develop during or after an infection and are not explained by any alternative diagnosis. Commonly

reported symptoms include headache, fatigue, sleep disturbances, concentration difficulties, and abdominal pain. Recognition of this condition and symptomatic treatment along with counselling is required. It is sometimes difficult to distinguish long COVID from pandemic fatigue in children.

Breast feeding of infants by COVID positive mother: Current evidence suggests that the chance of a new-born getting COVID-19 from their birth parent is low, especially when the parent takes precautionary measures such as wearing a mask and washing hands. Stable neonates/infants exposed to COVID-19 from mothers or other relatives should be roomed-in with their mothers and be exclusively breastfed.

Vaccination: Vaccination coverage to the adolescent group (15 to 18 years) was recently introduced by the Government, as the incidence of infection and complications are more in this age bracket. [3,4] Two doses of Covaxin (inactivated virus vaccine), over a four-week period are recommended. The safety and efficacy of Covaxin is much better in children as compared to the adult population. [5] Vaccination also prevents life-threatening complications like MIS-C in children. [6]

Psychological stress: COVID pandemic has been extremely challenging for children. Many activities considered healthy for development have been restricted. Online education, restricted meetings with friends/relatives, sedentary lifestyle, increased screen time and psychological stress are negatively impacting children. Stress due to isolation and loneliness should be recognised and combated by spending quality time with family, doing physical activities at home and maintaining a social circle of friends while practicing COVID-appropriate behaviour.

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In Focus

COVID-19: Treatment and Therapeutics

Over two years of the COVID-19 pandemic, we have been witness to ever changing treatment recommendations from various Indian and international medical bodies. Multiple drugs have been studied in various trials and we now have a much better understanding of COVID therapeutics

HCQS and Lopinavir/Ritonavir: During the early phase of pandemic, HCQS and Lopinavir/Ritonavir (LPV/r) were prescribed. However, soon evidence emerged that both these drugs were not beneficial in COVID-19 treatment.[1,2]

Azithromycin and Doxycycline: Antibiotics like Azithromycin and Doxycycline, which have long been used for treatment of atypical pneumonias, were also widely prescribed. However, scientific evidence was always lacking and the PRINCIPLE trial conducted in the UK found no benefit of Azithromycin and Doxycycline.[3]

Convalescent Plasma: Convalescent plasma was used based on the principle to supply readymade antibodies to neutralize the replicating virus. However, ICMR funded PLACID trial found no benefit of Convalescent plasma.[4]

Dexamethasone: Supported by the Dexamethasone arm of RECOVERY trial, Dexamethasone and other steroids in equivalent doses were the first intervention which provided mortality benefit, and they continue to be the cornerstone of management of moderate and severe COVID-19. In patients hospitalized with COVID-19, Dexamethasone reduced 28-day mortality among those receiving invasive mechanical ventilation (29.0% vs. 40.7%) or oxygen (21.5% vs. 25.0%), but not among patients not receiving supplemental oxygen.[5]

Remdesivir: ACTT-1 trial studied Remdesivir in hospitalized patients with pneumonia. Remdesivir was seen as superior to placebo in shortening the time of recovery in adults who were hospitalized with COVID-19 and had evidence of lower respiratory tract infection.(6) Maximum benefit of Remdesivir was seen in subgroup of patients on low flow oxygen and no benefit was found in patient on HFNC, mechanical ventilation and ECMO.[6] The SOLIDARITY trial conducted by the WHO studied various repurposed drugs including Remdesivir and found no mortality benefit with any of the study drugs. [7] Based on the above evidence most of the guidelines now recommend Remdesivir for moderate to severe disease (on low flow oxygen) but not

in patients on mechanical ventilation and ECMO.[8] In the PINETREE trial among non-hospitalized patients who were at high-risk for COVID-19 progression, a three-day course of Remdesivir resulted in an 87% lower risk of hospitalization or death than placebo [9] and this has led to NIH guidelines recommending it for high-risk mild disease patients.[10]

Ivermectin and Favipiravir: Ivermectin and Favipiravir were used to treat outpatient COVID-19 cases and also featured in several state government protocols. However, in a meta-analysis of RCTs, the use of Ivermectin was not associated with reduction in mortality[11] and therefore it is not recommended in the guidelines.[8] The data pertaining to Favipiravir use is very weak in studies and none of the guidelines suggest its routine use.

Tocilizumab and Baricitini: The second phase of COVID-19 illness and sudden worsening of respiratory function is due to immune dysregulation mediated via release of various cytokines including IL-6. IL-6 blockade has long been considered as a therapeutic intervention in management of severe COVID-19. Tocilizumab arm of the RECOVERY trial concluded in hospitalized COVID-19 patients with hypoxia and systemic inflammation, indicated that Tocilizumab improved survival. These benefits were seen regardless of the amount of respiratory support and were additional to the benefits of systemic corticosteroid.[12] In COVINTOC trial led by researchers from Medanta on post hoc analysis, it was observed that patients with severe disease would benefit from Tocilizumab.[13] Baricitinib, a JAK 1/2 inhibitor was studied in an RCT in Brazil, and 38% relative reduction in mortality was observed in Baricitinib arm compared to placebo.[14] Based on above evidence, guidelines now recommend Tocilizumab and Baricitinib for the treatment of severe COVID-19.[8]

Anticoagulants: Initially, COVID-19 was associated with increased risk of thrombosis and anticoagulation was studied in various trials. NIH and IDSA guidelines now recommend therapeutic dose of low molecular weight heparin for moderate disease patients and prophylactic dose anticoagulation for severe and critically ill COVID-19 patients. Non-hospitalized COVID-19 patients do not require anticoagulation and anticoagulation post-discharge is strictly based on IMPROVE score.

Monoclonal Antibodies: Monoclonal antibodies such as Casirivimab + Imdevimab (REGEN-COV) were studied in outpatient mild COVID-19 and they reduced the risk of COVID-19 related hospitalization or death from any cause by almost 70%.[15] In patients hospitalized with COVID-19, REGEN-COV reduced 28-day mortality among patients who were seronegative at baseline.[16] However with emergence of Omicron and significant number of mutations in spike protein, the neutralizing capacity of REGEN-COV is greatly reduced and should be used with caution. Sotrovimab is another monoclonal antibody which retains its activity against Omicron, however it is not available in India yet.

Molnupiravir: DCGI and ICMR have a difference of opinion on Molnupiravir. Scientific evidence backing the FDA and DCGI approval from the MOVE-OUT study is very weak.[17] Therefore, it should be used carefully when other treatment options are not available.

Therapies which work	Therapies which do not work
Remdesivir Dexamethasone / Steroids Anticoagulation Tocilizumab Baricitininb Sotrovimab (Not available in India) Paxlovid (Not available in India) Molnupiravir- Use only when no other option is available after an informed discussion with the patient. To be avoided in pregnancy and patients in childbearing age	HCQS Lopinavir / Ritonavir Doxycycline Azithromycin Favipiravir Ivermectin Vitamin C Zinc Colchicine Convalescent plasma
Monoclonal Antibody (Casirivimab + Imdevimab) - Active against alpha, beta, gamma and delta but no activity against Omicron.	

Undoubtedly, we have made significant progress in COVID-19 therapeutics. However, given the ever-evolving situation and new emerging variants, our search for COVID-19 therapeutics which are safe, affordable and effective against evolving variants of COVID-19 continues.

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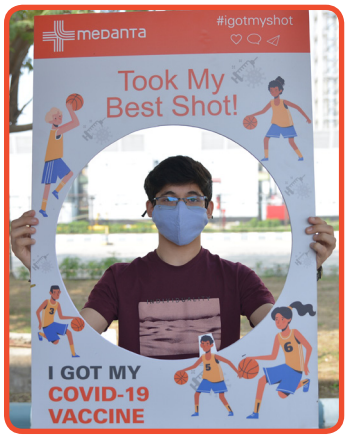

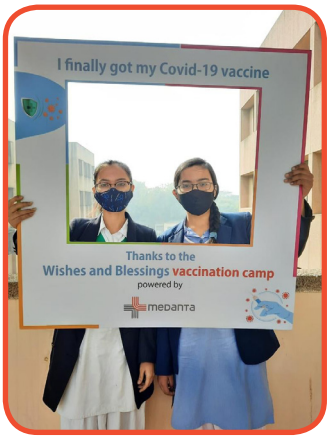

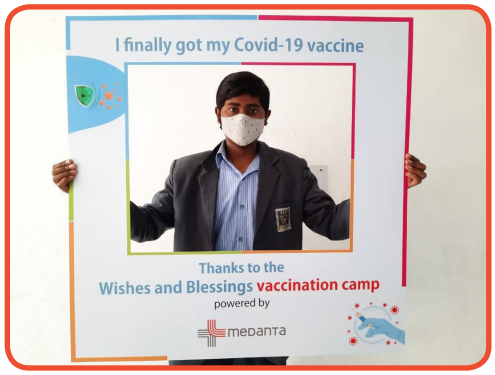

Medanta@Work

Furthering Access to COVID-19 Vaccination

To stop the spread of COVID-19, it is essential that more than 70% of the Indian population gets vaccinated. In congruence with this goal, the Government of India initiated vaccination for children between 15 to 18 years of age from January, 2021.

Medanta, a frontrunner in the battle against COVID-19 is going the extra mile to ensure easy accessibility of vaccines to children. From partnering with Resident Welfare Associations (RWAs), schools, NGOs, and local institutions to establishing dedicated vaccination centers and drive-throughs, Medanta is leaving no stone unturned to enhance access to the vaccine. Recently, Medanta partnered with a Delhi-based NGO Wishes and Blessings to organise a vaccination camp for underprivileged children wherein kids were vaccinated free of cost. All of these initiatives ensure that children can avoid long queues and get vaccinated in a safe and comfortable environment.

> "COVID-19 vaccines are the most effective way to protect children from this deadly pandemic. Vaccination will help children build natural immunity against the virus and bring us closer to achieving herd immunity. Vaccination must happen at a faster pace and we at Medanta are channelizing our efforts to make vaccines easily accessible to all."

Dr Naresh Trehan
Chairman and
Managing Director
Medanta

THE EXCHANGE

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Welcome Onboard

JAY PRABHA MEDANTA SUPER SPECIALTY HOSPITAL, PATNA

Dr. Prabhat Ranjan
Director, Urology & Kidney Transplant Surgery

Dr. Prabhat Ranjan is Director, Urology & Kidney Transplant Surgery in Jay Prabha Medanta Super Specialty Hospital, Patna. He completed MBBS from Rajendra Medical College, Ranchi and MS from PMCH, Patna. He pursued DNB (Urology) from MPUH, Nadiad. Dr. Ranjan has successfully established Urology department at two leading private hospitals in Patna. He started renal transplant program at a leading private hospital in Patna. He also pioneered RIRS surgery in Patna. Dr. Ranjan has performed 25 kidney transplants in the city. He specializes in endourology, laparoscopy, uro-oncology, andrology, paediatric urology, renal transplant and robotic surgery.

Dr. Ambuj Kumar
Consultant, Interventional Neurosurgery

Dr. Ambuj Kumar is Consultant, Interventional Neurosurgery in Jay Prabha Medanta Super Specialty Hospital, Patna. He completed his MBBS and MS from NSCB Medical College, Jabalpur. He did his MCH from AIIMS, New Delhi and Cerebrovascular and Endovascular Fellowship from Fujita Health University, Nagoya, Japan. He specializes in endoscopic brain surgery and minimally invasive spine surgery, aneurysm clipping and coiling, thrombectomy for acute ischaemic stroke and brain and spine tumour surgeries.
Dr. Kumar has also authored several papers in Indian and international publications of repute.

Dr. Pravir Sinha
Consultant, CTVS

Dr. Pravir Sinha is Consultant, CTVS in Jay Prabha Medanta Super Specialty Hospital, Patna. He completed MBBS from JSS Medical College, Mysore and DNB (Cardiothoracic Surgery) from Max Superspeciality Hospital, New Delhi. He specializes in performing adult cardiac surgeries, complex vascular surgeries, multivessel CABG, MICS, EVAR and TAVI.

Kudos

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A PROUD MOMENT

Medanta, Gurugram, has been awarded the State Level Energy Conservation Award under the Commercial building category above 1MW for 2019-2020 by the Government of Haryana