

# COVID-19 Pandemic – A Paediatric Perspective

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## ABSTRACT

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SARS CoV-2, the virus responsible for the current pandemic COVID-19 has resulted in 4.2 million cases and 2.9 lakhs deaths globally by mid- May 2020. Children are less likely to be symptomatic or develop severe symptoms with SARS-CoV-2 infection. Recent US reports show that rate of hospitalization is less in children (5.7%) when compared to adults (10%). Most common presenting complaints include fever, cough and sore throat; eight cases of Kawasaki disease/toxic shock syndrome like presentation with multi organ dysfunction has also been published from UK. For management, clinical categorization as A, B and C is helpful. Patients with comorbidities, on immunosuppressants, severe respiratory symptoms, altered sensorium and shock need hospitalization, close monitoring and care. Mainstay of diagnosis is with RT-PCR of nasopharyngeal swab. Treatment includes supportive care for category A, Hydroxychloroquine and Azithromycin for category B and C. In addition, if there is clinical worsening, Lopinavir/Ritonavir, Remdesivir (not available in India) and Tocilizumab may be considered. Appropriate protective gears and reduction of aerosol generating procedures are effective infection control strategies.

**Keywords:** SARS CoV 2, COVID-19, Children, pediatric, Asymptomatic

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## INTRODUCTION

In humans, coronaviruses cause common cold to more severe disease such as bronchitis, pneumonia, severe acute respiratory distress syndrome (ARDS), coagulopathy, multi organ failure and death.

Coronaviruses comprise a large family of enveloped, single stranded, zoonotic RNA viruses belonging to the family Coronaviridae, order Nidovirales. Those coronaviruses which are mainly found in mammals such as bats, rodents, civets and humans are classified into Alphacoronaviruses and Betacoronaviruses. Till the novel coronavirus emerged in last December, Coronaviruses namely HCoV2-229E, HKU1, NL63 and OC43 were the ones known to cause human disease. Those Coronaviruses found in birds are divided into *Gammacoronaviruses* and *Deltacoronaviruses*.

Coronaviruses are capable of rapid mutation and recombination leading to novel CoVs that can spread from animals to humans. This occurred in China in 2002 when the novel severe acute respiratory syndrome coronavirus (SARS-CoV) emerged by such a mutation and transmitted from civet cats or bats to humans. Another novel Coronavirus emerged in Saudi Arabia in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV), which was transmitted from dromedary camels to humans. Both of these viruses caused severe

respiratory infections in humans in various parts of the world for a considerable period of time.

The current Coronavirus pandemic started in Wuhan city, Hubei province, China, where The Health Commission of Hubei province first reported a pneumonia cluster in adults of unexplained aetiology on December 31, 2019. A local seafood and wet meat market was identified as a potential source. Later it was known the disease have human to human spread and WHO declared a Public Health Emergency of International Concern on January 30, 2020. The culprit was identified and named as Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) and on February 11, 2020 the clinical disease caused was given a nomenclature by the WHO as COVID-19.

In a preliminary report from CDC published on April 6, 2020, the incidence among children (0-18yrs) is recorded as 1.7% out of a cohort of around one and a half lakh cases of COVID-19. This is in striking contrast with the usual pattern of respiratory infections where infants and children has a higher propensity for infection. SARS-CoV-2 infection rate in children is seen to be less in reports from other countries as well. The current knowledge also tells as infections with milder symptoms are more common in children than adults when it comes to COVID-19 disease.

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In this review, we summarize epidemiologic, clinical and diagnostic findings, as well as treatment and prevention options for SARS-CoV-2 infections in humans with a focus on children.

## EPIDEMIOLOGY

As of May 14, 2020, more than 4.2 million cases of COVID-19 and 2.9 lakhs deaths have now been reported to WHO worldwide (WHO situation report 115). 216 countries, areas or territories are reported with cases. 1.18 Lakhs confirmed cases from South East Asia and 78,003 confirmed cases from India as of May 15, 2020.<sup>1</sup> The case fatality rate in China as on 16 April was estimated as 4% and now recent reports show it varies from 1% in Russia to 16% in Belgium among COVID-19 cases (3.2% in India).

The virus can be transmitted by an infected person or an asymptomatic carrier and is now proven as a highly contagious disease. Respiratory droplets are the main route of transmission, but can also be transmitted by contact (fomites) and digestive tract. The incubation period is about 1 to 14 days, and is suggested in a few reports that it could be up to 24 days. The Chinese Centers for Disease Control and Prevention reports that of the 72,314 cases reported as of February 11, 2020, only 2% were in individuals of less than 19 years of age. There are 3 case series of children who have been infected with SARS-CoV-2. The first included 20 children up to January 31, 2020, in the Province of Zhejiang, the second 34 children between January 19, 2020, and February 7, 2020, in the Province of Shenzhen, and the third 9 infants from different provinces in China.

In a more recent report from United States, it was observed that 73% of paediatric patients had symptoms of fever, cough, or shortness of breath compared with 93% of adults aged 18–64 years during the same period.<sup>2</sup> The need for hospitalisation in children was around 5.7%, lower than the percentages hospitalized among all adults aged 18–64 years (10%).<sup>2</sup> Most COVID-19 cases in children are not severe but serious COVID-19 illness resulting in hospitalization do happen in paediatrics also.

## CLINICAL FEATURES

Children with COVID-19 infection can be asymptomatic or can present with fever, cough, diarrhoea, watery nasal discharge, sore throat, fatigue, vomiting, breathlessness, it may rarely progress to coagulopathy, multi organ damage and death.<sup>3</sup> A case series with 34 children provides the most clinical details, none of the children had an underlying disease, 65% had common respiratory symptoms, 26% had mild disease and 9% were asymptomatic (Table 1). The most common symptoms were fever (50%) and

Table 1. Clinical Categories<sup>3</sup>

A	Mild sore throat/cough/rhinitis/diarrhoea
B	Fever and/or severe sore throat/cough/diarrhoea OR Category A plus two or more of the following <ul style="list-style-type: none"> <li>• Lung/heart/liver/kidney/neurological disease/hypertension/hematological disorders/uncontrolled diabetes/cancer/HIV-AIDS</li> <li>• On long term steroids/immunosuppressive drugs</li> <li>• Pregnant lady</li> <li>• Age more than 60 years</li> </ul> OR Category A plus cardiovascular disease
C	<ul style="list-style-type: none"> <li>• Breathlessness, chest pain, drowsiness, fall in blood pressure, haemoptysis, cyanosis (red flag signs)</li> <li>• Children with ILI (influenza like illness) with red flag signs (sommolence, high persistent fever, inability to feed well, convulsions, dyspnoea/respiratory distress etc)</li> <li>• Worsening of underlying chronic conditions</li> </ul>

\*Categorization should be reassessed every 24-48 hours for Category A & B

cough (38%).<sup>4</sup> A meta analysis from China cites fever (59%), cough (46%), whereas 26% were asymptomatic.<sup>5</sup> In another case series of 20 children, presentation was with low to moderate or no fever, rhinitis, cough, fatigue, headache, diarrhoea and, in more severe cases, with dyspnea, cyanosis and poor feeding, but the numbers were not specified. Deaths were not reported till mid of March, but then few paediatric confirmed cases of COVID-19 expired. According to the report by NCHS published by CDC, 12 cases of under 14 years (7 males and 5 females) expired in United States from January 2, 2020 till May 13, 2020.<sup>6</sup> In a series of 9 infants, only 4 were reported to have fever. One infant was asymptomatic. Additional asymptomatic children infected with SARS-CoV-2 outside these case series have also been described. Most infected children recover 1–2 weeks after the onset of symptoms.

Children have milder clinical symptoms than adults which could mean children might not be tested for SARS-CoV-2 as frequently as adults. It has therefore been suggested that asymptomatic or mildly symptomatic children might transmit the disease. A study prepublished in early March 2020 suggests that children are just as likely as adults to become infected with SARS-CoV-2 but are less likely to be symptomatic or develop severe symptoms.

A tertiary care centre in UK has reported a cluster of eight children presented with features similar to Atypical Kawasaki disease/ Toxic Shock Syndrome during last month.<sup>7</sup> The patients presented with a similar clinical picture comprising of high grade fever, conjunctivitis, rash, peripheral oedema, pain on the extremities etc. which progress to fluid refractory shock, requiring inotropes and mechanical ventilation, even though there was not much of respiratory involvement, in a significant number of cases from this group. Although

initially all of them tested negative for SARS-CoV-2 later two of them tested positive of which one child died. The authors of this communication has raised a suspicion this hyperinflammatory syndrome with involvement of multiple organ systems with striking similarity to Kawasaki disease could be a new phenomenon affecting previously asymptomatic children.

## LABORATORY FINDINGS

Laboratory findings from children are similar to those seen in infections caused by other coronaviruses. The white blood cell count is typically normal or reduced with decreased neutrophil and/or lymphocyte count during the early stages of the disease.<sup>4</sup> Thrombocytopenia may occur. C-reactive protein and procalcitonin levels are often normal or slightly elevated.<sup>9</sup> In severe cases, elevated liver enzymes, lactate dehydrogenase levels, as well as an abnormal coagulation and elevated D-dimers have been reported. In some patients low albumin levels and increased ferritin levels were also seen. In a case series of 34 children, the white blood cell count was normal in 83%, neutropenia and lymphopenia were each found in 1 case (3%). Progressive decline in the lymphocyte count occurs during the course of the illness. The lactate dehydrogenase level was elevated in 30% of cases. C-reactive protein and procalcitonin levels were each elevated in 1 case only (3%). A baseline ECG is indicated as rhythm abnormalities do occur in later stages of the disease in adults.<sup>10</sup>

In a series of 21 pregnant women affected by COVID-19 during late pregnancy, postnatal testing for RT-PCR (real-time polymerase chain reaction) of the amniotic fluid, placenta, cord blood and breast milk samples as well as the pharyngeal samples of the neonates to detect viral particles were negative in all of them. However in another series of 33 babies born to swab positive mothers three were affected which raises a remote suspicion of the possibility of vertical transmission of the disease.

On chest radiography, children mostly show bilateral patchy airspace consolidations often at the periphery of the lungs, peribronchial thickening and ground-glass opacities. Chest CT changes observed in children infected with SARS-CoV-2 include bilateral multiple patchy, nodular ground-glass opacities, speckled ground-glass opacities and/or infiltrating shadows in the middle and outer zone of the lung or under the pleura. These findings are unspecific and milder compared with those in adults.

## DIAGNOSIS

The main stay of diagnosis of coronavirus infections is real-time polymerase chain reaction (RT-PCR) on upper or lower respiratory secretions in children as well.<sup>11</sup> Whole genome sequencing allowed the rapid development of

molecular diagnostic tests for SARS-CoV-2. RT-PCR for genes encoding the internal RNA-dependent RNA polymerase and surface spike glycoprotein are commonly used worldwide.

### Case Definition (NCDC Definition)<sup>12</sup>

#### Suspect case

A. Patients with acute respiratory illness (fever, cough, breathing difficulty), AND with no other etiology that fully explains the clinical presentation AND at least one of the following:

- a history of travel to or residence in China in the 14 days prior to symptom onset, or
- patient is a health care worker who has been working in an environment where severe acute respiratory infections of unknown etiology are being cared for.
- worked or attended a health care facility where a confirmed case of 2019-nCoV is admitted in the last 14 days
- close contact with a confirmed case of 2019-nCoV in the 14 days prior to illness onset, or

B. A suspect case for whom testing for 2019-nCoV is inconclusive

#### Confirmed case

A person with laboratory confirmation of 2019-nCoV infection, irrespective of clinical signs and symptoms.

## TREATMENT

In Kerala, the State Medical Board has brought up an interim treatment guideline based on the WHO and ICMR guidelines which gets amended periodically as evidence comes in. The current recommendation is to test all patients/suspects with category B & C symptoms namely fever or/ and dyspnea apart from other symptoms like severe sore throat, cough etc if they are coming from a locality with community transmission or have a contact with a positive patient.

Supportive treatment including sufficient fluid and calorie intake, and additional oxygen supplementation should be used in the treatment of children infected with SARS-CoV-2. The aim is to prevent progression of the disease ARDS, organ failure and secondary nosocomial infections.

There is no current evidence from RCTs to recommend any specific anti-COVID-19 treatment for patients with suspected or confirmed COVID-19 infection. Treatment should be considered in symptomatic patients requiring hospitalization or those with conditions associated with severe disease. As children are more prone to bacterial pneumonia and fast progression empiric antibiotic therapy

should be offered to patients with severe suspected COVID pneumonia and sepsis within 1 hour of admission and appropriate de-escalation and modification may be done depending on culture reports and clinical judgement. Oseltamivir may be started in all children presenting with Influenza Like Illness (ILI) pending RT-PCR reports. Zinc inhibits coronavirus RNA polymerase activity and block replication of virus in cell cultures. Hence, Zinc 2mg per kg per day may be given. As with any viral infection in children avoid using NSAIDs other than paracetamol as well as systemic steroids. Steroids to be considered only in cases of refractory shock, Cytokine release Syndrome Grade 3 or 4 with no response to Tocilizumab.

Patients with Category B symptoms will receive Hydroxy Chloroquine 6.5mg/kg/dose (Max 400mg) PO BD day 1 followed by 3.5mg per kg PO BD (max 200mg/dose) for 4 days. QT prolongation > 500msec, porphyria, myasthenia gravis, retinal pathology, epilepsy are certain conditions in which HCQ is contraindicated. Azithromycin 10mg/kg on day 1 (Max 500mg) followed by 5mg/kg/day on days 2-5 is to be given along with HCQ.<sup>13</sup>

In patients with Category C symptoms who progresses to ARDS or MODS while on the above regimen addition of Lopinavir/ Ritonavir may be considered in case the child worsens as Remdesivir is not available in our country. Consider adding Tocilizumab to antiviral therapy for patients with rapidly worsening respiratory gas exchange, radiographic infiltrates by imaging (chest x-ray, CT scan, etc.) AND SpO<sub>2</sub> ≤93% on greater than 6 L/min O<sub>2</sub>. It may be offered to patients at high risk for cytokine storm. Other specific management (airway management, shock) may be required according to the case.<sup>8</sup>

### Other Strategies for Controlling in Hospital Spread

The need of the hour is rapid and effective strategies of infection control. One of the main challenges with novel CoVs is the high potential for nosocomial transmission. Health care settings seem to increase the risk of viral transmission due to aerosol-generating procedures such as nebulisation, suction, intubation and bronchoscopy. Appropriate hospital hygiene practices are therefore crucial to limit nosocomial outbreaks. The main aims are to effectively triage patients with fever and/or respiratory symptoms, take a meticulous contact history and to apply stringent infection control measures such as isolating patients and quarantine contacts as early as possible.<sup>14</sup> Ideally, each patient is placed in a single negative pressure room. If this is not possible, patients and health care workers should be cohorted. Protective gear should include water resistant gowns, disposable gloves, N95 masks and goggles or face shields. Only suction catheters and mechanical respirators with a closed-circuit system and viral filters should be used. In contrast, nebulizers, oxygen masks or nasal continuous positive airway pressure

systems should not be used in an open ward. During the pandemic as far as possible try to use MDI with spacer in the place of nebulisers so as to reduce the aerosol generation when we are treating children with asthma exacerbations. Needless to say, strict hand hygiene needs to be applied and visitors should be avoided or limited to an absolute minimum.

## CONCLUSION

COVID-19 is behaving in children in a very different manner when compared to other respiratory infections. Early reports from China showed similar attack rates among adults and children in households. Later it was told children remain as asymptomatic carriers and spread the disease. It was also noted that most of the children infected got it from either the household or a healthcare facility. Recently evidence is pouring in telling us children are less likely to get affected by SARS-CoV-2, like from a town in Italy where 86% of the population was screened and found around 2.6% of the citizens positive while none of them where children below 10 years of age. While the questions like whether children are comparatively immune or they are `super spreaders` are being debated the responsibility of individual physician is to be in the lookout for symptoms of COVID-19 in each child especially when there is a setting of a comorbidity or an immunocompromised state or a close relative is having the disease.

## END NOTE

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**Conflict of Interest:** None declared

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