

## COVID-19 in children: Epidemiology, presentation, diagnosis and management

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### Abstract

The new pandemic coronavirus disease (COVID-19) has affected children, including neonates, who mostly comprise of approximately 2% of total confirmed cases. Most children are asymptomatic or have mild disease and much lower mortality compared to adults for yet unknown reasons. Recovery from illness has largely been universal and <2% have severe disease requiring intensive care. Standardised guidelines from initial studies are now available for diagnosis, treatment, and prevention. Treatment is mostly supportive with no recommendations for any specific drugs so far. As the pandemic evolves, it is expected that more children will be diagnosed and treated with evolving newer regimens. Research should now focus on early diagnosis, better drugs for children, intensive care modalities, and a universal vaccine. New developments will help in better prevention asides from the other precautionary measures already being practiced.

**Keywords:** Children, COVID-19, SARS-CoV-2, Pandemic, Paediatrician, Pakistan.

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### Introduction

The new pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly across the globe since first described four months ago after an epidemic of pneumonia and deaths.<sup>1</sup> This novel coronavirus (formerly n-COV-19) was not previously seen in humans. It is most likely to have originated from animals and now easily transmitted between humans through close contact largely by droplet transmission and through fomites.

SARS-CoV-2 mainly causes respiratory infections with variable presentations.<sup>2,3</sup> The World Health Organization (WHO) declared it a Public Health Emergency of International Concern on 30th January 2020 and officially named this new disease as coronavirus disease 19 or

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'COVID-19'.<sup>4</sup> With the unprecedented rapid spread across countries and continents, WHO finally declared it a global pandemic on March 11, 2020. To date (May 3, 2020) there has been 3,506,729 confirmed cases with more than 247,470 deaths worldwide.<sup>5</sup> As the world grapples with rapidly-emerging new information about the genomics, epidemiology, presentation, diagnosis, treatment, outcome and prevention of this disease, health professionals worldwide are feverishly working to save lives. This review will focus on the paediatric aspects of coronavirus disease (COVID-19) from the current literature so far including from Pakistan. It is hoped that it may aid the paediatricians in Pakistan in early diagnosis, timely isolation, prevention, and management for optimised care.

### Epidemiology

Almost all ages of the paediatric population are affected, including neonate, with a median age of 7-11 years.<sup>2,3,6,7</sup> Among children, the largest proportion (56-84%) has been among the 9-19 years old. In one of the largest studies from China (n=72,314), the proportion of children (<19 years) affected by COVID-19 was 2% of all cases (n=4,212).<sup>2</sup> Another large Korean study (n=89,069) documented a total of 4.8% of children of the total confirmed cases.<sup>6</sup> In US, children made up 1.7% of total cases, with <15% being 1 year, 26% were 1-9 years, 59% were 10-17 years old.<sup>7</sup> In Pakistan the total confirmed CoVID-19 cases as of May 3, 2020 according to National Institute of Health, Islamabad are 20,084 and 457 (2.3%) deaths.<sup>8</sup> These include 7.1% children age <19 years with 0.6% deaths so far.

Despite the high incidence of coronavirus respiratory infections, such as 'the common cold', the lower incidence (1-5%) in children of COVID-19 cannot be fully explained.<sup>9</sup> The reasons for the disproportionately lower incidence is one of the mysteries of SARS-CoV-2.<sup>10</sup> More interesting has been the milder disease pattern and less severity.<sup>9-13</sup> Most studies point that outcome in children has been better than adults in terms of mortality, hospitalisation and intensive care.<sup>7,13</sup> Asymptomatic or milder cases may go undetected and may play a significant part in transmission.<sup>10-13</sup> Male gender (57-60%) is more common just as in adults.<sup>11</sup> Most of these children had infections in

family clusters contracting from adult households.<sup>7,10,12</sup>

Approximately one fourth (23%) of children may have underlying illnesses that may have been a risk for severe disease.<sup>7</sup> Risk factors reported in children are infants <1 year, congenital heart disease, blood disorders, immunosuppression, chronic kidney, liver and lung disease.<sup>7,10-13</sup> In adults mortality reported is high (related to age and underlying diseases) but in children only a few deaths have been documented.<sup>7,13</sup> The exact reasons for the relatively low incidence and lower mortality remain unknown. But it has been postulated that differences in immune function and expression/function of the cellular receptor in lungs for SARS-CoV-2 in elderly and children, "trained innate immunity", higher constitutional lymphocyte counts with less immune dysfunction in children appears to have a protective effect against the severity of SARS-CoV-2 infection.<sup>14</sup>

### Presentation

Based on severity the clinical classification of COVID-19 in children include asymptomatic upper respiratory tract infection (URTI), mild pneumonia and severe pneumonia.<sup>15,16</sup> The experts' consensus statement from the National Health Committee on Novel Coronavirus Infection Pneumonia Diagnosis and Treatment Standards have given clinical classification.<sup>15</sup> A study of 1391 children from Wuhan showed 16% were asymptomatic, 19% had URTI and 65% had pneumonia especially those with severe COVID-19.<sup>13</sup> Another large study of 2135 children also documented that >90% had asymptomatic, mild or moderate disease.<sup>16</sup> Among symptomatic children most common manifestations seen were fever, cough, anosmia, body aches, irritability and abdominal pain.<sup>7,10-16</sup> Less common features seen are rhinorrhoea, fatigue, vomiting, and diarrhoea. Physical examination noted pharyngeal erythema, dyspnoea and crackles or rales. Illness severity was age-dependent and overall 0.6% are critical but in infants <1 year 11% are critical.<sup>16</sup> Common complications reported include shock, acute respiratory distress syndrome (ARDS) and multi-organ failure.<sup>11-13</sup> Overall the complication rates have been low (<2% compared to 5%), in children compared to adults.<sup>11-13</sup> Large series of children with COVID-19 have shown remarkably very low mortality of 0.05% to 0.07%.<sup>13,16</sup>

### Approach to Diagnosis

Different screening criteria are used for case definition and testing depending on geographic location. The WHO and Chinese criteria for diagnosis take into account the following epidemiological history and clinical manifestations:<sup>17,18</sup>

### Suspect Case

- 1) A patient with acute respiratory tract infection (sudden onset of at least one of the following: cough, fever, shortness of breath) AND with no other aetiology that fully explains the clinical presentation AND with a history of travel or residence in a country/area reporting local or community transmission\* during the 14 days before symptom onset; OR
- 2) A patient with an acute respiratory illness AND having been in close contact with a confirmed or probable COVID-19 case in the last 14 days before onset of symptoms; OR
- 3) A patient with severe acute respiratory infection (fever and at least one sign/symptom of respiratory disease (e.g., cough, fever, shortness breath)) AND requiring hospitalisation (SARI) AND with no other aetiology that fully explains the clinical presentation.

\*However, once local or community transmission has been reported like Pakistan, all children presenting with symptoms of acute respiratory infection in any healthcare setting may be considered as suspected cases.

### Probable case

1. A suspect case for whom testing for the COVID-19 virus is inconclusive; OR
2. A suspect case for whom testing could not be performed for any reason.

### Confirmed case

A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.

### Laboratory and Radiologic Features

Common laboratory findings (25-65%) noted in most paediatric patients with COVID-19 included normal blood counts, lymphopenia, increased C-reactive protein, increased procalcitonin and increased lactate dehydrogenase.<sup>11-13,16</sup> In those with severe disease, high ferritin, elevated liver function tests, D-dimers, and creatinine kinase may be found.<sup>11,15,16</sup> Radiologic findings may be normal or non-specific but studies have reported pneumonia in the majority (65%) of children.<sup>11,13</sup> Chest x-ray changes reported include normal to lower lobe and peripheral opacities that are mostly bilateral.<sup>11,13,15,16</sup> Chest computed tomography (CT) may show changes similar to adults with abnormal variable findings of peripheral bilateral (multilobar or multifocal) ground-glass opacification (GGO) in 33%, bilateral or unilateral patchy infiltrates and areas of consolidation.<sup>11,13,16</sup>

Asymptomatic children have been reported to have abnormal CT findings.

## Diagnosis

Confirmation of COVID-19 in children is via a positive SARS-CoV-2 RNA by reverse-transcriptase polymerase chain reaction (PCR) of respiratory samples of either upper or lower respiratory tract such as nasopharyngeal (preferable), throat, sputum and tracheal or bronchial lavage.<sup>19</sup> A single sample may be falsely negative and therefore repeat sampling may be warranted in case of strong suspicion. Other methods being evaluated including stool PCR, immunodiagnosics, and ultra-rapid tests in both adult and paediatric populations. Other viral and bacterial may need to be excluded as differential diagnosis but may exist as co-pathogen(s).

## Clinical Classification

For case management the following clinical classification has been developed:<sup>18</sup>

### 1. Mild cases

The clinical symptoms were mild, and there was no sign of pneumonia on imaging

### 2. Moderate cases

Children with fever and respiratory symptoms with radiological findings of pneumonia

### 3. Severe cases

Children meeting any of the following criteria:

a) Tachypnoea (respiratory rate (RR)  $\geq$  60 breaths/min for infants aged below 2 months; RR  $\geq$  50 breaths/min for infants aged 2-12 months; RR  $\geq$  40 breaths/min for children aged 1-5 years, and RR  $\geq$  30 breaths/min for children above 5 years old) independent of fever and crying;

b) Oxygen saturation  $\leq$  92% on finger pulse oximeter taken at rest;

c) Laboured breathing (moaning, nasal fluttering, and infrasternal, supraclavicular and intercostal retraction), cyanosis, and intermittent apnoea;

d) Lethargy and convulsion;

e) Difficulty feeding and signs of dehydration.

### 4. Critical cases

Children meeting any of the following criteria:

a) Respiratory failure and requiring mechanical

ventilation;

b) Shock;

c) Other organ failures that require ICU care.

## Management

The definitive clinically proven treatments of COVID-19 are yet to be defined especially in children and mostly not recommended. Management is directed at prevention of transmission to others, supportive care, and monitoring for deterioration especially after 5-7 days of symptom onset.<sup>13,15,16</sup> Most children with mild to moderate disease need supportive care only at home like any URTI clinical syndromes. Instructions must be given to maintain hydration, use of antipyretics, and a healthy diet. Only 6-20% of children may require hospitalisation for oxygenation and 0.58-2% need intensive care including mechanical ventilation employing "lung-protective ventilation strategy" and other intensive support.<sup>7,13,15,16</sup> Hospitalisation is recommended in symptomatic children with moderate to severe disease requiring oxygen, intensive care, clinical deterioration, or those with risk factors.<sup>18,20</sup> Other therapies such as antibiotics, steroids, and immunoglobulins are not used routinely unless specific indication exists.

Limited studies in adults show that the exact role of specific medications remains unclear.<sup>18,20-22</sup> These include some antivirals including anti-HIV drugs, remdesivir, antimalarial drugs chloroquine and hydroxychloroquine, immunoglobulins, interferon, immunomodulatory agents such as tocilizumab, steroids and COVID-19 convalescent plasma. Almost all these studies have been scrutinised for evidence, potential benefits, harms, and limitations.<sup>22</sup> Given early phase of the pandemic and paucity of scientific evidence Infectious Diseases Society of America (IDSA) has aptly put this as "among patients who have been admitted to the hospital with COVID-19, the IDSA guideline panel recommended the use of specific medication in the context of a clinical trial."<sup>22</sup> Some of these potential drugs may be considered in children as an off-label treatment or within the context of a clinical trial. Hopefully the numerous clinical trials (692 to date) now being explored will give a much-needed evidence-based decision of the right cure or treatment in terms of resolution of symptoms or radiologic findings, negativity of PCR, reduction in mechanical ventilation use, hospital stay and mortality.<sup>23</sup>

## Neonates

COVID-19 in neonates has been described in various case reports and series.<sup>24,25</sup> These are significant for mostly

mild disease and remarkably few deaths so far. Vertical transmission has not been documented. The most likely exposure is during or after delivery. Most of these neonates have presented 1-14 days after exposure. Illness may include asymptomatic, mild, or severe disease. Nonspecific symptoms included irritability, poor feeding, temperature instability, tachypnoea, grunting, cough, and gastrointestinal symptoms such as vomiting, diarrhoea, and abdominal distension. Laboratory findings are mostly normal or non-specific and have included mild lymphopenia or leucopenia, elevated liver enzymes, LDH, and creatinine kinase. Chest X-ray or ultrasound findings of the lungs may show pneumonia.

Management for SARS-CoV-2 PCR positive asymptomatic neonates is supportive and requires monitoring for clinical deterioration.<sup>24-26</sup> Management for SARS-CoV-2 PCR positive symptomatic neonates is mostly supportive care in single rooms, incubator care, and treatment of complications. Some of these neonates may require mechanical ventilation and extracorporeal membrane oxygenation (ECMO) etc. Antibiotics, intravenous immunoglobulin (IVIG), steroids, interferon are mostly not required and not recommended. Currently, there are no antivirals recommended for use in neonates. Transmission SARS-CoV-2 from mother to neonate during breastfeeding has not been documented and therefore may be continued even in PCR positive asymptomatic mother with precautions such as putting on facemask and hand hygiene. Alternatively expressed breast milk may be given by another caregiver.<sup>26</sup>

## Prevention

Children, fortunately, have been spared of the direct adverse effects of this pandemic but if prolonged it can have serious consequences. Experts fear that the global threat to child health will be indirect socio-economic consequences resulting in increasing poverty, malnutrition, health issues, and poor schooling. Paediatricians must play a role in advocating preventive aspects for COVID-19 and also its consequences. SARS-CoV-2 can only be prevented effectively by following infection control measures in healthcare and home settings such as clinics and daycare.<sup>27</sup> Paediatricians must encourage families and children to stay home and follow advice on lockdowns and avoiding mass gatherings. Children should be taught regular hand hygiene, cough etiquettes, not to touch their mouth, nose and eyes and avoiding going out of home. Washing their toys regularly and their rooms are also important. For children who are exposed to monitoring for fever and other respiratory symptoms for at least 14 days after exposure will identify early-infected children to exclude from contact with

others. Regular physical exercises and a good healthy diet must be ensured. Currently there is no vaccine available but trials are already underway and there is hope that a vaccine may be ready in 12-18 months.<sup>28</sup>

## Conclusions

Paediatric COVID-19 has a low incidence, is fortunately mild, has low complication rates, and low mortality from preliminary data from Pakistan. Treatment is largely supportive but must be directed to early identification of infected children to halt transmission. Available literature on clinical presentation, classification, diagnosis, management, and prevention has now translated into guidelines for paediatricians to manage these children and neonates for optimal care.

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