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Managing COVID-19 disease in pediatric patients

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■ ABSTRACT

Children are less likely to be infected with SARS-CoV-2 than adults and often have a milder course of COVID-19 disease and a lower case fatality rate. Children account for an estimated 1% to 5% of those diagnosed with COVID-19. Even so, preschool-aged children, infants, and children with underlying health conditions may still be at risk for severe disease and complications. Unique aspects of COVID-19 presentation and disease course in children and possible vertical transmission to newborns from COVID-19-positive mothers are discussed.

■ WORLD EXPERIENCE WITH COVID-19 IN CHILDREN

Thus far, studies have shown that children are less likely to be infected with SARS-CoV-2 than adults and often have a milder course of COVID-19 disease and a lower case fatality rate. Children account for an estimated 1% to 5% of those diagnosed with COVID-19.¹ Even so, preschool-aged children, infants, and children with underlying health conditions may still be at risk for severe disease and complications.²

A large retrospective study of 2,135 confirmed or suspected COVID-19 cases in children reported to the Chinese Center for Disease Control and Prevention showed milder clinical manifestations in this population.³ Patients were classified as being asymptomatic (4.4%) or as having mild (51.0%), moderate (38.7%), severe (5.2%), or critical disease (0.6%) based on clinical features, laboratory testing, and imaging. Severe disease was defined as the presence of dyspnea, central cyanosis, and an oxygen saturation of less than 92%. Critical disease was defined as the

presence of acute respiratory distress syndrome, respiratory failure, or shock. Younger children were more at risk for severe illness than older children—half of the children with critical disease were less than 1 year old. There was no significant difference in cases between boys and girls.

Similarly, morbidity data available in the United States showed that 2,572 (1.7%) of the 149,082 reported cases of COVID-19 disease (as of April 2, 2020) occurred in pediatric patients (younger than 18 years of age).⁴ The median age of these patients was 11 years, and infants younger than 1 year of age made up 15% (398) of the pediatric cases.

Among the 184 (7.2%) children for whom exposure information was available, 168 (91%) were infected by a positive close contact within the household or community.⁴ Signs and symptoms of fever, cough, and shortness of breath were less commonly reported in children than in adults (56% vs 71%, 54% vs 80%, and 13% vs 43%, respectively). Among 345 pediatric patients with information on underlying comorbidities, 80 (23%) had at least 1 underlying health condition, most commonly chronic lung disease (including asthma), cardiovascular disease, or immunosuppression. This subset of patients and infants is more likely to require hospitalization, including intensive care.

As of May 15, 2020, there are reports from Europe and the United States of children and teenagers who developed a multisystem inflammatory condition with features similar to those of Kawasaki disease and toxic shock syndrome with temporal association to COVID-19, termed *Multisystem Inflammatory Syndrome in Children* (MIS-C).⁵ These patients typically require hospitalization and, at times, intensive care. Please refer to World Health Organization scientific brief on MIS-C related to COVID-19.

There are scarce data on children from Italy, Iran, and South Korea. One case series of 9 children from

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Iran reported a high probability of direct transmission from a family member.⁶ All children presented with fever and respiratory symptoms such as cough, tachypnea, and chest wall retractions. None presented with gastrointestinal symptoms. This case series reported an overall good prognosis of COVID-19 in children.

It is also important to note that COVID-19 diagnoses in children may be underreported due to varying testing prioritization as well as cases being largely asymptomatic or with mild symptoms at the time of presentation.

■ UNIQUE ASPECTS OF COVID-19 PRESENTATION AND COURSE IN CHILDREN

Signs and symptoms in children are usually less severe than those in adults and are similar to those seen with respiratory tract infections, including fever, cough, shortness of breath, and pharyngeal erythema.⁷ Although gastrointestinal symptoms have been described in adult patients, diarrhea and vomiting are less commonly reported in children.^{2,4,7}

One anecdotal report described pernio-like lesions or acro-ischemic lesions on the toes and sometimes on the fingers of asymptomatic older children.⁸ These round, painful lesions were a few millimeters in size with a clear demarcation at the metatarsal-phalangeal level. The lesions can initially have a reddish-purple color and become bullous, black, or both over the ensuing weeks.

Coinfection with other respiratory pathogens has been described in children with COVID-19 (eg, influenza, mycoplasma, respiratory syncytial virus, and cytomegalovirus), and providers should consider these when ordering tests. Results of chest radiography are usually normal in pediatric patients or may show patchy infiltrates similar to that seen with viral pneumonias. Computed tomography scans generally show unilateral or bilateral subpleural ground-glass opacities and consolidations with surrounding halo sign. The consolidation with surrounding halo sign was seen in 50% of pediatric patients in 1 study and is a unique finding described in children with COVID-19.⁹

Laboratory findings vary. In one study of 20 pediatric cases,⁹ the white blood cell count was normal in 14 patients and lymphopenia (< 45% of lymphocyte) was noted in 7 patients. Procalcitonin levels were elevated (> 0.05 mg/L) in 16 patients whereas C-reactive protein levels were elevated (> 3 mg/L) in 7 patients. Only 5 patients had elevated levels of transaminase (> 40 IU/L) and creatine-kinase myocardial band (CK-MB > 25 IU/L).

A meta-analysis of laboratory findings in 66 pediatric patients aged 2 weeks to 17 years also reported that most had normal leukocyte counts (69.6%), neutrophil counts (89.4%), and normal C-reactive protein (86.4%) and procalcitonin (89.4%) levels.¹⁰ Only 2 infants had lymphopenia (3%).

The reasons why children are not as severely ill as adults when infected with COVID-19 are largely unknown, but there are multiple theories. First, children are generally well taken care of by caregivers and, hence, may have a smaller chance of being exposed to the pathogen itself. Second, it is possible that children have higher levels of antibodies against viruses due to higher rates of respiratory infections during winter. Third, their immune systems are less mature than those of adults, which may lead to a less robust cytokine response to the pathogen. Finally, the binding ability of angiotensin converting enzyme II—which is a known cell receptor for COVID-19—is reduced in children.^{3,11}

Because most pediatric cases are mild, treatment with supportive care is usually sufficient. Currently, there are no antiviral agents approved by the US Food and Drug Administration (FDA) for use in either children or adults to treat COVID-19. For severely sick pediatric patients, recent guidelines from the Pediatric Infectious Disease Society suggest using remdesivir on a case-by-case basis, taking into consideration the respiratory support needs and individual risk factors of disease progression, including young age, immune status, and underlying cardiovascular and pulmonary diseases. Formal studies of this drug are underway. The use of antivirals in children and adults with COVID-19 needs to be tested in clinical trials or through the FDA's Expanded Access Program for Investigational Drugs.¹²

Although most manifestations of COVID-19 in children are benign and self-limiting, there have been increasing reports of a small subset of older children and young adults with multisystem inflammatory syndrome, which emphasizes the need to detect and report these cases early as they are often sick and require intensive care with a multidisciplinary approach. Please see the World Health Organization commentary on MIS-C for full diagnostic criteria and treatment guidelines.⁵

Given the large numbers of COVID-19–positive children who are asymptomatic or with a mild clinical presentation, the importance of social distancing, use of cloth face masks (except in children under the age of 2 or for those who cannot remove the mask without assistance), and proper hand hygiene should

be emphasized as these patients likely play an important role in disease transmission.

■ IS THERE A RISK OF VERTICAL TRANSMISSION?

A few studies (case reports and series) have described possible vertical transmission to newborns from COVID-19–positive mothers. Of 33 neonates delivered at Wuhan Children's Hospital to COVID-19–positive mothers, 3 (9%) were clinically symptomatic and tested positive via nasopharyngeal and anal swabs at day 2 of life.¹³ Strict infection prevention procedures were followed during delivery and, thus, vertical transmission was suspected.

Another series from China reported elevated IgM antibody and cytokine levels at birth in infants born to COVID-19–positive mothers. The infants remained asymptomatic and tested negative via nasopharyngeal swab and serum PCR.¹⁴

A study from China retrospectively reviewed 9 pregnant women with COVID-19 nasopharyngeal swab-positive disease who gave birth and reported negative viral detection in cord blood, placental tissue, serum, vaginal mucus, amniotic fluid, and breast milk,^{15,16} providing evidence against vertical transmission.

Even though overall vertical transmission seems less likely due to low viremia rates, leading to a small chance of placental seeding, all studies are limited by their small sample sizes. Further studies are needed to better understand the risk of perinatal transmission.

To date, there is no clear evidence of intrauterine vertical transmission. However, there is a plausible risk of infection occurring during and after delivery. The US Centers for Disease Control and Prevention and the American Academy of Pediatrics currently recommend that newborns born to COVID-19–positive mothers or those who are suspected to be positive should be considered persons under investigation and tested using nasal and throat swabs via molecular assays at 24 hours of age and again at 48 hours if they are still in the care facility. They should be separated from their mothers, if possible, to minimize the risk of postnatal infection and kept in areas away from infants whose mothers are negative for COVID-19.¹⁷ They can be fed expressed breastmilk from their mothers as no studies have found the virus in breastmilk thus far.^{15–17}

After discharge, COVID-19–positive mothers are encouraged to maintain a 6-foot distance from their newborn infants, as possible, and use proper hand hygiene and masks while providing care to their newborn until they are afebrile for 72 hours and 7 days out from symptom onset.¹⁷ Providers should continue

optimal newborn care and prioritize immunizations of infants and young children, after discharge, while following measures of social distancing.¹⁸

■ VISITORS IN HEALTHCARE SETTINGS

Many pediatric healthcare systems, including Cleveland Clinic Children's Hospital, have instituted strict visitor restrictions to both inpatient and outpatient locations. Many limit visitors to 1 parent each day during the hospital stay (except for end-of-life situations), visitors are screened and temperature taken prior to entering the facilities. All visitors are encouraged to wear cloth masks at all times, respect social distancing, and practice hand hygiene. If visitors are for patients with COVID-19, they are typically required to wear personal protective equipment.

■ REFERENCES

1. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr*. Published online March 23, 2020. doi:10.1111/apa.15270
2. Cruz AT, Zeichner SL. COVID-19 in children: initial characterization of the pediatric disease. *Pediatrics* 2020; 145(6):e20200834. doi:10.1542/peds.2020-0834
3. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics* 2020; 145(6):e20200702. doi:10.1542/peds.2020-0702
4. CDC COVID-19 Response Team. Coronavirus disease 2019 in children – United States, February 12–April 2, 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69(14):422–426. doi: 10.15585/mmwr.mm6914e4
5. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. Scientific brief. May 15, 2020. Accessed June 3, 2020. <https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>
6. Rahimzadeh G, Ekrami Noghabi M, Kadkhodaei Elyaderani F, et al. COVID-19 infection in Iranian children: a case series of 9 patients. *J Pediatr Rev* 2020; 8(2):139–144. doi:10.32598/jpr.8.2.139
7. Centers for Disease Control and Prevention. Information for Pediatric Healthcare Providers. Updated May 29, 2020. Accessed June 3, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html>
8. Mazzotta F, Troccoli T. Acute acro-ischemia in the child at the time of COVID-19. *Eur J Pediatr Dermatol* 2020; April 6. Accessed June 3, 2020. <https://www.fip-ifp.org/wp-content/uploads/2020/04/acroischemia-ENG.pdf>
9. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *Pediatr Pulmonol* 2020; 55(5):1169–1174. doi:10.1002/ppul.24718
10. Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. *Clin Chem Lab Med* Published online March 16, 2020. doi:10.1515/cclm-2020-0272
11. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 2020; 395(10229):1033–1034. doi:10.1016/S0140-6736(20)30628-0
12. Choitos K, Hayes M, Kimberlin DW, et al. Multicenter initial guidance on use of antivirals for children with COVID-19/SARS-CoV-2. *J Pediatric Infect Dis Soc* 2020 April 22. doi:10.1093/jpids/piaa045
13. Zeng L, Xia S, Yuan W, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatr* 2020; March 26. doi:10.1001/jamapediatrics.2020.0878

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14. **Zeng H, Xu C, Fan J, et al.** Antibodies in infants born to mothers with COVID-19 pneumonia. *JAMA* 2020; 323(18):1848–1849. doi:10.1001/jama.2020.4861
 15. **Liu W, Wang Q, Zhang Q, et al.** Coronavirus disease 2019 (COVID-19) during pregnancy: a case series. *Preprints* 2020; 2020020373. Accessed on June 3, 2020. <https://www.preprints.org/manuscript/202002.0373/v1>
 16. **Wang W, Xu Y, Gao R, et al.** Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA* 2020; 323(18):1843–1844. doi:10.1001/jama.2020.3786
 17. **Puopolo KM, Hudak ML, Kimberlin DW, Cummings J.** Initial guidance: management of infants born to mothers with COVID-19. Published online April 6, 2020. Accessed June 3, 2020. <https://www.sigo.it/comunicati-covid-19/initial-guidance-management-of-infants-born-to-mothers-with-covid-19>
 18. **Centers for Disease Control and Prevention.** Coronavirus disease 2019: Caring for pregnant women. Updated April 6, 2020. Accessed June 3, 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-guidance.html#anchor_1582067955833