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Managing COVID-19 infection 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 illness and a lower case fatality rate. Children account for an estimated 1% to 5% of those diagnosed with COVID-19.[1] Even so, pre-school–aged children, infants, and children with underlying health conditions may still be at risk for severe disease and complications.[2] Unique aspects of COVID-19 presentation and 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 illness and a lower case fatality rate. Children account for an estimated 1% to 5% of those diagnosed with COVID-19.[1] Even so, pre-school–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 2,143 confirmed or suspected COVID-19 infections in children reported to the Chinese Center for Disease Control and Prevention showed milder clinical manifestations in children.[3] Patients were classified as being asymptomatic (4.4%) or as having mild (50.9%), moderate (38.8%), 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 a year old. There was no significant difference in cases between boys and girls.

Similarly, morbidity data available in the United States showed that 2572 (1.7%) of the 149,082 reported cases of COVID-19 infection (as of April 2, 2020) occurred in pediatric patients (less than 18).[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 co-morbidities, 80 (23%) had at least one underlying health condition, most commonly chronic lung disease (including asthma), cardiovascular disease, or immunosuppression. This subset of patients and infants are more likely to require hospitalization, including intensive care.

There is scarce data on children from Italy, Iran, and South Korea. One case series of 9 children from Iran reported a high probability of direct transmission from a family member.5 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 infection in children.

It is also important to note that COVID-19 diagnosis in children may be underreported due to

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varying testing prioritization as well as 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.[6] While gastrointestinal symptoms have been described in adult patients, diarrhea and vomiting are less commonly reported in children.[2,4,6]

One anecdotal report described pernio-like lesions or acro-ischemic lesions on the toes, and sometimes the fingers, of asymptomatic older children.[7] 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.

Co-infection with other respiratory pathogens has been described in children with COVID-19 (eg, influenza, mycoplasma, respiratory syncytial virus, and cytomegalovirus), and providers should consider this 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 one study and is a unique finding described in children with COVID-19.[8]

Laboratory findings vary. In one study of 20 pediatric cases,[8] the white blood cell count was normal in 14 patients; lymphopenia (< 45%) 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 of transaminase (> 40 IU/L) and creatine-kinase MB (> 25 IU/L).

A meta-analysis of laboratory findings in 66 pediatric patients ages 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.[9] 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.[3,10]

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 for the treatment of 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.[11]

Given the large numbers of COVID-19-postive 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.[12] 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.[13]

A study from China retrospectively reviewed 9

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COVID-19 nasopharyngeal swab-positive pregnant women who gave birth and reported negative viral detection in cord blood, placental tissue, serum, vaginal mucus, amniotic fluid, and breast milk,[14,15] 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 are 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.[16] They can be fed expressed breastmilk from their mothers as no studies have found the virus in breastmilk thus far.[14–16]

COVID-19—positive mothers are also encouraged to maintain a distance of 6 feet from their newborn infants after discharge and use proper hand hygiene and masks while providing newborn care until they are afebrile for 72 hours and 7 days out from symptom onset.[16] Providers should continue optimal newborn care and prioritize immunizations of infants and young children, after discharge, while following measures of social distancing.[17]

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