COVID-19 in Children, Pregnancy and Neonates: A Review of Epidemiologic and Clinical Features

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Abstract: The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has spread rapidly across the globe. In contrast to initial reports, recent studies suggest that children are just as likely as adults to become infected with the virus but have fewer symptoms and less severe disease. In this review, we summarize the epidemiologic and clinical features of children infected with SARS-CoV-2 reported in pediatric case series to date. We also summarize the perinatal outcomes of neonates born to women infected with SARS-CoV-2 in pregnancy. We found 11 case series including a total of 333 infants and children. Overall, 83% of the children had a positive contact history, mostly with family members. The incubation period varied between 2 and 25 days with a mean of 7 days. The virus could be isolated from nasopharyngeal secretions for up to 22 days and from stool for more than 30 days. Co-infections were reported in up to 79% of children (mainly mycoplasma and influenza). Up to 35% of children were asymptomatic. The most common symptoms were cough (48%; range 19–100%), fever (42%; 11–100%) and pharyngitis (30%; 11–100%). Further symptoms were nasal congestion, rhinorrhea, tachypnoea, wheezing, diarrhea, vomiting, headache and fatigue. Laboratory test parameters were only minimally altered. Radiologic findings were unspecific and included unilateral or bilateral infiltrates with, in some cases, ground-glass opacities or consolidation with a surrounding halo sign. Children rarely needed admission to intensive care units (3%), although 9% of children had required mechanical ventilation. Children rarely needed admission to intensive care units (3%), although 9% of children had required mechanical ventilation. The incubation period varied between 2 and 25 days (mean 7 days, median 6 and 11 days, respectively).9,15,16 Several studies reported that the nasopharyngeal or throat swabs can be positive before the onset of symptoms.7,11,14 However, false-negative swabs have also been reported.10 We did not include single details17,24–26 or studies which were retracted.27 The age of the children ranged from 1 day to 16 years, 55% (183) were male. The majority of diagnoses were made by real-time polymerase chain reaction on nasopharyngeal or other respiratory samples. Overall, 83% (275, range 52–100%) of children had a positive contact history, mostly with family members. Three studies reported incubation periods which varied between 2 and 25 days (mean 7 days, median 6 and 11 days, respectively).9,15,16 Several studies reported that the nasopharyngeal or throat swabs can be positive before the onset of symptoms.7,11,14 However, false-negative swabs have also been described.10 There were 4 studies which did consecutive sampling: real-time polymerase chain reaction on respiratory samples remained positive between 1 and 22 days and in stool between 5 and over 30 days.8,9,14,17 Viral shedding from the gastrointestinal tract might last longer and also be greater than that from the respiratory tract.14

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes the disease termed coronavirus disease 2019 (COVID-19), emerged in China in early December 2019.4 The outbreak was declared a public health emergency of international concern by the World Health Organization on January 30, 2020.2 The virus has rapidly spread causing a global pandemic with a major burden on the health care system and economy. During the early stages of the outbreak, it was thought that children were rarely affected by SARS-CoV-2 which could have been as a result of their lower nosocomial exposure and less frequent contact with animals.3 However, a number of reports suggest that children are just as likely as adults to become infected with SARS-CoV-2 but have fewer symptoms and less severe disease, as well as a much lower case-fatality rate.4,5 Many of the initial studies in China were done in adults hospitals, so it is not surprising that the numbers of children reported were small.9 Furthermore, as many children with mild disease might not be tested, the true rate of infection and viral carriage is likely underestimated.

In this review, we summarize the epidemiologic characteristics and clinical features of children infected with SARS-CoV-2 reported in pediatric case series to date. We also summarize perinatal outcomes of infants born to women infected with SARS-CoV-2 during pregnancy. Understanding the clinical presentation of this virus in this age group is important for early identification of children with SARS-CoV-2 to provide optimal medical care and to help control the pandemic.

PEDIATRIC CASE SERIES

We found 11 case series, including a total of 333 children (range 6–171 children) with confirmed SARS-CoV-2 infections (Tables 1–4).7–17 All of the series are from China. One case series included only infants3 and one only children who were admitted to an intensive care unit.16 In 2 of the studies, there were patients that overlapped14 and further duplicate reporting of patient could not be excluded in 2 other studies.7,11 We did not include single case reports,18–23 publications which did not give enough clinical details18–20 or studies which were retracted.11 The age of the children ranged from 1 day to 16 years, 55% (183) were male. The majority of diagnoses were made by real-time polymerase chain reaction on nasopharyngeal or other respiratory samples. Overall, 83% (275, range 52–100%) of children had a positive contact history, mostly with family members. Three studies reported incubation periods which varied between 2 and 25 days (mean 7 days, median 6 and 11 days, respectively).9,15,16 Several studies reported that the nasopharyngeal or throat swabs can be positive before the onset of symptoms.7,11 However, false-negative swabs have also been described.10 There were 4 studies which did consecutive sampling: real-time polymerase chain reaction on respiratory samples remained positive between 1 and 22 days and in stool between 5 and over 30 days.8,9,14,17 Viral shedding from the gastrointestinal tract might last longer and also be greater than that from the respiratory tract.14

Three studies investigated for co-infections (Table 1).11,16 One study only for influenza A and B, which was found in 1 of 8 children16 and the other 2 studies for a broader range of pathogens, which were found in 45% and 79% of children.11,15

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**TABLE 1.** Epidemiologic Features of Pediatric Patients With COVID-19 (as of March 27, 2020)

| Number of children | Location                  | Time period               | Age Range                                                                 | Male (%) | Specimens for RT-PCR or RNA sequencing | Transmission | Incubation period Range | Shedding duration Range | Co-infections |
|--------------------|---------------------------|----------------------------|---------------------------------------------------------------------------|----------|----------------------------------------|--------------|--------------------------|------------------------|---------------|
| 171                | Wuhan Children's Hospital, China | Jan 28 to Feb 26, 2020 | Median 7 y                                                                | 61% (104)| Pharyngeal                            | 90% (154)    | Mean 7 d 2–10 d          | Median 12 d 3–22 d    | Total          |
| 36                 | 3 hospitals in Zhejiang, China | Jan 17 tp to March 1, 2020 | Mean 8 y 1–16 y                                                           | 36% (13) | NP or throat                           | 89% (32)     | NR                       | Median 6 d 18–30 d   | Mycoplasma     |
| 10                 | Shanghai Children's Hospital, China | Jan 19 to Feb 3, 2020 | Mean 6 y 3 m–11 y                                                        | 40% (4)  | NP or rectal, sputum, blood            | 80% (8)      | Median 7 d 2–10 d        | Median 12 d 18–30 d  | Influenza A/B   |
| 26                 | Shenhen Third People's Hospital, China | Jan 16 to Feb 8, 2020 | Mean 7 y 1–13 y                                                           | 65% (17) | Throat                                | 100% (26)    | Median 11 d 8–25 d       | Median 15 d 10–15 d  | RSV           |
| 20                 | Wuhan Children's Hospital, China | Jan 23 to Feb 8, 2020 | Median 2 y 1–15 y                                                         | 65% (13) | NP                                    | NR           | Median 6 d 5–10 d        | Median 28 d 23–33 d  | CMV           |
| 9                  | Tongji Children's Hospital, China | Jan 7 to Jan 15, 2020   | Median 3 y 1–7 y                                                          | 33% (2)  | NP or rectal                          | 100% (9)     | Median 11 d 8–25 d       | Median 15 d 10–15 d  | EBV           |
| 10                 | Nationwide study in China | Dec 8 to Feb 20, 2020   | Median 7 m 2–11 m                                                         | 22% (2)  | Throat or lower respiratory           | 60% (6)      | Median 6 d 5–10 d        | Median 15 d 10–15 d  | Parainfluenza   |
| 34                 | Guangzhou Children's Medical Center, China | Dec to Jan 1, 2020     | Median 6 y 1–12 y                                                         | 70% (7)  | NP                                    | 52% (18)     | Median 11 d 8–25 d       | Median 15 d 10–15 d  | Adenovirus     |
| 8                  | 4 hospitals in Western China | Jan 24 to Feb 24, 2020   | Median 3 y 2 m–15 y                                                       | 41% (14) | Throat or lower respiratory           | 60% (6)      | Median 6 d 5–10 d        | Median 15 d 10–15 d  |               |
| 3                  | Qingdao, Shandong Province, China | Jan 17 to Feb 23, 2020 | Median 8 y 1–6 y                                                          | 66% (2)  | Throat, stool                         | 100% (3)     | NR                       | NR                     |               |

*Preprint.
†Patients in this study are possibly also reported in the study by Lu et al.
‡Three patients overlap with the study by Lu et al.
CMV, cytomegalovirus; EBV, Epstein-Barr virus; NR, not reported; NP, nasopharyngeal; RSV, respiratory syncytial virus; RT-PCR, real-time polymerase chain reaction.
China and further deaths have now been reported in Europe and an 14-year-old boy has been reported in an epidemiologic study from biotics and traditional Chinese medicine.8,10,12,15–17 The hospital (±lopinavir), interferon, glucocorticoids, immunoglobulin, anti-

surrounding halo sign in the latter (Table 3).

Typical laboratory findings were minor changes in white blood cell counts (reports of both increased and decreased lymphocyte and, less commonly, neutrophil counts), as well as mildly elevated inflammatory markers (erythrocyte sedimentation rate, C-reactive protein or procalcitonin), liver enzymes, creatine kinase, lactate dehydrogenase or D-dimers (Table 3).

### SARS-CoV-2 Infection During Pregnancy, Vertical Transmission and Perinatal Outcomes

There are 9 small case series (all from China) and 2 case reports including a total of 65 pregnant women (67 neonates) who were infected with SARS-CoV-2 during pregnancy (Table 5). The number of women in each case series varied between 2 and 16 (median 7). Two women were infected at 25 and 27 weeks of pregnancy, the remaining during the third trimester. Three women were discharged, the remaining delivered between 30 and 40 weeks of pregnancy, mostly by Cesarean section (88% (56). Fetal distress was reported in 31% (20). A total of 38% (724) women delivered preterm. Maternal complications included premature rupture of membranes 12% (8), pre-eclampsia 3% (2), gestational hypertension 6% (4), gestational diabetes 5% (3), hypothyroidism 3% (2), tachycardia 2% (1) and abnormal umbilical cord 3% (2). Two women (3%) were admitted to intensive care unit for mechanical ventilation, one of whom developed multi-organ failure and died. A further death due to COVID-19 of a preexisting condition (leukemia and hydronephrosis, respectively). A 10-month-old girl admitted to an intensive care unit developed intussusception, encephalopathy, septic shock and multiple organ dysfunction, and died. A further death due to COVID-19 of a 14-year-old boy has been reported in an epidemiologic study from China and further deaths have now been reported in Europe and the USA.

### DISCUSSION

This review confirms that, compared with adults, children with SARS-CoV-2 infection have milder clinical symptoms and fewer laboratory and radiologic abnormalities. The same findings...
| Laboratory and Radiologic Findings of Pediatric Patients With COVID-19 | Lu et al<sup>7</sup> | Qiu et al<sup>8</sup> | Cai et al<sup>9</sup> | Tang et al<sup>10</sup>‡ | Xia et al<sup>11</sup>† | Liu et al<sup>12</sup> | Wei et al<sup>13</sup> | Xu et al<sup>14</sup> | Zhang et al<sup>15</sup>* | Sun et al<sup>16</sup‡ | Xing et al<sup>17</sup>* |
|---------------------------------------------------------------|------------------|-------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| **Laboratory findings**                                        |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Leucocytosis                                                  | 0 NR             | 20% (2)           | 15% (4)          | 10% (2)          | 0 NR             | 0 NR             | 0 NR             | 13% (1)          | 0 NR             | 0 NR             | 0 NR             |
| (>12 G/L)                                                     |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Leukopenia                                                    | 20% (45)         | 19% (7)           | 20% (2)          | 20% (5)          | 88% (5)          | NR 30% (3)       | NR 13% (1)        | 0 NR             | 0 NR             | 0 NR             |                  |
| (<5.5 G/L)                                                   |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Neutrophilia                                                  | 0 NR             | 10% (1)           | NR 0 NR 0        | 0 NR             | 0 NR             | 0 NR             | 0 NR             | 13% (1)          | 0 NR             | 0 NR             |
| (>7 G/L)                                                     |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Neutropenia                                                   | 0 NR             | 20% (2)           | NR NR 0          | 20% (2)          | 50% (3)          | NR 10% (1)        | NR 26% (2)         | 3% (1)           | 3% (1)           | 3% (1)           |
| (<1.5 G/L)                                                   |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Lymphocytosis                                                 | 0 NR             | 10% (1)           | NR NR 0 NR 13%  | 15% (3)          | 0 NR             | 20% (2)          | 50% (17)         | 26% (2)          | 100% (3)         | 0 NR             |
| (>4 G/L)                                                     |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Lymphopenia                                                   | 4% (6)           | 31% (11)          | 0 NR NR 35% (7) | 15% (3)          | 0 NR             | 20% (2)          | 50% (17)         | 26% (2)          | 100% (3)         | 0 NR             |
| (<1.2 G/L)                                                   |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Thrombocytosis                                                | NR NR            | 20% (2)           | Abnormal in 31%  | NR 0 NR 10% (1)  | NR 0 NR          | 10% (1)          | NR 38% (3)        | 0 NR             |                  |                  |
| (<350 G/L)                                                   |                  |                   |                 |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated ESR                                                 | NR 0             | 27% (7)           | NR NR 33% (2)    | 30% (3)          | 0 NR             | 10% (1)          | NR 38% (3)        | 0 NR             |                  |                  |
| (>15 mm/h)                                                   |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated CRP                                                 | 20% (33)         | 3% (1)            | 20% (2)          | 19% (5)          | 35% (7)          | 83% (5)          | NR 30% (3)        | 63% (5)          | 33% (1)          | 0 NR             |
| (>10 mg/L)                                                   |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated PCT                                                 | 2% (0)           | 17% (6)           | 0 0              | 80% (14)         | NR 0             | 50% (5)          | NR 63% (5)        | 33% (1)          | 0 NR             |                  |
| (>0.05 ng/mL)                                                |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated ALAT                                                | 12% (21)         | 6% (2)            | 10% (1)          | 12% (3)          | 25% (5)          | 17% (1)          | NR 10% (1)        | 50% (4)          | NR 25% (4)       | 0 NR             |
| (>45 U/L)                                                    |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated ASAT                                                | 15% (25)         | 8% (3)            | 20% (2)          | 12% (3)          | NR 67% (4)       | 20% (2)          | 0 NR             | 25% (2)          | 0 NR             |                  |
| (>50 U/L)                                                    |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated CK                                                 | 3% (1)           | NR 0 NR 0         | NR NR 3% (1)     | NR 0 NR          | 30% (3)          | NR 0 NR          | 25% (2)          | 0 NR             |                  |                  |
| (>170 U/L)                                                   |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated CK-MB                                               | NR 31% (11)      | 50% (5)           | NR 75% (15)      | NR NR NR 50% (3)| 10% (1)          | NR 25% (2)       | 33% (1)          | 0 NR             |                  |                  |
| (>300 U/L)                                                   |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated LDH                                                 | 0 NR             | 30% (3)           | 46% (12)         | NR 50% (3)       | 20% (2)          | 3% (1)           | 33% (1)          | 0 NR             |                  |                  |
| (>300 U/L)                                                   |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Elevated D-dimers                                            | 14% (21)         | 3% (3)            | 0 NR NR 50% (3) | 10% (1)          | NR 25% (2)       | 3% (1)           | 33% (1)          | 0 NR             |                  |                  |
| (>0.6 mg/L)                                                  |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Prolonged PT                                                 | 0 NR             | 0 NR NR 0         | NR NR 0          | 0 NR             | 0 NR             | 0 NR             | 0 NR             |                  |                  |                  |
| (>0.6 mg/L)                                                  |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| **Chest CT findings**                                         |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |                  |
| Normal                                                       | 0 NR             | 0                | 20% (4)          | 17% (1)          | NR 50% (5)       | 18% (6)          | 0 NR             | 33% (1)          |                  |
| Ground-glass opacities                                       | 33% (56)         | 53% (19)          | 31% (8)          | 60% (12)         | 33% (2)          | 50% (5)          | 3% (1)           | 75% (6)          | 33% (1)          |
| Bilateral infiltrates                                        | 19% (32)         | NR 42% (11)       | 30% (6)          | 0 NR             | 41% (14)         | 25% (2)          | 33% (1)          |                  |                  |
| Interstitial abnormalities                                   | 12% (21)         | NR 27% (7)        | 50% (19)         | 50% (3)          | NR 41% (14)      | 75% (6)          | 0 NR             |                  |                  |
| Consolidation with surrounding halo sign                     | 2% (2)           | NR 0              | 50% (10)         | 0 NR             | 0 NR             | 0 NR             | 0 NR             |                  |                  |
| Nodules                                                      | 0 NR             | 0                | 15% (3)          | 0 NR             | 0 NR             | 0 NR             | 0 NR             |                  |                  |
| 'White-lung'                                                 | 0 NR             | 0                | 0                | 0 NR             | 0 NR             | 0 NR             | 0 NR             |                  |                  |
| Preprint.                                                     |                  |                   |                  |                  |                  |                  |                  |                  |                  |                  |
| *Patients in this study are possibly also reported in the study by Lu et al.† |
| †These patients overlap with the study by Lu et al.‡ |
| §Specified normal values incorrect.¶ |
| Likely the wrong unit was specified.¶ |
| ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; CRP, C-reactive protein; CK, creatinine kinase; CT, computer tomography; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; NR, not reported; ns, not specified; PCT, procalcitonin; PT, prothrombin time. |
### TABLE 4. Management and Outcomes of Pediatric Patients With COVID-19

| Study     | ICU admission | Two co-existing conditions§ | O2 requirement | Drug treatment |
|-----------|---------------|------------------------------|---------------|---------------|
| Lu et al.7 | 1.8% (3)      |                              | 2% (4)        | NR            |
| Qiu et al.8| 0             |                              | 17% (6)       | Interferon-alpha |
| Cai et al.9| 9% (3)        |                              | 82% (28)      | Antibiotics   |
| Tang et al.10*| 100% (8)     |                              | 17% (1)       | Interferon-alpha |
| Xia et al 11†| 100% (8)     |                              | NR            | Ribavirin      |
| Liu et al 12| 0             |                              | 75% (6)       | Lopinavir/ribavirin |
| Wei et al13| 100% (8)      |                              | NR            | Oseltamivir    |
| Xu et al14| 100% (8)      |                              | NR            | Glucocorticoids |
| Zhang et al15*| 100% (8)     |                              | NR            | Immunoglobulin |
| Sun et al 16‡| 100% (8)     |                              | NR            | Traditional Chinese medicine |
| Xing et al 17*| 100% (8)     |                              | NR            | Interferon nebulization |
| Duration of hospitalization | NR | Mean 13 d | Median 8 d | 5.13 d |
| Deaths | 0% (0.6) | 0 | 0 | 0 | 0 |

*Preprint. †Patients of this study are possibly also reported in the study by Lu et al.7 ‡Three patients overlaps with the study by Lu et al.7 §Hydronephrosis 1, leukemia on maintenance chemotherapy 1.

NR, not reported; NP, nasopharyngeal; ns, not specified.

**Note:** The sixth potential explanation related to angiotensin-converting enzyme 2 (ACE2) receptors that are one of the main receptors for the entry of SARS- and SARS-CoV-2 into human cells.59,60 It has been suggested that adults who are taking ACE inhibitors or angiotensin receptor blockers for arterial hypertension might have a higher number of ACE2 receptors, potential making them more susceptible to SARS-CoV-2.71 However, this theory remains controversial.53 It has been postulated that children have less ACE2 receptors with lower affinity compared with adults and therefore might be less affected by SARS-CoV-2.74 ACE2 is important in regulating the immune response, especially in the lungs. In animal studies, it has been shown to protect against SARS-CoV-1 and influenza-associated lung injury.75-77 For Pseudomonal lung infections, it has been shown that a dynamic variation of pulmonary ACE2 is required for protection against lung injury.78 The interaction between ACE2 concentration and the number and affinity of ACE2 receptor is likely complex and might also be influenced by genetics.79,80

There are several hypotheses for why children infected with SARS-CoV-2 have less severe symptoms (Table 6). One potential explanation is differences in the immune system between children and adults, especially elderly adults.52 Mice models of infections with SARS-CoV show that both CD4 and CD8 T cells, as well as antibodies, play an important role in virus clearance.48-50 Children have a stronger innate immune response, higher proportion of total lymphocytes and absolute numbers of T and B cells, as well as natural killer cells, which might help to fight the virus.53 However, children are often described to have an ‘immature’ immune system and, for infections with other respiratory tract viruses, for example, respiratory syncytial virus or influenza, infants and children are at higher risk for serious disease and hospital admission.52 This suggests that protective immunity against SARS-CoV-2 differs to that against other common respiratory viruses.

Furthermore, children have a less proinflammatory cytokine response and are less prone to develop acute respiratory distress syndrome.51,52 It is therefore possible that the cytokine storm which plays an important role in the pathogenesis of severe COVID-19 in adults, is attenuated in this age group.53

The second factor that may contribute to the reduced severity of COVID-19 is the lower prevalence in children of the co-morbidities that have been associated with severe disease, such as diabetes, chronic lung, heart and kidney problems or arterial hypertension.

The third potential explanation for the milder symptoms of SARS-CoV-2 infections in children is that common circulating coronaviruses are frequent in this age group, responsible for approximately 8% of acute respiratory tract infections.56-58 Pre-existing immunity and cross-reacting antibodies to SARS-CoV-2 may play a protective role. Despite the fact that most individuals develop antibodies to common circulation coronaviruses during childhood,59-62 reinfections later in life occur,63,64 suggesting waning immunity against coronaviruses and increased susceptibility in adults.

The fourth potential explanation is the higher mucosal colonization by viruses and bacteria, which could limit colonization and growth of SARS-CoV-2 through microbial interactions and competition.65,66

A fifth hypothesis for the less severe symptoms in children is that children are usually infected by an adult, which means that they are infected by a second or third generation of the virus. For SARS- and MERS-CoV, these following generations have been described to have decreased pathogenicity.67,68

The sixth potential explanation related to angiotensin-converting enzyme 2 (ACE2) receptors that are one of the main receptors for the entry of SARS- and SARS-CoV-2 into human cells.69,70 It has been suggested that adults who are taking ACE inhibitors or angiotensin receptor blockers for arterial hypertension might have a higher number of ACE2 receptors, potential making them more susceptible to SARS-CoV-2.71 However, this theory remains controversial.73 It has been postulated that children have less ACE2 receptors with lower affinity compared with adults and therefore might be less affected by SARS-CoV-2.74 ACE2 is important in regulating the immune response, especially in the lungs. In animal studies, it has been shown to protect against SARS-CoV-1 and influenza-associated lung injury.75-77 For Pseudomonal lung infections, it has been shown that a dynamic variation of pulmonary ACE2 is required for protection against lung injury.78 The interaction between ACE2 concentration and the number and affinity of ACE2 receptor is likely complex and might also be influenced by genetics.79,80
### TABLE 5. Case Series of Pregnant Women With COVID-19 (as of March 27, 2020)

|                      | Chen et al³⁰ | Liu et al³⁵* | Li et al³¹* | Chen et al³² | Fan et al³³ | Zhu et al³⁴ | Wang et al³⁶ | Yu et al³⁸ | Zeng et al³⁷ |
|----------------------|--------------|--------------|-------------|--------------|-------------|-------------|-------------|------------|-------------|
| **Number of women**  | 9            | 13           | 16          | 4            | 2           | 9           | 1           | 7          | 3           |
| **Number of infants**| 9            | 13           | 17          | 4            | 2           | 9           | 1           | 7          | 3           |
| **Location**         | Wuhan University Hospital, China | Different hospitals in China outside Wuhan | Hubei Provincial Maternal and Child Health Center, Wuhan, China | Tongji Medical College, Wuhan, China | Renmin Hospital of Wuhan University, China | Maternal and Child Health Hospital of Hubei Province, China | Sunnou Municipal Hospital, China | Tongji Medical College, Wuhan, China | Wuhan Children's Hospital, China |
| **Time period**      | Jan 20 to Jan 31, 2020 | Dec 8 to Feb 25, 2020 | Jan 24 to Feb 29, 2020 | ns | 17 Jan to Feb 19, 2020 | Feb 2, 2020 | Jan 1 to Feb 8, 2020 | Dec to Mar 10, 2020 |
| **Gestational age**  | Median 37 + 2, Range 36 + 0 to 39 + 4 | Median 30, 25–38 | Mean 38 + 0, 33 + 6 to 40 + 4 | Median 38 + 6, Range 37 + 2 to 39 + 0 | Median 36 + 5 and 39 + 0 | Median 34 + 5, 31 + 0 to 39 + 0 | Median 39 + 1, 37 + 0 to 41 + 2 |
| **Maternal complications** | 44% (4) PROM 22% (2) Pre-eclampsia 11% (1) Gestational hypertension 11% (1) | 16% (2) PROM 8% (1) Admission to ICU for mechanical ventilation, multi-organ failure 8% (1) | 69% (1) PROM 6% (1) Pre-eclampsia 6% (1) Gestational hypertension 19% (3) Gestational diabetes 19% (3) Hypothyroidism 12% (2) Tachycardia 6% (1) | 0 | 0 | 56% (5) PROM 33% (3) Abnormal umbilical cord 22% (2) Admission to ICU for mechanical ventilation 100% (1) | 0 | 33% (1) PROM 33% (1) |
| **Fetal distress**   | 22% (7) | 23% (3) | 6% (1) | 0 | 0 | 60% (6) | 100% (1) | 0 | 67% (2) |
| **Cesarean section** | 100% (9) | 77% (10) | 88% (14) | 75% (3) | 100% (2) | 70% (7) | 100% (1) | 100% (7) | 100% (3) |
| **Preterm deliveries** (s<37 weeks) | 44% (4) | 46% (6) | 24% (6) | 0 | 0 | 60% (6) | 100% (1) | 0 | 67% (2) |
| **Specimens for RTPCR** | Amniotic fluid, cord blood, breast milk, neonatal throat swabs in 6, all negative | NR | Neonatal throat swabs in 3, all negative | Neonatal throat swab in 3, all negative | Vaginal swabs, amniotic fluid, placenta tissues, maternal serum, cord blood, breast milk, neonatal nasopharyngeal swabs in 3, all negative | Pharyngeal swabs in 9, all negative | Amniotic fluid, placenta tissues, cord blood, neonatal throat swab, gastric juice and stool negative | Neonatal throat swab in 3, 1 positive on day 2 | Neonatal nasopharyngeal and anal swab positive in 3, positive on day 2 and 4 |
| **Fetal complications** | Low birth weight 22% (2) | NR | 18% (3) | 0 | 0 | 20% (2) | NR | 0 | 67% (2) |
|                       | Rash 0 | NR | 0 | 50% (2) | 0 | 0 | 0 | 0 | 33% (1) |
|                       | Asphyxia 0 | 0 | 0 | 25% (1) | 100% (2) | 60% (6) | 0 | 0 | 100% (3) |
|                       | Resp distress or pneumonia 0 | 0 | 0 | 25% (1) | NR | NR | 0 | 0 | NR |
|                       | O₂ requirement 0 | 0 | 0 | 25% (1) | NR | NR | 0 | 0 | 33% (1) |
|                       | Mechanical ventilation 0 | 0 | 0 | (noninvasive) | NR | NR | 0 | 0 | 0 |
|                       | DIC 0 | 0 | 0 | 0 | 0 | 20% (2) | 0 | 0 | 0 |
|                       | Death 0 | 0 | 8% (1) | 0 | 0 | 10% (1) | 0 | 0 | 0 |

*Preprint.
DIC, disseminated intravascular coagulation; ICU, intensive care unit; ns, not specified; PROM, premature rupture of membranes; RTPCR, real-time polymerase chain reaction.
The majority of children included in this review had a reported adult or family contact infected with SARS-CoV-2. It is still uncertain whether asymptomatic children transmit the virus and therefore the role of children as a reservoir for SARS-CoV-2 and for transmission of the virus remains unclear. However, it has been reported that even asymptomatic children can have high viral loads of SARS-CoV-2 and can excrete the virus in stool for a prolonged period. An unpublished data suggests that the clinical features of COVID-19 in children varies in different countries. While in Asian countries and Europe children have been reported to have milder disease, recent data from the US reports that, by March 27, 2020, at least 35 children needed mechanical ventilation and one infant died. It has been suggested that this could be due to differences in Bacillus-Calmette-Guérin vaccination policies, as this vaccine’s off-target immunomodulatory effects might alter the immune response to SARS-CoV-2.

The influence of SARS-CoV-2 infection on pregnancy and neonatal outcomes is also unclear. SARS- and MERS-CoV cause more severe disease in pregnant women compared with non-pregnant women. To date, this has not been reported for SARS-CoV-2. Nevertheless, 3% of pregnant women infected were reported adult or family contact infected with SARS-CoV-2. It is unclear if some of the reported maternal and neonatal complications are due to the virus or were iatrogenic (eg, decision for a Cesarean leading to preterm delivery and neonatal respiratory problems). Nevertheless, 1 case-control study reported that the number of pre-term deliveries were higher in SARS-CoV-2-infected women compared with non-infected women. Furthermore, fetal distress and preterm ruptures of membranes have been reported in SARS-CoV-2 infected women. The one healthy neonate and 3 neonates who developed pneumonia and tested positive for SARS-CoV-2 on day 2 of life and the three neonates who had Immunoglobulin M against SARS-CoV-2 at birth, despite strict infection control and prevention procedures during delivery and separation of mother and infants, suggests the possibility of vertical transmission of SARS-CoV-2.

There is no evidence for the presence of SARS-CoV-2 in genital fluids. However, the virus can be isolated from feces, meaning it is possible that vaginal delivery poses a greater risk for infection of the infant. Most of the women delivered by Cesarean section as recommended in Chinese guidelines. It is still unclear whether the virus can be transmitted through breast milk. However, close contact during breast-feeding, might risk droplet or contact transmission from the mother to the neonate.

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