REVIEW ARTICLE

Obstetrics

Delivery in pregnant women infected with SARS-CoV-2: A fast review

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Abstract

Background: Few case reports and clinical series exist on pregnant women infected with SARS-CoV-2 who delivered.

Objective: To review the available information on mode of delivery, vertical/peripartum transmission, and neonatal outcome in pregnant women infected with SARS-CoV-2.

Search strategy: Combination of the following key words: COVID-19, SARS-CoV-2, and pregnancy in Embase and PubMed databases.

Selection criteria: Papers reporting cases of women infected with SARS-CoV-2 who delivered.

Data collection and analysis: The following was extracted: author; country; number of women; study design; gestational age at delivery; selected clinical maternal data; mode of delivery; selected neonatal outcomes.

Main results: In the 13 studies included, vaginal delivery was reported in 6 cases (9.4%; 95% CI, 3.5–19.3). Indication for cesarean delivery was worsening of maternal conditions in 31 cases (48.4%; 95% CI, 35.8–61.3). Two newborns testing positive for SARS-CoV-2 by real-time RT-PCR assay were reported. In three neonates, SARS-CoV-2 IgG and IgM levels were elevated but the RT-PCR test was negative.

Conclusions: The rate of vertical or peripartum transmission of SARS-CoV-2 is low, if any, for cesarean delivery; no data are available for vaginal delivery. Low frequency of spontaneous preterm birth and general favorable immediate neonatal outcome are reassuring.

KEYWORDS
Cesarean delivery; COVID-19; Neonatal outcome; Pregnancy; Review; SARS-CoV-2; Vaginal delivery; Vertical transmission

1 | INTRODUCTION

Midwives and obstetricians face a new challenge posed by the recent outbreak of COVID-19. In this early phase of the epidemic, few data are available on the effect of COVID-19 on pregnant women. The risk of intrauterine and peripartum transmission of the virus to the fetus is also largely unknown.

Until now, most of the guidelines are based on previous experience with other highly pathogenic coronaviruses, namely severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).1–3

A recent consensus stated that there is no clear evidence on timing of optimal delivery, safety of vaginal delivery, or whether cesarean delivery prevents vertical transmission at the time of delivery. Therefore, mode and timing of delivery should be individualized based on obstetric indications and maternal–fetal status.2

During recent weeks, some case reports and clinical series have been published on mode of delivery, immediate neonatal outcome, risk of infection of the newborn, and breastfeeding in pregnant women infected with COVID-19.4–6 These series, although of few cases, may offer initial information to direct clinical practice.
The aim of the present article was to review the available information with special focus on mode of delivery, vertical/peripartum transmission, and immediate neonatal outcome of pregnant women infected with SARS-CoV-2.

2 | MATERIALS AND METHODS

We searched PubMed (National Library of Medicine, Washington, DC) and Embase (Elsevier) databases from January 1 up to March 31, 2020, using a combination of the following key words: COVID-19, SARS-CoV-2, and pregnancy. We also reviewed the reference lists of retrieved articles to search for other pertinent studies. Two authors (FP and RB) reviewed the papers and independently selected the articles eligible for systematic review. Studies were selected if they met the following criteria: clinical studies, studies reporting original data, studies reporting SARS-CoV-2 infected women who delivered.

2.1 | Data extraction

A PICOS (Patient, Intervention, Comparator, Outcome, Study) design structure was used to develop the study questions and the inclusion/exclusion criteria. The question was: "What is the mode of delivery and the obstetric and immediate neonatal outcomes in SARS-CoV-2 infected pregnant women?" (Table 1).

For each study, the following information was extracted: first author’s last name; year; country; number of women who delivered; study design; gestational age at delivery; selected clinical maternal data (maternal age, comorbidity, diagnosis of pneumonia, treatment); mode of delivery; selected neonatal outcomes (birthweight, 5-minute Apgar score, admission to neonatal intensive care unit [NICU] neonatal diseases; SARS-CoV-2 positivity).

2.2 | Data synthesis

The primary outcomes assessed were frequency of preterm birth (<37 weeks of gestation), vaginal delivery, Apgar score at 5 minutes <7, and newborn infection. For each study with binary outcomes, we calculated the 95% confidence intervals (CIs) of the estimated proportion.

3 | RESULTS

The initial search retrieved 41 abstracts from PubMed and 23 from Embase. After exclusion of unrelated abstracts of review papers, guidelines, and commentaries, 17 papers were selected for extensive review. Two studies reported data only on maternal outcome.7,8

Another paper was published without peer review.9 One study was published in Chinese.10 Therefore, a total of 13 studies were included.4–6,11–20 Table 2 presents their main methodological characteristics. Six studies were case reports and seven were retrospective clinical series.

A total of 64 pregnant women who delivered were reported in the studies (seven women admitted to hospital but who did not deliver at the time of publication were also reported).

Table 3 presents the maternal characteristics and clinical conditions. Pneumonia was present in 49/61 (80.3%; 95% CI, 68.2–89.4) cases for which the information was available. For cases with available information, oxygen support was needed by 29/35 (82.9%; 95% CI, 66.4–93.4) and 2/31 (6.5%; 95% CI, 0.8–2.4) were admitted to a critical care unit (CCU).

Table 4 presents mode of delivery data. Vaginal delivery was reported in six (9.4%) cases (95% CI, 3.5–19.3). Indication for cesarean delivery was worsening of maternal conditions in 31 women (48.4%; 95% CI, 35.8–61.3); cases reported by Liu et al.14 and Zeng et al.19 are not included since the indication for cesarean section was unclear in the text.

Preterm birth (<37 weeks of gestation) was observed in 19 cases among the 48 for which the information on gestational age at delivery was available (39.6%; 95% CI, 25.8–54.7). In only two cases, reported by Zhu et al.,5 delivery was due to spontaneous preterm labor (1 twin pregnancy and 1 premature rupture of membranes).

Table 5 presents data on the immediate neonatal outcome and the frequency of SARS-CoV-2 positivity in the newborns. Low birthweight (<2500 g) was observed in 10 newborns (10/37 [27.0%] for which information was available; 95% CI, 13.8–44.1). In all cases, 5-minute Apgar score was greater than 7. One neonatal death due to disseminated intravascular coagulation (DIC) syndrome was reported. The death occurred in a singleton male neonate born by cesarean delivery at 34 + 5 weeks of gestation and weighing 2200 g. The cause of death was multiple organ failure and DIC.

Considering respiratory disease in newborns, one case of pneumonia, one low-grade fever and haziness in both lung fields, one high-density nodular shadow under the pleura of the right lung, six shortness of breath, and two cases of neonatal respiratory distress syndrome were reported.

Wang et al.15 reported a case of neonatal COVID-19 infection with pharyngeal swabs testing positive by rRT-PCR assay 36 hours after cesarean delivery; whether the case is a vertical transmission from mother to child remains to be confirmed.

Dong et al.11 reported a case of a neonate delivered by cesarean in which SARS-CoV-2 IgG and IgM levels were elevated at 2 hours old.

### Table 1: PICOS criteria for inclusion and exclusion of studies.

| Parameter | Inclusion criteria | Data extraction |
|-----------|--------------------|-----------------|
| Patient   | Women treated for SARS-CoV-2 infection | Location, age, clinical characteristics |
| Intervention | Delivery | Mode of delivery |
| Comparator | None | |
| Outcome   | Neonatal outcome | Birth weight, Apgar score, neonatal disease, NICU admission, SARS-CoV-2 positivity |
| Study     | Case reports/observational studies | Type of study design |
Results from five RT-PCR tests on nasopharyngeal swabs taken from 2 hours to 16 days old were negative. Two other newborns delivered by cesarean with elevated IgM antibodies to SARS-CoV-2 virus, but negative throat swab result by RT-PCR have also been reported.\textsuperscript{19} Finally, Yu et al.\textsuperscript{17} reported the case of a RT-PCR positive test in a newborn 36 hours after cesarean birth.

### TABLE 2  
| Authors, year, country | Type of study | Aim | Assessment | Cases (No.) |
|------------------------|---------------|-----|------------|-------------|
| Chen et al., 2020, China\textsuperscript{4} | Retrospective clinical series | IVT | AF, CB, ITS, M | 9 |
| Chen et al., 2020, China\textsuperscript{20} | Retrospective clinical series | -- | -- | 5 |
| Dong et al., 2020, China\textsuperscript{11} | Case report | IVT | IGM-IGG, INPS, M, VS | 1 |
| Fan et al., 2020, China\textsuperscript{12} | Case report | IVT | AF, CB, IGG, INPS, M, PT, VS | 2 |
| Lee et al., 2020, Korea\textsuperscript{18} | Case report | IVT | AF, CB, INPS, PT | 1 |
| Li et al., 2020, China\textsuperscript{13} | Case report | IVT | AF, CB, IB, IOPS, IS, IU, M, PT | 1 |
| Liu et al., 2020, China\textsuperscript{14} | Retrospective clinical series | IVT | Nr | 10/+3\textsuperscript{a} |
| Liu et al., 2020, China\textsuperscript{15} | Retrospective clinical series | -- | -- | 11/+4\textsuperscript{a} |
| Wang et al., 2020, China\textsuperscript{16} | Case report | IVT | CB, IOPS, M, PT | 1 |
| Wang et al., 2020, China\textsuperscript{5} | Case report | IVT | AF, CB, IGG, IS, ITS, PT | 1 |
| Yu et al., 2020, China\textsuperscript{17} | Case report | IVT | IB, IGM-IGG, ITS | 7 |
| Zeng et al., 2020, China\textsuperscript{19} | Retrospective clinical series | IVT | IOPS | 6 |
| Zhu et al., 2020, China\textsuperscript{6} | Retrospective clinical series | IVT | -- | Nr |

Abbreviations: IVT, intrauterine vertical transmission; AF, amniotic fluid; CB, cord blood; ITS, infant throat swab; M, milk; INPS, infant nasopharyngeal swab; PT, placenta tissues; VS, vaginal swab; IOPS, infant oropharyngeal swab; IB, infant blood; IS, infant stool; IU, infant urine; IGI, infant gastric juice; Nr, not reported.

\textsuperscript{a}Patients with pregnancy in progress.

\textsuperscript{b}Nine mothers and 10 neonates.

4  | **DISCUSSION**

The results of this fast review of the available data on mode of delivery and immediate neonatal outcome in pregnant women infected with SARS-CoV-2 suggest that the risk of vertical or peripartum transmission of the virus to the newborn is limited, if any.

### TABLE 3  
| Authors | Maternal age, y | Comorbidities | Antiviral therapy | Pneumonia | Oxygen support | CCU admission |
|---------|-----------------|---------------|------------------|-----------|---------------|--------------|
| Chen et al.\textsuperscript{4} | 26–40 | 2 GH/9 | 6/9 | 9/9 | 9/9 | 0/9/9 |
| Chen et al.\textsuperscript{20} | 25–31 | 2GD, 1GH/5 | 5\textsuperscript{b}/5 | 5\textsuperscript{b}/5 | 0/5 | Nr |
| Dong et al.\textsuperscript{11} | 29 | 0/1 | 1/1 | 1\textsuperscript{b}/1 | 1/1 | Nr |
| Fan et al.\textsuperscript{12} | 29, 34 | 0/2 | 2/2 | 2/2 | Nr | Nr |
| Lee et al.\textsuperscript{18} | 28 | 0/1 | 0/1 | 1/1 | 0/1 | 0/1 |
| Li et al.\textsuperscript{13} | 30 | 0/1 | 1/1 | 1\textsuperscript{b}/1 | Nr | Nr |
| Liu et al.\textsuperscript{14} | 22–36 | 0/13 | Nr | 1/13 | Nr | 1/13 |
| Liu et al.\textsuperscript{15} | 23–40 (mean, SD, 32 +– 5) | 1 GD, 1VR/11 | 11\textsuperscript{c}/11 | 11/11 | 11/11 | Nr |
| Wang et al.\textsuperscript{16} | 34 | 0/1 | 1\textsuperscript{b}/1 | 1\textsuperscript{b}/1 | Nr | Nr |
| Wang et al.\textsuperscript{6} | 28 | 0/1 | 1/1 | 1/1 | 1/1 | 1/1 |
| Yu et al.\textsuperscript{17} | 29–34 (mean 32) | 2\textsuperscript{c}/7 | 7/7 | 7/7 | 7/7 | 0/7 |
| Zeng et al.\textsuperscript{19} | Nr | Nr | Nr | Nr | Nr | Nr |
| Zhu et al.\textsuperscript{5} | 25–35 (mean 30) | 0/9 | 3\textsuperscript{d}/9 | 9/9 | Nr | Nr |

Abbreviations: CCU, critical care unit; GH, gestational hypertension; GD, gestational diabetes; VR, mitral and tricuspid valve replacement; Nr, not reported.

\textsuperscript{a}No mechanical ventilation.

\textsuperscript{b}Computed tomography scan with typical images of viral pneumonia.

\textsuperscript{c}After delivery.

\textsuperscript{d}1 hypothyroidism, 1 polycystic ovary syndrome.
We identified two cases of newborn infection, confirmed positive by rRT-PCR assay, out of 64 reported cases. To our knowledge, another case of a newborn infected with SARS-CoV-2 (not included in this review) has been reported by the National Health Commission of the People’s Republic of China, in which the diagnosis was made at 17 days of life. In all cases, postpartum neonatal infection acquired through an infected contact was impossible to exclude.

IgM antibodies to SARS-CoV-2 were found in three cases. Caution in interpreting these findings has been suggested, including the possibility that IgM positivity could represent a laboratory artifact. These findings suggest that transmission in utero is possible. However, SARS-CoV-2 was not found in amniotic fluid or cord blood and this finding is based on very few cases.

Data on virus transmission are based substantially on women who delivered by cesarean. This aspect is relevant. In fact, vertical transmission of infection usually occurs during intraterine life via the placenta, or during delivery via ingestion or aspiration of cervicovaginal secretions, and in the postpartum period via breastfeeding. The risk of ingestion or aspiration of cervicovaginal secretions or contact with perineal infected tissue is higher with vaginal delivery. In this review we identified 19 women who delivered preterm, although spontaneous vaginal preterm birth was reported in only two cases. Therefore, there is reassuring evidence that COVID-19 infection of the mother did not markedly increase the risk of spontaneous preterm birth.

Regarding maternal conditions, we note that COVID-19 infection in pregnancy seems to be less severe than other coronavirus infections such as SARS or MERS. We identified two women who needed intensive care. The proportion of women requiring CCU admission seems to be similar to that reported in the general population affected by COVID-19. However, worsening of maternal condition was the cause of emergency cesarean delivery in about 45% of women. Diabetes and hypertension are considered determinants of worse prognosis in cases of infection. However, we were unable to analyze this in detail; the few cases reported with diabetes did not need CCU admission.

Finally, newborn outcome deserves some consideration. In all reported cases the 5-minute Apgar score was greater than 7 and generally 9 or 10 (data not shown in table). Furthermore, the frequency of NICU admission was low and due to medically induced preterm birth. However, one neonatal death and several cases of respiratory symptoms or diseases were reported by pharyngeal or nasopharyngeal swabs, although these tested negative for SARS-CoV-2 by rRT-PCR assay, except in one case.

Very few reported cases provided information on the risk of newborn infection during breastfeeding. Guidelines suggest allowing breastfeeding for infected women who wear a mask. Preliminary data suggest that the virus is not detectable in milk.

In conclusion, this review of the literature suggests that the rate of vertical or peripartum transmission of SARS-CoV-2 is low, if any, for cesarean delivery. Crucially, no data were available for vaginal delivery. Likewise, breastfeeding was not generally reported; thus, the risk

| Authors          | Gestational age, w | Cesarean for maternal COVID-19 infection | Cesarean for obstetric indication | Vaginal delivery | Preterm birth |
|------------------|--------------------|----------------------------------------|----------------------------------|------------------|---------------|
| Chen et al.       | 36–39              | 9/11                                   | 7/11                             | —                | 4/9           |
| Chen et al.      | 38–40              | —                                      | 2/5                              | 3/5              | 0/5           |
| Dong et al.      | 37                 | 1/1                                    | —                                | —                | 0/1           |
| Fan et al.       | 36, 37             | 2/2                                    | —                                | —                | 1/2           |
| Lee et al.       | 37                 | —                                      | 1/1                              | —                | 0/1           |
| Li et al.        | 35                 | —                                      | 1/1                              | —                | 1/1           |
| Liu et al.       | Nr                 | 5/10                                   | 5/10                             | —                | 6/10          |
| Liu et al.       | Nr                 | 9/11                                   | 1/11                             | 1/11             | Nr            |
| Wang et al.      | 40                 | 1/1                                    | —                                | —                | 0/1           |
| Wang et al.      | 30                 | 1/1                                    | —                                | —                | 1/1           |
| Yu et al.        | 37–41              | 7/7                                    | —                                | —                | 0/7           |
| Zeng et al.      | Nr                 | 6/6                                    | —                                | —                | Nr            |
| Zhu et al.       | 31–39              | 1/9                                    | 6/9                              | 2/9              | 6 (2 twins)/10|

Abbreviation: Nr, not reported.

1In 7 cases, cesarean delivery for maternal COVID-19 infection and obstetric indication: 1 history of cesarean delivery, 1 pre-eclampsia, 2 fetal distress, 1 history of stillbirth, 2 premature rupture of membranes.
2Also fetal distress.
3No obstetric indication.
43 fetal distress, 1 PROM, 1 stillbirth.
51 premature rupture of membranes, 4 fetal distress, 1 cholecystitis and fever.
62 premature rupture of membranes, 3 fetal distress, 2 twins.
7Unclear in the text.

TABLE 4 Mode of delivery and preterm birth in pregnant women in the included studies.
of transmission during breastfeeding is unknown. Low frequency of spontaneous preterm birth and generally favorable immediate neonatal outcomes are reassuring.

**AUTHOR CONTRIBUTIONS**

FP and EF designed the study. FP and RB reviewed the identified papers. FP and RB drafted the manuscript. PM, SG, AF and EF revised the manuscript. All authors reviewed and approved the final manuscript.

**CONFLICTS OF INTEREST**

The authors have no conflicts of interest.

**REFERENCES**

1. Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus disease 2019 (COVID-19) and pregnancy: What obstetricians need to know. Am J Obstet Gynecol. 2020[Epub ahead of print].
2. Chen D, Yang H, Cao Y, et al. Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection. Int J Gynaecol Obstet. 2020[Epub ahead of print].
3. Schwartz DA. COVID-19, SARS-CoV-2 and pregnancy: Does the past predict the present? ContagionLive. 2020. https://www.contagionlive.com/news/covid19-sarscov2-and-pregnancy-does-the-past-predict-the-present. Accessed March 30, 2020.
4. Chen H, Guo J, Wang C, et al. Clinical characteristics and intratumerine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. Lancet. 2020;395:809–815.
5. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Transl Pediatr. 2020;9:51–60.
6. Wang X, Zhou Z, Zhang J, Zhu F, Tang Y, Shen X. A case of 2019 novel coronavirus in a pregnant woman with preterm delivery. Clin Infect Dis. 2020[Epub ahead of print].
7. Liu H, Liu F, Li J, Zhang T, Wang D, Lan W. Clinical and CT imaging features of the COVID-19 pneumonia: Focus on pregnant women and children. J Infect. 2020[Epub ahead of print].
8. Wen R, Sun Y, Xing QS. A patient with SARS-CoV-2 infection during pregnancy in Qingdao, China. J Microbiol Immunol Infect. 2020 [Epub ahead of print].

9. Liu W, Wang Q, Zhang Q, et al. Coronavirus disease 2019 (COVID-19) during pregnancy: A case series. Preprints 2020, 2020020373. https://www.preprints.org/manuscript/202002.0373/v1. Accessed March 28, 2020.

10. Zhang L, Jiang Y, Wei M, et al. Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province [in Chinese]. Zhonghua Fu Chan Ke Za Zhi. 2020;55:E009. [Epub ahead of print].

11. Dong L, Tian J, He S, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. JAMA. 2020 [Epub ahead of print].

12. Fan C, Lei D, Fang C, et al. Perinatal transmission of COVID-19 associated SARS-CoV-2: Should we worry? Clin Infect Dis. 2020 [Epub ahead of print].

13. Li Y, Zhao R, Zheng S, et al. Lack of vertical transmission of severe acute respiratory syndrome coronavirus 2, China. Emerg Infect Dis. 2020. [Epub ahead of print].

14. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. J Infect. 2020. [Epub ahead of print].

15. Liu D, Li L, Wu X, et al. Pregnancy and perinatal transmission of women with coronavirus disease (COVID-19) pneumonia: A preliminary analysis. AJR Am J Roentgenol. 2020 [Epub ahead of print].

16. Wang S, Guo L, Chen L, et al. A case report of neonatal COVID-19 infection in China. Clin Infect Dis. 2020 [Epub ahead of print].

17. Yu N, Li W, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: A retrospective, single-centre, descriptive study. Lancet Infect Dis. 2020 [Epub ahead of print].

18. Lee DH, Lee J, Kim E, Woo K, Park HY, An J. Emergency cesarean section on severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) confirmed patient. Korean J Anesthesiol. 2020 [Epub ahead of print].

19. Zeng H, Xu C, Fan J, et al. Antibodies in infants born to mothers with COVID-19 pneumonia. JAMA. 2020 [Epub ahead of print].

20. Chen S, Liao E, Shao Y. Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia. J Med Virol. 2020 [Epub ahead of print].

21. Schwartz DA. An analysis of 38 pregnant women with 2 COVID-19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: Maternal coronavirus infections and pregnancy outcomes. Arch Pathol Lab Med. 2020 [Epub ahead of print].

22. National Health Commission of the People’s Republic of China. Transcript of Press Conference on Feb 7, 2020. http://www.nhc.gov.cn/xcs/s3574/202002/5bc099fc9144445297e8776838e57d8c.shtml. Accessed February 7, 2020.

23. Kimberlin DW, Stagno S. Can SARS-CoV-2 infection be acquired in utero?: More definitive evidence is needed. JAMA. 2020 [Epub ahead of print].

24. Silasi M, Cardenas I, Racicot K, Kwon JY, Aldo P, Mor G. Viral infections during pregnancy. Am J Reprod Immunol. 2015;73:199–213.

25. Guan W-J, Ni Z-J, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020 [Epub ahead of print].

26. Center for Disease Control Coronavirus Disease (COVID-19) and Breastfeeding. https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/maternal-or-infant-illnesses/covid-19-and-breastfeeding.html. Accessed April 6, 2020.