A systematic review of pregnant women with COVID-19 and their neonates

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Received: 11 July 2020 / Accepted: 27 March 2021 / Published online: 2 April 2021
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Abstract

Background In December 2019, a novel coronavirus disease (COVID-19) emerged in Wuhan, China, with an incredible contagion rate. However, the vertical transmission of COVID-19 is uncertain.

Objectives This is a systematic review of published studies concerning pregnant women with confirmed COVID-19 and their neonates.

Search strategy We carried out a systematic search in multiple databases, including PubMed, Web of Science, Google Scholar, Scopus, and WHO COVID-19 database using the following keywords: (Coronavirus) OR (novel coronavirus) OR (COVID-19) OR (COVID19) OR (COVID 19) OR (SARS-CoV2) OR (2019-nCoV)) and ((pregnancy) OR (pregnant) OR (vertical transmission) OR (neonate) OR (newborn) OR (placenta) OR (fetus) OR (Fetal)). The search took place in April 2020.

Selection criteria Original articles published in English were eligible if they included pregnant patients infected with COVID-19 and their newborns.

Data collection and analyses The outcomes of interest consisted of clinical manifestations of COVID-19 in pregnant patients with COVID-19 and also the effect of COVID-19 on neonatal and pregnancy outcomes.

Main results 37 articles involving 364 pregnant women with COVID-19 and 302 neonates were included. The vast majority of pregnant patients were in their third trimester of pregnancy, and only 45 cases were in the first or second trimester (12.4%). Most mothers described mild to moderate manifestations of COVID-19. Of 364 pregnant women, 25 were asymptomatic at the time of admission. The most common symptoms were fever (62.4%) and cough (45.3%). Two maternal deaths occurred. Some pregnant patients (12.1%) had a negative SARS-CoV-2 test but displayed clinical manifestations and abnormalities in computed tomography (CT) scan related to COVID-19. Twenty-two (6.0%) pregnant patients developed severe pneumonia. Two maternal deaths occurred from severe pneumonia and multiple organ dysfunction. Studies included a total of 302 neonates from mothers with COVID-19. Of the studies that provided data on the timing of birth, there were 65 (23.6%) preterm neonates. One baby was born dead from a mother who also died from COVID-19. Of the babies born alive from mothers with COVID-19, five newborns faced critical conditions, and two later died. A total of 219 neonates underwent nasopharyngeal specimen collection for SARS-CoV-2, of which 11 tested positive (5%). Seventeen studies examined samples of the placenta, breast milk, umbilical cord, and amniotic fluid, and all tested negative except one amniotic fluid sample.

Conclusions A systematic review of published studies confirm that the course of COVID-19 in pregnant women resembles that of other populations. However, there is not sufficient evidence to establish an idea that COVID-19 would not complicate pregnancy.

Keywords COVID-19 · Immunity · Neonates · Pregnancy · SARS-CoV2 · Vertical transmission
Background

The World Health Organization (WHO) announced the novel coronavirus disease (COVID-19) as a Pandemic on March 7, 2020, when the number of confirmed cases just exceeded 100,000 [1]. As of April 21, 2020, COVID-19 has reached all over the world, with about 180,000 deaths of a total of more than 2 million confirmed cases. Moreover, it seems there is an underestimation in the mortality rate of this infectious disease. Studies estimate the real mortality rate to be about 6% in China, rising to about 15% in other countries [2]. Therefore, COVID-19 is, in general, a life-threatening condition.

COVID-19 can affect multiple organs and systems [3–11], although it mainly involves the respiratory system, where its involvement can cause a wide range of symptoms from a common cold to severe respiratory distress [12–15]. In particular, the disease is more severe and deadly in older age groups and people who have pre-existing comorbidity. The immunopathogenesis of the disease is not clear [16–21]. However, as for other infectious conditions, immune dysregulation might increase the risk of severe illness and death from COVID-19 [21–27].

Pregnancy is a particular condition that can have significant effects on the biological systems of a woman’s body. Notably, pregnant women acquire changes so that their immune system will be able to tolerate pregnancy. These changes mostly place the maternal immune system under a down-regulated condition. As a result, pregnant women are generally considered vulnerable to infectious diseases.

Whereas its transmission mainly occurs through human-to-human contact, the novel coronavirus has shown its potential to transmit via multiple transmission routes [28] and affect both children and adults [13, 29]. It, however, remained unclear whether or not this potentially fatal virus can vertically be transmitted and what are the possible effects of the disease on the pregnancy outcomes.

Methods

The present systematic review was developed according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement [14]. Before the study begins, the authors developed the study protocol that is available on request.

Literature search

We carried out a systematic search in multiple databases, including PubMed, Web of Science, Google Scholar, Scopus, and WHO COVID-19 database using the following keywords: (Coronavirus) OR (novel coronavirus) OR (COVID-19) OR (COVID19) OR (COVID 19) OR (SARS-CoV2) OR (2019-nCoV)) and ((pregnancy) OR (pregnant) OR (vertical transmission) OR (neonate) OR (newborn) OR (placenta) OR (fetus) OR (Fetal)). The search took place in April 2020 (Fig. 1).

Selection criteria

We sought studies that investigated the potential effect of COVID-19 on pregnancy and neonatal health. Original articles published in English were eligible if they included pregnant patients infected with COVID-19 and their newborns. The outcomes of interest consisted of clinical manifestations of COVID-19 in pregnant patients with COVID-19 and also, the effect of COVID-19 on neonatal and pregnancy outcomes.

Data extraction

For pregnant women infected with COVID-19, we extracted the following data: article title, author, study type, country, number of pregnant women with COVID-19, clinical manifestations of disease in pregnant women, the trimester of pregnancy, diagnostic technique, potential complications related to COVID-19, delivery, and the maternal outcome(s) of COVID-19. For neonates born from mothers with COVID-19, data on the article title, author, study type, country, number of neonates, neonatal maturity, clinical presentation, neonatal complications, a diagnostic test for COVID-19, Apgar score, and neonatal outcome were extracted. Finally, for pregnancy outcomes, we collected data on the article title, author, study type, country, placental test for viral nucleic acid, and pregnancy complications.

Results

Literature search

The systematic search yielded a total of 1068 search results, of which 785 discrete records remained for screening after removing duplicates. During title and abstract screening, we selected 48 articles for detailed review. In the detailed review process, we excluded thirteen articles with the following reasons for exclusion: seven articles not provided data on pregnant patients or neonatal outcomes [28, 30–35], three studies lacked data on neonates or vertical transmission [36–38], one study reported a 17-day neonate who had exposure to parents complaining of fever and cough [39], one study was not original research [40], and the full-text was not available for one article [41].
Also, we carried out an additional search through reviewing reference lists of 35 included articles from systematic search and related review articles and found two additional articles [42, 43]. Finally, a total number of 37 studies, including case reports and case series, were eligible to be included in this systematic review [42–76]. Tables 1, 2, 3 provide an overview of the characteristics of the included studies. Below is a narrative synthesis of studies that included pregnant women with confirmed COVID-19 and their neonates.

Clinical presentation of COVID-2019 in pregnant women

Of 37 studies, two provided no data on clinical symptoms of pregnant patients [43, 44]. A total of 364 pregnant women was, thus, included in the data synthesis of clinical manifestations of COVID-19 in pregnant women.

Of 364 pregnant women, 25 were asymptomatic at the time of admission. The most common symptoms were fever (62.4%) and cough (45.3%). The other common symptoms
| Article title                                                                 | Author          | Study type | Country | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (= N) | Diagnosing technique                                    | Complications due to viral infection | Delivery | The maternal outcome(s) of disease in pregnant patients |
|------------------------------------------------------------------------------|-----------------|------------|---------|--------------------|--------------------------------------------------------|---------------------------------------|----------------------------------------|--------------------------------------|----------|----------------------------------------------------------|
| Pregnant women with new coronavirus infection: a clinical characteristics and placental pathological analysis of three cases | Chen et al.     | Case study | China   | 3                  | Fever (= 3)                                            | Third trimester (= 3)                  | 2 cases; positive nucleic acid test through throat swab, 1 case: clinical confirmation | None                                 | Cesarean section (= 3) | 2 patients cured and discharged; one underwent isolation treatment |
| Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia    | Zhu et al.      | Case study | China   | 9                  | Fever (= 7) Cough (= 4) Cholecystitis (= 1) Diarrhea (= 1) | Third trimester*                      | Chest CT scan and throat swab nucleic acid testing** | None                                 | Cesarean section (= 7) | Vaginal delivery (= 2) Cured and discharged |
| Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records | Chen et al.     | Case study | China   | 9                  | Fever (= 7) Cough (= 4) Myalgia (= 3) Sore throat (= 2) Malaise (= 2) | Third trimester CT scan of lung and throat swab nucleic acid testing | None | Cesarean section (= 9) | Cured and discharged |
| Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province | Zhang et al.    | Case–control | China   | 16 (45 Controls) | 15 moderate case and 1 severe case of pneumonia | Third trimester Clinical diagnosis and throat swab nucleic acid detection | Severe case (= 1) | Cesarean section (= 16) | Cured and discharged |
| Article title                                                                 | Author         | Study type | Country     | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (\(=N\)) | Diagnosing technique                  | Complications due to viral infection | Delivery               | The maternal outcome(s) of disease in pregnant patients |
|------------------------------------------------------------------------------|----------------|------------|-------------|--------------------|--------------------------------------------------------|-------------------------------------------|--------------------------------------|----------------------------------|------------------------|-------------------------------------------------------------|
| Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy | Liu et al.     | Case Study | China       | 13                 | Fever (\(=10\)) Fatigue (\(=3\)) Cough (\(=2\)) Sore throat (\(=1\)) | Third trimester (\(=11\)), Less than 28 weeks GA (\(=2\)) | Clinical symptoms and throat swab nucleic acid detection | Severe pneumonia and intubation (\(=1\)) | Cesarean section (\(=10\)) | Still pregnant (\(=3\)) | Cured and discharged |
| Lack of vertical transmission of severe acute respiratory syndrome Coronavirus 2, China | Li et al.      | Case Report | China       | 1                  | Cough and temperature of 37.2 °C | Third trimester | Clinical symptoms and throat swab nucleic acid detection | None | Cesarean section | Cured and discharged |
| A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery | Wang et al.    | Case Report | China       | 1                  | Fever | Third trimester | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None | Cesarean section | Cured and discharged |
| A case report of neonatal COVID-19 infection in China                        | Wang et al.    | Case report | China       | 1                  | Fever | Third trimester | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None | Cesarean section | Cured and discharged |
| Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry?  | Fan et al.     | Case report | China       | 2                  | Fever (\(=2\)) Nasal congestion (\(=2\)) Chill (\(=1\)) Sore throat (\(=1\)) Abdominal rush (\(=1\)) | Third trimester | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None | Cesarean section (\(=2\)) | One case still in the hospital One case cured and discharged |
Table 1 (continued)

| Article title                                                                 | Author          | Study type | Country  | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (=N) | Diagnosing technique                                      | Complications due to viral infection | Delivery            | The maternal outcome(s) of disease in pregnant patients |
|-----------------------------------------------------------------------------|-----------------|------------|----------|--------------------|-------------------------------------------------------|----------------------------------------|------------------------------------------------------------|--------------------------------------|---------------------|----------------------------------------------------------|
| Clinical analysis of pregnant women with 2019 Novel Coronavirus Pneumonia   | Chen et al.     | Case series| China    | 5                  | Fever (=5) Coryza (=1) Sputum (=1) Cough (=1)         | Third trimester (=5)                   | Clinical symptoms and Chest CT scan and SARS-CoV-2 quantitative RT-PCR | None                   | Cesarean section (=2) Vaginal delivery (=3) | No death was reported |
| Possible vertical transmission of SARS-CoV-2 From an infected mother to her newborn | Dong et al.     | Case report| China    | 1                  | Fever and Nasal congestion                           | Third trimester                        | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None                   | Cesarean section                                      | Cured and discharged |
| Lung ultrasound and computed tomographic findings in a pregnant woman with COVID-19 | Kalafat et al. | Case report| Turkey   | 1                  | Cough and shortness of breath                        | Third trimester                        | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | Severe pneumonia and intubation | Cesarean section                                      | Still in hospital   |
| Coronavirus disease 2019 (COVID-19) during pregnancy: a case series         | Liu et al.      | Case series| China    | 3                  | Fever (=2) Cough (=1)                                | Third trimester (=3)                   | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None                   | Cesarean section (=2) Vaginal delivery (=1) | No death was reported |
| Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia; a case–control study | Li et al.       | Case–control| China    | 16                 | Fever (=12)                                         | Third trimester (=16)                  | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None                   | Cesarean section (=14) Vaginal delivery (=2) | No death was reported |


| Article title                                                                 | Author                  | Study type   | Country     | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (=N) | Diagnosing technique                              | Complications due to viral infection | Delivery | The maternal outcome(s) of disease in pregnant patients |
|-----------------------------------------------------------------------------|-------------------------|--------------|-------------|--------------------|-------------------------------------------------------|--------------------------------------|----------------------------------------|-------------------------------------|----------|------------------------------------------------------|
| A pregnant woman with COVID-19 in Central America                          | Zambrano et al.         | Case report  | The United States, USA | 1                  | Fever, headache, myalgia, and cough                   | Third trimester                      | Clinical symptoms and throat swab nucleic acid detection | None                               | Vaginal delivery | No death was reported                                  |
| Pregnancy and perinatal outcomes of women with coronavirus disease (COVID-19) pneumonia: a preliminary analysis | Liu et al.              | Cross-sectional | China       | 15                 | Fever (=13) Cough (=9) Fatigue (=4) Muscle ache (=3) Dyspnea (=1) Sore throat (=1) Diarrhea (=1) No clinical symptoms (=1) Post-partum fever (=1) | Third trimester (=13) Second trimester (=2) | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None                               | Cesarean section (=10) Vaginal delivery (=1) Still pregnant (=4) | All patients survived          |
| Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-center, descriptive study | Yu et al.               | Retrospective study | China       | 7                  | Fever (=6) Cough (=1) Dyspnea (=1) Diarrhea (=1) | Third trimester (=7) | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None                               | Cesarean section (=7) | Cured and discharged (=7) |
| Article title                                                                 | Author                        | Study type   | Country     | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (N) | Diagnosing technique | Complications due to viral infection | Delivery | The maternal outcome(s) of disease in pregnant patients |
|-------------------------------------------------------------------------------|-------------------------------|--------------|-------------|--------------------|--------------------------------------------------------|---------------------------------------|----------------------|--------------------------------------|-----------|----------------------------------------------------------|
| Neonatal early-onset infection with SARS CoV-2 in 33 neonates born to mothers With COVID-19 in Wuhan, China | Zeng et al.                   | Cohort study | China       | 33                 | Fever on admission (=8) Cough (=10) Post-partum fever (=5) | Third trimester | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None                                  | Cesarean section (=26) Vaginal delivery (7) | No death was reported |
| Mortality of a pregnant patient diagnosed with COVID-19: a case report with clinical, radiological, and histopathological findings | Karami et al.                 | Case report  | Iran        | 1                  | Fever Myalgia Cough                                      | Third trimester | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | Multiple organ dysfunction and death | Vaginal delivery | Not survived |
| Unlikely SARS-CoV-2 vertical transmission from mother to child: a case report | Peng et al.                   | Case report  | China       | 1                  | Fever Fatigue Shortness of breath                        | Third trimester | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | Not reported                          | Cesarean section | Survived |
| Severe COVID-19 during pregnancy and possible vertical transmission          | Alzamora et al.              | Case report  | The United States, USA | 1              | Fever (low grade) Shortness of breath Malaise            | Third trimester | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | Severe pneumonia and intubation | Cesarean section | No death was reported |
| Article title                                                                 | Author            | Study type | Country | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (= N) | Diagnosing technique                                                                 | Complications due to viral infection | Delivery | The maternal outcome(s) of disease in pregnant patients |
|------------------------------------------------------------------------------|-------------------|------------|---------|--------------------|------------------------------------------------------|---------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------|----------|----------------------------------------------------------|
| Preterm delivery in a pregnant woman with critical COVID-19 pneumonia and vertical transmission | Zamanian et al.   | Case report | Iran    | 1                  | Fever, Myalgia, Nausea, Cough, Dyspnea, Anorexia      | Third trimester                      | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection          | Severe pneumonia and intubation       | Cesarean section | Not survived                                             |
| Vaginal delivery report of a healthy neonate born to a convalescent mother with COVID-19 | Xiong et al.      | Case report | China   | 1                  | Fever, Cough, Shivering                               | Third trimester                      | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection          | Not reported                         | Vaginal delivery | Healthy and discharged                                   |
| Association of COVID-19 infection with pregnancy outcomes in healthcare workers and general women | Khan et al.       | Case series | China   | 17                 | Cough (= 6), Fever (= 3), Diarrhea (= 3), Nasal congestion (= 2), Shortness of breath (= 2), Sputum production (= 1) | Third trimester (= 17)                | Clinical symptoms and Chest CT scan and/or throat swab nucleic acid detection       | Not reported                         | Cesarean section (= 17) | No case of death was reported                           |
| Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth | Khan et al.       | Case report | China   | 3                  | Fever (= 2), Cough (= 3), Chest tightness (= 1)       | Third trimester (= 3)                | Clinical symptoms throat swab nucleic acid detection                                | Not reported                         | Vaginal delivery (= 3) | No case of death was reported                           |
| Article title                                                                 | Author      | Study type       | Country        | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (N) | Diagnosing technique | Complications due to viral infection | Delivery | The maternal outcome(s) of disease in pregnant patients |
|-----------------------------------------------------------------------------|-------------|------------------|----------------|-------------------|------------------------------------------------------|-------------------------------------|---------------------|--------------------------------------|-----------|----------------------------------------------------------|
| Clinical characteristics of 19 neonates born to mothers with COVID-19    | Liu et al.  | Retrospective    | China          | 19                | Fever (= 11) Cough (= 5) Diarrhea (= 2)               | Third trimester (19)                 | Clinical diagnosis (9) Laboratory confirmed (10) | Not reported                          | Cesarean section (= 18) Vaginal delivery (1) | No case of death was reported          |
| COVID-19 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals | Breslin et al. | Cohort study | The United States, USA | 43                | No symptoms (= 14) Fever (= 14) Cough (= 19) Myalgias or fatigue (= 11) Dyspnea (= 7) Chest pain (= 5) Headache (= 8) | Third trimester (43)                 | Clinical symptoms and throat swab nucleic acid detection | Severe case (4) Intubation and ICU admission (2) | Cesarean section (8) Vaginal delivery (10) Discharge for continuing pregnancy (25) | No case of death was reported          |
| Clinical features and outcomes of pregnant women suspected of Coronavirus Disease 2019 | Yang et al. | Case–control    | China          | 13 (42 controls) | Prenatal fever (2) Postpartum Fever (8) Cough (2) | Third trimester                     | Clinical symptoms and Chest CT scan and/or throat swab nucleic acid detection | Not reported                          | Cesarean section (9) Vaginal delivery (4) | No case of death was reported          |
| Asymptomatic COVID-19 in pregnant woman with typical chest CT manifestation: a case report | Renbin et al. | Case report | China          | 1                 | Asymptomatic                                          | Third trimester                     | Chest CT scan and throat swab nucleic acid detection | Not reported                          | Cesarean section                         | No case of death was reported          |
| Article title                                                                 | Author        | Study type | Country  | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (= N) | Diagnosing technique                                                                 | Complications due to viral infection | Delivery | The maternal outcome(s) of disease in pregnant patients |
|------------------------------------------------------------------------------|---------------|------------|----------|--------------------|-------------------------------------------------------|----------------------------------------|---------------------------------------------------------------------------------------|--------------------------------------|----------|----------------------------------------------------------|
| Chest CT Findings in a Pregnant patient with 2019 Novel Coronavirus Disease  | Liao et al.   | Case report | China    | 1                  | Fatigue Cough                                         | Third trimester                        | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection           | Not reported                        | Cesarean section | No case of death was reported                             |
| Infants born to mothers with a new Coronavirus (COVID-19)                   | Chen et al.   | Case report | China    | 4                  | Fever (= 3) Cough (= 2) Headache (= 2)                | Third trimester (= 4)                  | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection           | Not reported                        | Cesarean section (= 3) Vaginal delivery (= 1) | No case of death was reported                             |
| Anesthetic management for emergent cesarean delivery in a parturient with recent diagnosis of Coronavirus Disease 2019 (COVID-19); a case report | Song et al.   | Case report | China    | 1                  | Fever Cough Myalgia                                    | Third trimester                        | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection           | Not reported                        | Cesarean section | No case of death was reported                             |
| Clinical characteristics and risk assessment of newborns born to mothers with COVID-19 | Yang et al.   | Case series | China    | 7                  | Fever (= 5) Cough (= 1) Diarrhea (= 1) Abdominal pain (= 1) | Third trimester (= 7)                  | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection           | Not reported                        | Cesarean section (= 7)                                 | No case of death was reported                             |
| COVID-19 in pregnancy: early lessons                                        | Breslin et al.| Case series | The United States, USA | 7                  | Fever (= 2) Cough (= 3) Myalgia (= 3) Headache (= 2) Asymptomatic (= 2) | Third trimester (= 7)                  | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection           | Intubation and ICU admission (= 2) | Cesarean Section (= 2) No report of other 5 patients     | No case of death was reported                             |
Table 1 (continued)

| Article title | Author | Study type | Country | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (=N) | Diagnosing technique | Complications due to viral infection | Delivery | The maternal outcome(s) of disease in pregnant patients |
|---------------|--------|------------|---------|--------------------|--------------------------------------------------------|----------------------------------------|----------------------|-------------------------------------|----------|--------------------------------------------------------|
| Antibodies in infants born to mothers with COVID-19 Pneumonia | Zeng et al. | Case study | China | 6 | Mild clinical presentations (=6) | Third trimester (=6) | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None | Cesarean section (=6) | No case of death was reported |
| Novel Coronavirus infection in newborn babies under 28 days in China | Zhang et al. | Case series | China | 4 | Fever (=3) | Third trimester (=4) | Clinical symptoms and Chest CT scan and throat swab nucleic acid detection | None | Cesarean section (=4) | No case of death was reported |
| Clinical characteristics of pregnant women with Covid-19 in Wuhan, China | Chen et al. | Retrospective study | China | 118 | Fever (=84) | Third trimester (=75) | 84 women confirmed with Nucleic acid testing and 34 others diagnosed with CT scan | 9 severe case and 1 need of mechanical ventilation | Cesarean section (=63) | No case of death was reported |
| Article title | Author | Study type | Country | Number of patients | Clinical features of the disease in pregnant patients | The onset of disease presentation (=N) | Diagnosing technique | Complications due to viral infection | Delivery | The maternal outcome(s) of disease in pregnant patients |
|---------------|--------|------------|---------|--------------------|-----------------------------------------------------|---------------------------------------|---------------------|-------------------------------|----------|-----------------------------------------------------|
| **Summary**   |        |            |         | Total number of cases: 386 | Fever (=227/364) Cough (=165/364) Asymptomatic (25/364) Fatigue (=26/364) Dyspnea (=21/364) Chest tightness (21/364) Headache (=20/364) Diarrhea (=17/364) Myalgia (=13/364) Sore throat (5/364) Malaise (=3/364) | Third trimester (=341) Second trimester (=45) | Clinical + CT scan + oropharyngeal swab NAT | Severe pneumonia (=22) Number of death (=2) | Cesarean section (=257) Vaginal delivery (=42), Continuing pregnancy (=73) Spontaneous abortion (=3) Ectopic pregnancy (=2) Induced abortion (=4) | Number of death: 2 |

*NAT* Nucleic Acid testing, *CT* computed tomography

*4 cases before delivery, 2 cases on the day of delivery, 3 cases after delivery

**Mother of twins, with typical clinical and chest CT finding of nCoV-2019 pneumonia confirmed as a nCoV-2019 after rule out of other causes although NAT was negative

***3 patients cured and discharged to continue the pregnancy, 9 patients gave birth and then cured and discharged, 1 patient with severe pneumonia intubated
Table 2  Characteristics of neonates born from pregnant women with COVID-19 included in the systematic review

| Article title                                                                 | Author            | Study type | Country | Number of neonates | Neonatal maturity (=N) | Neonatal clinical presentations (=N) | Neonatal complications | Neonate test for nCoV-2019 | Apgar score | Neonatal outcome          |
|-------------------------------------------------------------------------------|-------------------|------------|---------|--------------------|------------------------|-------------------------------------|------------------------|-----------------------------|-------------|---------------------------|
| Pregnant women with new coronavirus infection: clinical characteristics and placental pathological analysis of three cases | Chen et al.       | Case study | China   | 3                  | Mature infants (2)     | No remarkable clinical problem was reported | No complications were reported | Negative                    | Not reported | Healthy and discharged    |
| Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia     | Zhu et al.        | Case study | China   | 10 (2 twins)       | 4 full terms, 6 premature (2 SGA AND 1 LGA) | Respiratory distress (6), GI tract symptoms (4), Fever (2), Increased heart rate (1), Vomiting (1) | Death (1)** DIC (1)** | Negative                    | 5th min Apgar score: 10 (6) 9 (2) 8 (2) | Cured (5)   | In hospital (4) Died (1)    |
| Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records | Chen et al.       | Case study | China   | 9                  | Full-term babies (5), birth at 36th week of gestational age (4*) | No remarkable clinical problem was reported | No complications were reported | Negative                    | All babies with 5th min Apgar score of 9 to 10 | None of the neonates needed special treatment |
| Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province | Zhang et al.      | Case–control | China   | 10                 | Full-term babies (9) Premature babies (1) | 3 neonate developed bacterial pneumonia | No complications were reported | Negative                    | Not reported | None of the neonates needed special treatment. No neonatal death |

**DIC** = disseminated intravascular coagulopathy
### Table 2 (continued)

| Article title                                                                 | Author            | Study type | Country | Number of neonates | Neonatal maturity (\(= N\))                  | Neonatal presentations (\(= N\)) | Neonatal complications | Neonate test for nCoV-2019 | Apgar score | Neonal outcome                        |
|------------------------------------------------------------------------------|-------------------|------------|---------|--------------------|-----------------------------------------------|---------------------------------|--------------------------|-------------------------------|-------------|--------------------------------------|
| Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy | Liu et al.        | Case Study | China   | 10                 | Full-term babies (= 4), Premature babies (= 6) | 9 neonates survived with no remarkable clinical problem, 1 died due to ARDS and MODS | 1 neonate died due to MODS | Negative          | 1st min Apgar score: 10 for all nine alive babies | 1 dead neonate because of MODS |
| Lack of Vertical transmission of severe acute respiratory syndrome Coronavirus 2, China | Li et al.         | Case Report | China   | 1                  | Premature baby in 35th week of GA             | No remarkable clinical problem was reported | No complications were reported | Negative          | Not reported | Healthy and discharged                |
| A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery | Wang et al.       | Case report | China   | 1                  | Premature baby in 30th week of GA             | No remarkable clinical problem was reported | No complications were reported | Negative          | 5th min Apgar score: 10               | Healthy and discharged                |
| A case report of neonatal COVID-19 infection in China                         | Wang et al.       | Case report | China   | 1                  | Full-term baby                                | COVID-19 Pneumonia               | No complications were reported | Positive          | 5th min Apgar score: 9               | Healthy and discharged                |
| Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry?   | Fan et al.        | Case report | China   | 2                  | Full-term neonate (= 1) 36th week and 5 days of GA (= 1) | Mild neonatal pneumonia and lymphopenia (= 1) Low-grade Fever and diffuse haziness of lungs without patchy consolidation which cured with antibiotic | No complications were reported | Negative          | 5th min Apgar score: 10               | Healthy and discharged                |
| Article title                                                                 | Author                 | Study type  | Country     | Number of neonates | Neonatal maturity (= N)                                      | Neonatal clinical presentations (= N) | Neonatal complications                                      | Neonate test for nCoV-2019 Result | Diagnostic method | Apgar score | Neonatal outcome |
|-----------------------------------------------------------------------------|------------------------|-------------|-------------|--------------------|-------------------------------------------------------------|--------------------------------------|-------------------------------------------------------------|----------------------------------|-------------------|--------------|-----------------|
| Clinical analysis of pregnant women with 2019 Novel Coronavirus pneumonia   | Chen et al.            | Case series | China       | 5                  | Full-term neonate (= 5)                                     | Fetal tachycardia (= 1)               | No complications were reported                             | Negative                        | Neonatal throat swab nucleic acid testing | 5th min Apgar score: 10 (= 5) | Healthy       |
| Possible vertical transmission of SARS-CoV-2 From an infected mother to her newborn | Dong et al.            | Case report | China       | 1                  | 34 weeks and 5 days                                        | Elevated IgM antibody***              | No complications were reported                             | Negative                        | Neonatal throat swab nucleic acid testing | 5th min Apgar score: 10 | Healthy and discharged |
| Lung ultrasound and computed tomographic findings in a pregnant woman with COVID-19 | Kalafat et al.         | Case report | Turkey      | 1                  | 35 weeks and 3 days                                        | No remarkable clinical problem was reported | No complications were reported                             | Negative                        | Neonatal throat swab nucleic acid testing | 5th min Apgar score: 9 | Healthy       |
| Title: Coronavirus disease 2019 (COVID-19) during pregnancy: a case series  | Liu et al.             | Case series | China       | 3                  | Full-term neonates (= 3)                                   | Chorioamnionitis and meconium aspiration syndrome (= 1) | No complications were reported                             | Negative                        | Neonatal throat swab nucleic acid testing | 5th min Apgar score: 9 (= 3) | Survived (= 3) |
| Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case–control study | Li et al.              | Case-control | China       | 17                 | Full-term (= 13) Premature (= 4) LBW (= 3)                 | Intrauterine fetal distress (= 2)     | No complications were reported                             | Negative                        | Neonatal throat swab nucleic acid testing (= 3)*** | 5th min Apgar score: 10 (= 17) | No death was reported |
| Article title                                                                 | Author                        | Study type     | Country          | Number of neonates | Neonatal maturity (\(= N\)) | Neonatal clinical presentations (\(= N\)) | Neonatal complications | Neonate test for nCoV-2019 | Apgar score | Neonatal outcome |
|------------------------------------------------------------------------------|-------------------------------|----------------|------------------|--------------------|-------------------------------|------------------------------------------|------------------------|--------------------------------|-------------|-----------------|
| A pregnant woman with COVID-19 in Central America                           | Zambrano et al.               | Case report    | United States, USA| 1                  | 32 weeks of GA               | No remarkable clinical problem was reported | No complications were reported         | Negative                        | 5th min Apgar score: 9 | No death was reported   |
| Pregnancy and Perinatal outcomes of women with Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis | Liu et al.                    | Cross-sectional| China            | 11                 | Full-term (= 8) Preterm delivery (= 3) | No remarkable clinical problem was reported | No complications were reported         | Negative                        | Not reported**** | No death was reported   |
| Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-center, descriptive study | Yu et al.                     | Retrospective study | China            | 7                  | Full-term (= 7) Mild shortness of breath (= 1) | Mild pulmonary infection in a neonate with positive COVID-19 test | Negative (= 2) Positive (= 1)**** | Neonatal throat swab nucleic acid testing | 5th min Apgar score: 9 -10 (= 7) | No death was reported   |
| Article title | Author | Study type | Country | Number of neonates | Neonatal maturity (\(=N\)) | Neonatal clinical presentations (\(=N\)) | Neonatal complications | Neonate test for nCoV-2019 Result | Apgar score | Neonatal outcome |
|---------------|--------|------------|---------|--------------------|-----------------------------|--------------------------------|------------------------|-----------------------------------|------------|-----------------|
| Neonatal early-onset infection with SARS CoV-2 in 33 neonates born to mothers With COVID-19 in Wuhan, China | Zeng et al. | Cohort study | China | 33 | Full-term (\(=29\)) Preterm (\(=4\)) | Fever (\(=2\); both with positive COVID-19) Shortness of breath (\(=4\); 3 with negative COVID-19 and one positive) Cyanosis (\(=3\); 2 with negative COVID-19 and one with positive) Feeding intolerance (\(=3\); 2 with negative COVID-19 and one with positive) | Asphyxia (\(=2\); one neonate with negative COVID-19 infection and one neonate with positive COVID-19 infection) Pneumonia (\(=3\); all 3 with positive COVID-19) Respiratory distress syndrome (\(=4\); 3 with negative COVID-19 and one positive) Requiring mechanical ventilation: 1 baby with COVID-19 positive | Negative (\(=30\)) Positive (\(=3\)) | Not reported****** | No death was reported |
| Article title                                                                 | Author          | Study type | Country       | Number of neonates | Neonatal maturity (= N) | Neonatal clinical presentations (= N) | Neonatal complications | Neoneate test for nCoV-2019 Result | Diagnostic method | Apgar score | Neonatal outcome |
|------------------------------------------------------------------------------|-----------------|------------|---------------|--------------------|------------------------|----------------------------------------|------------------------|-----------------------------------|-------------------|-------------|------------------|
| Mortality of a pregnant patient diagnosed with COVID-19: a case report with clinical, radiological, and histopathological findings | Karami et al.   | Case report | Iran           | 1                  | Stillbirth             | –                                      | –                      | Not reported                     | Not reported      | Apgar score: 0  | Fetal death     |
| Unlikely SARS-CoV-2 vertical transmission from mother to child: a case report | Peng et al.     | Case report | China          | 1                  | Preterm                | Mild respiratory distress          | None                   | Negative                         | Neonatal throat and anal and swab and sputum and serum nucleic acid testing | 5th min Apgar score: 10 | Survived     |                   |
| Severe COVID-19 during pregnancy and possible vertical transmission          | Alzamora et al. | Case report | The United States, USA | 1 | Preterm                  | Mild respiratory distress And sporadic cough | Intubation because of mother’s sedation | Positive                     | Neonatal throat swab nucleic acid testing (16 h after delivery) | 5th min Apgar score: 8 | No death was reported |                   |
| Preterm delivery in a pregnant woman with critical COVID-19 pneumonia and vertical transmission | Zamanian et al. | Case report | Iran           | 1                  | Preterm                | Fever                                 | None                   | Positive                         | Neonatal throat swab nucleic acid testing | 5th min Apgar score: 9 | Survived     |                   |
| Vaginal delivery report of a healthy neonate born to a convalescent mother with COVID-19 | Xiong et al.    | Case report | China          | 1                  | Full-term              | No remarkable clinical problem was reported | None                   | Negative                         | Neonatal throat and anal swab nucleic acid testing | 5th min Apgar score: 10 | Healthy and discharged |                   |
Table 2 (continued)

| Article title                                                                 | Author          | Study type  | Country | Number of neonates | Neonatal maturity \((= N)\) | Neonatal clinical presentations \((= N)\) | Neonatal complications | Neonatal test for nCoV-2019 \(\text{Result} \) | Diagnostic method | Apgar score | Neonatal outcome |
|-------------------------------------------------------------------------------|-----------------|-------------|---------|--------------------|-----------------------------|-------------------------------|-----------------------|---------------------------------|-----------------|--------------|-----------------|
| Association of COVID-19 infection with pregnancy outcomes in healthcare workers and general women | Khan et al.     | Case series | China   | 17                 | Full-term \((= 14)\) Preterm \((= 3)\) | Neonatal pneumonia \((= 5)\) 2 case of COVID-19 which one of them developed pneumonia | No serious complications were reported | Negative \((= 15)\) Positive \((= 2)\) | Neonatal throat and anal swab nucleic acid testing | 5th min Apgar score: 9–10 | No case of death was reported |
| Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth | Khan et al.     | Case report  | China   | 3                  | Full-term \((= 2)\) Preterm \((= 1)\) | No remarkable clinical problem was reported | None | Negative \((= 3)\) | Neonatal throat and anal swab nucleic acid testing | 5th min Apgar score: 9–10 | No case of death was reported |
| Clinical characteristics of 19 neonates born to mothers with COVID-19         | Liu et al.      | Retrospective study | China   | 19                 | Full-term \((= 17)\) Preterm \((= 2)\) | No remarkable clinical problem was reported | None | Negative \((= 19)\) | Neonatal throat and anal swab nucleic acid testing | 5th min Apgar score: 9 | No case of death was reported |
| Article title                                                                 | Author                  | Study type | Country            | Number of neonates | Neonatal maturity (\(= N\)) | Neonatal clinical presentations (\(= N\)) | Neonatal complications | Neonate test for nCoV-2019 Result | Diagnostic method | Apgar score | Neonatal outcome                   |
|------------------------------------------------------------------------------|-------------------------|------------|--------------------|---------------------|-----------------------------|------------------------------------------|------------------------|-----------------------------------|-------------------------------|---------------|----------------------------------|
| COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals | Breslin et al.          | Cohort study | The United States, USA | 18                  | Full-term (\(= 17\)) Premature (\(= 1\)) | Respiratory distress (\(= 1\)) One patient with congenital disease | None                    | Negative (\(= 18\); including one intermediate result which considers as negative because of low detection) | Neonatal throat and anal swab nucleic acid testing | 5th min Apgar score: 9–10 | All healthy and discharged        |
| Clinical features and outcomes of pregnant women suspected of Coronavirus Disease 2019 | Yang et al.             | Case-control | China              | 20******            | Mean ± SD GA: 38.2 ± 2.3 | Fever (\(= 1\) from COVID-19 positive mother) | None                    | Negative | Neonatal throat and anal swab nucleic acid testing | Not reported | No case of death was reported |
| Asymptomatic COVID-19 in a pregnant woman with typical chest CT manifestation: a case report | Renbin et al.           | Case report  | China              | 1                   | Full-term                  | No remarkable clinical problem was reported | None                    | Negative | Neonatal throat swab nucleic acid testing | Not reported | Healthy and discharged           |
| Chest CT findings in a pregnant patient with 2019 Novel Coronavirus Disease | Liao et al.             | Case report  | China              | 1                   | Preterm                    | No remarkable clinical problem was reported | None                    | Negative | Neonatal throat and anal swab nucleic acid testing | Not reported | No case of death was reported |
| Article title                                                                 | Author     | Study type   | Country          | Number of neonates | Neonatal maturity (= N) | Neonatal clinical presentations (= N) | Neonatal complications | Neonate test for nCoV-2019 Result | Diagnostic method | Apgar score | Neonatal outcome                        |
|------------------------------------------------------------------------------|------------|--------------|------------------|--------------------|-------------------------|----------------------------------------|------------------------|-------------------------------------|-------------------|-------------|-----------------------------------------|
| Infants born to mothers with a new Coronavirus (COVID-19)                    | Chen et al.| Case report  | China            | 4                  | Full-term (= 4)          | No remarkable clinical problem was reported | None                   | Negative (= 4) | Neonatal throat and anal swab nucleic acid testing | Not reported      | No case of death was reported         |
| Anesthetic management for emergent cesarean delivery in a parturient with recent diagnosis of Coronavirus Disease 2019 (COVID-19): a case report | Song et al.| Case report  | China            | 1                  | Preterm (= 1)           | No remarkable clinical problem was reported | None                   | Negative   | Neonatal throat swab nucleic acid testing | 5th min Apgar score: 9 | Healthy and discharged                  |
| Clinical characteristics and risk assessment of newborns born to mothers with COVID-19 | Yang et al.| Case series  | China            | 7                  | Full-term (= 3)         | Mild respiratory distress syndrome (= 2) Vomiting and hypoglycemia (= 1) | None                   | Negative (performed for 6 neonates) | Neonatal throat swab nucleic acid testing | 5th min Apgar score: 9–10 | No case of death was reported         |
| COVID-19 in pregnancy: early lessons                                         | Breslin et al.| Case series | The United States, USA | 2                  | Full-term (= 2)         | No remarkable clinical problem was reported | None                   | Negative (performed for one neonate) | Neonatal throat swab nucleic acid testing | Not reported      | No case of death was reported         |
| Antibodies in Infants Born to mothers with COVID-19 Pneumonia               | Zeng et al.| Case study   | China            | 6                  | Not reported            | No remarkable clinical problem was reported*          | None                   | Negative (6) | Neonatal throat and serum swab nucleic acid testing | Not reported      | No case of death was reported         |
| Novel Coronavirus infection in newborn babies under 28 days in China         | Zhang et al.| Case series  | China            | 2                  | Full-term (= 2)         | Shortness of breath (= 1)                 | None                   | Positive    | Neonatal throat swab nucleic acid testing | Not reported      | No case of death was reported         |
Table 2 (continued)

| Article title                                                                 | Author               | Study type       | Country     | Number of neonates | Neonatal maturity (\(= N\)) | Neonatal clinical presentations (\(= N\)) | Neonatal complications | Neonate test for nCoV-2019 | Apgar score | Neonatal outcome |
|-------------------------------------------------------------------------------|----------------------|------------------|-------------|--------------------|------------------------------|-------------------------------------------|------------------------|---------------------------|-------------|------------------|
| Clinical characteristics of pregnant women with Covid-19 in Wuhan, China    | Chen et al.          | Retrospective study | China       | 70 (2 set of twins)| Full-term (= 56) Preterm (= 14) | No remarkable clinical problem was reported | None                   | Negativeϕ                | 5th min Apgar score: 8-9ϕ | Survived     | No case of death was reported |
| Total results                                                                 |                      |                  |             | Total number of neonates: 302 | Full-term (= 210/276) Premature (= 65/276) stillbirth (= 1) | DIC (= 2) MODS (= 1) Negatives (= 208) And positive (= 11) |                      |                           |             |                  |

MODS Multiple organ dysfunction syndrome, ARDS Acute respiratory distress syndrome, DIC Disseminated intravascular coagulation, GA gestational age, SGA Small for gestational age, LGA Large for gestational age, LBW low birth weight, C-Section Cesarean section

We considered GA < 37 weeks as preterm delivery
*One complicated with pre-eclampsia, one with history of 2 stillbirth, one with history of 2 previous c-sections and irregular contractures, and one with premature rupture of membranes
**One neonate in which first symptom was increased heart rate developed refractory shock and gastric bleeding which lead to death, another neonate with shortness of breath and moaning and later with DIC that cured
***SARS-CoV-2 IgG level: 140.32 AU/mL and IgM level: 45.83 AU/mL 2 h after birth and also 16 days after birth repeated test revealed IgG level of 69.94 AU/mL and IgM level of 11.75 AU/mL
****The specimens collected from three neonates whom delivered by cesarean section
*****The study claimed that no COVID-19 infection was represented in neonates but did not clarify by which method -clinical or nucleic acid testing-
******Specimens collected from three neonates and positive sample was collected 36 h after birth
*******Except one of infected neonates with confirmed COVID-19 infection born with need of resuscitation and Apgar score of 3, 4, 5 in 1, 5 and 10 min
*********The total number of neonates were 57 and 20 neonates tested for COVID-19 but study did not clarify how many neonates belong to the case group
**********2 neonates had elevated serum IgM levels
ϕNasopharyngeal swab was taken from 8 neonates
ϕϕApgar score was measured for 66 neonates
### Table 3  A summary of studies on pregnancy outcomes in pregnant women with COVID-19 included in the systematic review

| Article title                                                                 | Author          | Study type | Country | Placental test for nCoV-2019 nucleic acid | Pregnancy complications                                                                 | Further information                                                                 |
|-------------------------------------------------------------------------------|-----------------|------------|---------|------------------------------------------|----------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Pregnant women with new coronavirus infection: clinical characteristics and placental pathological analysis of three cases | Chen et al.     | Case study  | China   | Negative RT-PCR                           | Not reported                                                                           | Umbilical cord and fetal membranes were tested and went negative                      |
| Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia     | Zhu et al.      | Case study  | China   | Not reported                              | Not reported                                                                           | Premature rupture of membranes (= 3), One polyhydramnios, One oligohydramnios         |
|                                                                                 |                 |            |         |                                          |                                                                                        |                                                                                        |
| Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records | Chen et al.     | Case study  | China   | Not reported                              | Premature rupture of membranes (= 2), Fetal distress (= 2)                              | All amniotic fluid, cord blood, breastmilk samples from six patients were negative (3 cases has unsuccessful sample collection) |
| Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province | Zhang et al.    | Case–control | China   | Not reported                              | Not reported                                                                           | Pre-eclampsia (= 1), PROM (= 3), Fetal distress (= 1), Premature birth (= 3), Asphyxia (= 1) |
| Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy  | Liu et al.      | Case study  | China   | Not reported                              | Not reported                                                                           | Fetal distress (= 3), PROM (= 1), Stillbirth (= 1)                                     |
| Lack of vertical transmission of severe acute respiratory syndrome Coronavirus 2, China | Li et al.       | Case report | China   | Negative RT-PCR                           | Not reported                                                                           | Serum, urine, feces, amniotic fluid, umbilical cord blood and placenta, and breast milk samples were negative |
| A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery    | Wang et al.     | Case report | China   | Negative RT-PCR                           | Not reported                                                                           | Amniotic fluid and cord blood were negative                                           |
| A case report of neonatal COVID-19 infection in China                          | Wang et al.     | Case report | China   | Negative RT-PCR                           | Not reported                                                                           | Cord blood and mother’s breast milk were negative                                      |
| Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry?    | Fan et al.      | Case report | China   | Negative RT-PCR                           | Not reported                                                                           | Umbilical cord blood, amniotic fluid, vaginal swabs, and mother’s breast milk were negative |
| Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia     | Chen et al.     | Case series | China   | Not reported                              | Pre-eclampsia (= 1) Gestational diabetes (= 2)                                          | Not reported                                                                           |
| Article title                                                                 | Author                  | Study type         | Country          | Placental test for nCoV-2019 nucleic acid Result | Pregnancy complications | Further information                                                        |
|-----------------------------------------------------------------------------|-------------------------|--------------------|------------------|-----------------------------------------------|--------------------------|---------------------------------------------------------------------------|
| Possible vertical transmission of SARS-CoV-2 from an infected mother to her  | Dong et al.             | Case report        | China            | Not reported                                  | Not reported             | Mother’s vaginal discharge and breastmilk were negative for COVID-19 PCR test result |
| newborn                                                                     |                         |                    |                  |                                               |                          |                                                                           |
| Lung ultrasound and computed tomographic findings in a pregnant woman with   | Kalafat et al.          | Case report        | Turkey           | Negative                                      | RT-PCR                   | Breast milk and cord blood were negative                                 |
| COVID-19                                                                    |                         |                    |                  |                                               |                          |                                                                           |
| Coronavirus disease 2019 (COVID-19) during pregnancy: a case series          | Liu et al.              | Case series        | China            | Negative                                      | RT-PCR                   | Breast milk, cord blood, amniotic fluid, neonatal serum, and mothers’ vaginal mucosa were negative |
| Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia:  | Li et al.               | Case–control       | China            | Not reported                                   | Not reported             | gestational diabetes mellitus (= 3)                                      |
| a case–control study                                                        |                         |                    |                  |                                               |                          | PROM (= 1)                                                               |
|                                                                             |                         |                    |                  |                                               |                          | gestational hypertension (= 3), hypothyroidism (= 2), pre-eclampsia (= 1) |
|                                                                             |                         |                    |                  |                                               |                          | Sinus tachycardia (= 1)                                                  |
|                                                                             |                         |                    |                  |                                               |                          | Fetal distress (= 2)                                                     |
|                                                                             |                         |                    |                  |                                               |                          |                                                                           |
| A pregnant woman with COVID-19 in Central America                           | Zambrano et al.         | Case report        | United States,   | Not reported                                   | Not reported             | Neonaute’s blood sample was negative                                     |
|                                                                             |                         |                    | USA              |                                               |                          |                                                                           |
| Pregnancy and perinatal outcomes of women with Coronavirus Disease          | Liu et al.              | Cross-sectional    | China            | Not reported                                   | Not reported             | Placenta previa (= 1)                                                    |
| (COVID-19) pneumonia: a preliminary analysis                                 |                         |                    |                  |                                               |                          |                                                                           |
| Clinical features and obstetric and neonatal outcomes of pregnant patients  | Yu et al.               | Retrospective study| China            | Not reported                                   | Not reported             | Uterine scarring (= 3)                                                   |
| with COVID-19 in Wuhan, China: a retrospective, single-center, descriptive   |                         |                    |                  |                                               |                          | Hypothyroidism (= 1)                                                     |
| study                                                                       |                         |                    |                  |                                               |                          |                                                                           |
| Neonatal Early-Onset Infection with SARS CoV-2 in 33 Neonates Born to      | Zeng et al.             | Cohort study       | China            | Not reported                                   | Not reported             | PROM (= 3)                                                               |
| Mothers With COVID-19 in Wuhan, China                                       |                         |                    |                  |                                               |                          |                                                                           |
Table 3 (continued)

| Article title                                                                                                                                                                                                 | Author               | Study type       | Country              | Placental test for nCoV-2019 nucleic acid Result | Pregnancy complications | Further information                                                                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|------------------|----------------------|------------------------------------------------|-------------------------|-------------------------------------------------------------------------------------|
| Mortality of a pregnant patient diagnosed with COVID-19: A case report with clinical, radiological, and histopathological findings                                                                                   | Karami et al.        | Case report      | Iran                 | Not reported                                    | Not reported            | Not reported                                                                         |
| Unlikely SARS-CoV-2 vertical transmission from mother to child: a case report                                                                                                                                   | Peng et al.          | Case report      | China                | Negative                                        | RT-PCR                  | Not reported                                                                         |
| Severe COVID-19 during pregnancy and possible vertical transmission                                                                                                                                           | Alzamora et al.      | Case report      | The United States, USA | Not reported                                    | Not reported            | Diabetes mellitus                                                                   |
| Preterm delivery in a pregnant woman with critical COVID-19 pneumonia and vertical transmission                                                                                                | Zamanian et al.      | Case report      | Iran                 | Not reported                                    | Not reported            | Not reported                                                                         |
| Vaginal delivery report of a healthy neonate born to a convalescent mother with COVID-19                                                                                                                     | Xiong et al.         | Case report      | China                | Negative                                        | RT-PCR                  | Amniotic fluid was negative                                                          |
| Association of COVID-19 infection with pregnancy outcomes in healthcare workers and general women                                                                                                             | Khan et al.          | Case series      | China                | Not reported                                    | Not reported            | 5 women with other complications                                                     |
| Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth                                                                  | Khan et al.          | Case report      | China                | Not reported                                    | Not reported            | The cord blood sample was negative                                                   |
| Clinical characteristics of 19 neonates born to mothers with COVID-19                                                                                                                                          | Liu et al.           | Retrospective study | China               | Not reported                                    | Not reported            | Breast milk sample, amniotic fluid, and cord blood were negative                     |
| COVID-19 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals                                                      | Breslin et al.       | Cohort study     | The United States, USA | Not reported                                    | Not reported            | PROM                                                                                |

Negative RT-PCR: Not reported.
| Article title                                                                 | Author            | Study type    | Country   | Placental test for nCoV-2019 nucleic acid | Pregnancy complications | Further information                                      |
|------------------------------------------------------------------------------|-------------------|---------------|-----------|------------------------------------------|--------------------------|----------------------------------------------------------|
| Clinical features and outcomes of pregnant women suspected of Coronavirus Disease 2019 | Yang et al.       | Case–control  | China     | Not reported                             | Not reported             | Not reported                                             |
| Asymptomatic COVID-19 in a pregnant woman with typical chest CT manifestation: a case report | Renbin et al.     | Case report   | China     | Not reported                             | Not reported             | Not reported                                             |
| Chest CT findings in a pregnant patient with 2019 Novel Coronavirus Disease | Liao et al.       | Case report   | China     | Negative RT-PCR                          | Not reported             | Amniotic fluid and cord blood were negative             |
| Infants born to mothers with a new Coronavirus (COVID-19)                     | Chen et al.       | Case report   | China     | Not reported                             | Placenta (=1)            | Not reported                                             |
| Anesthetic management for emergent cesarean delivery in a parturient with recent diagnosis of Coronavirus Disease 2019 (COVID-19): a case report | Song et al.       | Case report   | China     | Not reported                             | Not reported             | Not reported                                             |
| Clinical characteristics and risk assessment of newborns born to mothers with COVID-19 | Yang et al.       | Case series   | China     | Not reported                             | Not reported             | Cord blood and amniotic fluid were negative             |
| COVID-19 in pregnancy: early lessons                                          | Breslin et al.    | Case series   | The United States, USA                   | Not reported             | Type 2 diabetes mellitus (=2)                         | Not reported                                             |
| Antibodies in infants born to mothers with COVID-19 pneumonia                 | Zeng et al.       | Case study    | China     | Not reported                             | Not reported             | Not reported                                             |
| Novel Coronavirus infection in newborn babies under 28 Days in China          | Zhang et al.      | Case series   | China     | Not reported                             | Not reported             | Not reported                                             |
| Clinical characteristics of pregnant women with Covid-19 in Wuhan, China      | Chen et al.       | Retrospective study | China    | Not reported                             | Not reported             | Breast milk of three mothers were negative              |
| Total results                                                                 |                   |               |           | All samples examined were negative       | RT-PCR                   |                                                          |

RT-PCR Reverse transcription-polymerase chain reaction, PROM Premature rupture of membranes
included myalgia, diarrhea, dyspnea, headache, and chest tightness. There were two women with specific presentations: one with Cholecystitis [50] and another with oil intolerance [67].

For nearly all pregnant women, the diagnosis was made based on a combination of clinical symptoms, nucleic acid testing for the novel coronavirus, and computed tomography (CT). As for the general population, some pregnant patients \( n = 44 \) had a negative SARS-CoV-2 test but displayed clinical manifestations and abnormalities in CT scan related to COVID-19 [50, 53, 55].

Twenty-two (6.0%) pregnant patients developed severe pneumonia. Among them, 10 cases (2.8%) required mechanical ventilation and therefore were admitted to the intensive care unit (ICU) [42, 44, 53, 58, 60, 63, 65, 73, 74]. Two of these ten patients died from severe pneumonia and multiple organ dysfunction [65, 73].

The vast majority of patients were in their third trimester of pregnancy, and only 45 cases were in the first or second trimester (12.4%). Of the total number of 299 births, there were 257 (86%) cesarean sections, and 42 (14%) vaginally completed. Zhang L et al. and Breslin et al. reported obstetric reasons such as premature rupture of membrane, fetal distress, and other indications for the Cesarean section [44, 60]. Chen et al. reported that 38 of 63 cases who underwent cesarean sections claimed to have a fear of COVID-19 [53]. There were three cases of spontaneous abortions, two ectopic pregnancy, and four induced abortions. Pregnant women seeking induced abortion were most afraid of COVID-19 and its potential effects on pregnancy outcomes [53].

**Neonatal outcomes**

Thirty-seven studies included a total of 302 neonates from mothers with COVID-19. Two studies have not indicated the timing of birth [43, 57]. Of the studies that provided data, there were 210 full-term and 65 preterm neonates.

Karami et al. reported the death of a mother from COVID-19 and also her fetus [65]. The dead baby was born with an Apgar score of 0, did not respond to resuscitation, and was not considered for COVID-19 diagnostic tests. Of the babies born alive from mothers with COVID-19, five newborns faced critical conditions. One of them presented with a fast heart rate developed gastric bleeding and refractory shock later and died. The second complicated case was a premature newborn born from a mother, who had a diagnosis of severe COVID-19 pneumonia [50]. This neonate showed shortness of breath at presentation and developed disseminated intravascular coagulation (DIC). This case could be cured. The third neonate died due to the multiple organ dysfunction syndrome and could not survive [58]. The nasopharyngeal samples of these three babies were all negative for SARS-CoV-2 RNA detection. The fourth one suffered from pneumonia and needed intubation at birth. Sixteen hours after birth, the neonate tested positive for SARS-CoV-2 RNA with throat swab nucleic acid testing [74]. This neonate was later extubated and discharged without any complications. The fifth one was a premature baby with the gestational age of 31 weeks and 2 days. This neonate had an Apgar score of 3, 4, and 4 at the first, fifth, and tenth minute after delivery and required resuscitation [66]. This neonate was later confirmed as a definite case of COVID-19 and developed DIC. Vital signs were successfully stabilized on the day of 14. This neonate had close contact with the mother after delivery.

Except for the babies mentioned above, most babies born alive had a 5-min Apgar score of 8 and 9 (Table 2). A total of 219 neonates underwent nasopharyngeal specimen collection for SARS-CoV-2 nucleic acid testing. Of them, 11 tested positive, and two of which were described above. A study by Wang S et al. reported a neonate with a positive throat specimen for COVID-19 [48]. This neonate had early close contact with COVID-19 positive mother, and the specimen was collected 36 h after birth, while the placental and cord blood specimens taken at birth were negative. Yu N et al. collected nasopharyngeal swab from three neonates, of which one was positive for COVID-19 [56]. This specimen was collected 36 h after birth, and that no nucleic acid testing was performed for the placenta, cord blood, or other pregnancy products.

In a cohort study of 33 neonates, there were two neonates with a positive test [66]. Both neonates survived. None of the placenta, cord blood, and other pregnancy products were tested for COVID-19 in this study. Zamanian et al. reported another newborn with a positive test who had fever without any further complications. By the end of the study, the neonate was healthy and stable [73]. Also, the other four COVID-19 positive neonates did not develop any complications and survived [46]. Seventeen studies reported the collection of the amniotic fluid, cord blood, placenta, and breast milk samples, and all tested negative except one amniotic fluid sample. Zamanyan et al. reported a pregnant woman with COVID-19 infection and her positive newborn. Nucleic acid testing was done on the cord blood and amniotic fluid samples [73]. Whereas no viral RNA was detected in the cord blood, the amniotic fluid was positive for viral RNA.

**Pregnancy outcomes**

In a case–control study by Zhang et al., there was no difference between 16 pregnant women with COVID-19 and 45 pregnant women without COVID-19 in terms of pregnancy complications, including eclampsia, fetal distress, and premature rupture of membrane (Table 3) [44].
Discussion

This systematic review included 386 pregnant women with COVID-19. There were 257 cesarean sections and 42 vaginal delivery. This relatively higher rate of cesarean sections would reflect the existence of indications for a cesarean section as well as the role of fear of vertical transmission. Most women represented common symptoms, and two deaths occurred (death rate of 0.5%). While COVID-19 has, to date, caused a total number of 163,097 deaths out of 2.4 million confirmed cases, corresponding to the mortality rate of about 7% [77]. Therefore, compared to the general population, pregnant women have not shown a more aggressive form of COVID-19.

Among the total number of 302 neonates from mothers with COVID-19, there were nasopharyngeal specimens collected from 219 neonates, of which 11 tested positives for SARS-CoV-2. One study reported a positive SARS-CoV-2 for amniotic fluid samples [73]. Interestingly, two studies reported high IgM levels in neonates who tested negative for SARS-CoV2 [43, 69]. Because there is no possibility of IgM transfer through the placenta, this laboratory data can be suggestive of vertical transmission of COVID-19. More studies are required to investigate the potential of COVID-19 to be transmitted via the vaginal route and the possible association between maternal infection with COVID-19 and long-term child health.

Nearly all mothers were healthy women without underlying severe diseases such as diabetes mellitus, cardiovascular disease, and autoimmune diseases. Therefore, further research is necessary to evaluate whether or not ethnicity/race, maternal comorbidities, and pregnancy stage would influence the course of COVID-19 in pregnancy and how this, in turn, would affect delivery complications.

Finally, one crucial issue which remained unresolved is the psychosocial effects of the COVID-19 outbreak on mental health during pregnancy. Pregnant women frequently report psychosocial stress, depression, and panic disorder. In particular, there is a direct correlation between the level of antenatal psychosocial stress and the risk of poor pregnancy outcomes in the manner that the higher the antenatal psychosocial stress, the greater the risk of poor pregnancy outcomes. Therefore, pregnancy might positively impact pregnant women’s psychological status when choosing delivery method. Another possible reason for the difference in results is the method of data gathering. This study is a systematic review including studies pertinent to different countries. At the time of systematic search by the last of April 2020, many studies reporting pregnant women with COVID-19 were case reports, case series, or studies with a low sample size. Still, the two mentioned studies were at a grander scale, which may effectuate the result. On the other hand, in our study, there is no patient from England or Germany, and most of the patients are from China. Although the CRONOS register is a large-scale registry, it lacks clinically important details, such as signs, symptoms, and history, about every individual registered in this program.

Since December 2019, COVID-19 has been a resident of the world. Early efforts ranged from the development of diagnostic assays [80–83] and specific therapeutics [84–102] to optimizing health monitoring [103, 104]. Despite this effort, in addition to our knowledge and experience from the recent outbreaks [105], it mainly relied on non-pharmacological interventions to control the pandemic, e.g., quarantine and social isolation [106, 107]. Such a condition triggers stress [108]. The stress was, in particular, of high level at the time when the outbreak was initiated. Growing knowledge about different aspects of the disease, namely about the origin and pathogenesis of disease varying dependent on the immunogenetic background and the presence of comorbidities [4, 109–120], could protect against the stress and related damage, which is potentially critical in pregnant women and their neonates. Our review included studies conducted in the first six months of the pandemic when there was a high degree of stress and fear. This explains why the cesarean rate we calculated is relatively high, and also one can simply predict its reduction over time.

A major limitation is the lack of data in developing countries. Perinatal care is a crucial issue in less developed countries, while pregnant women in these countries may not have feasible access to health care facilities. Besides, insufficient perinatal care leads to a high rate of perinatal adverse events [122] while worsening during the pandemic. It is, therefore, important to gather enough data on pregnant women and their neonates in these countries. However, when this study was carried out, the data on less developed countries were too scarce, which may be because of lack of diagnostic facilities in these countries, insufficient referring, or reporting system. So further investigations are necessary to discover.
the impact of COVID-19 on perinatal events in developing countries.

**Conclusion**

The present systematic review suggests that clinical features and prognosis of pregnant women with COVID-19 may not be worse than the general population as well as some previous studies [121]. Still, this result should not lead to pregnant women ignore their suspect signs and symptoms to present themselves to medical care centers. It is crucial to provide optimum health care for pregnant women during the COVID-19 pandemic and follow their health status, especially respiratory signs and symptoms. The current evidence suggests that clinical features, diagnosis, and prognosis of COVID-19 in pregnant women are not different from those of the disease reported in society. Despite the high rate of contagion of COVID-19, vertical transmission of the novel coronavirus may remain a missing piece of the puzzle due to a lack of sufficient evidence. International collaboration remains a fundamental component of any future attempt to solve the puzzle [123–127].

**Author contributions** MM: Conceptualized the study, conducted database search, search results screening, detailed review, and prepared the initial draft. AS: Prepared the final draft. NR: Supervised the project and critically appraised the manuscript. All authors have read and approved the manuscript.

**Declarations**

**Conflict of interest** The authors declare that they have no conflicts of interest.

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