



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

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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].

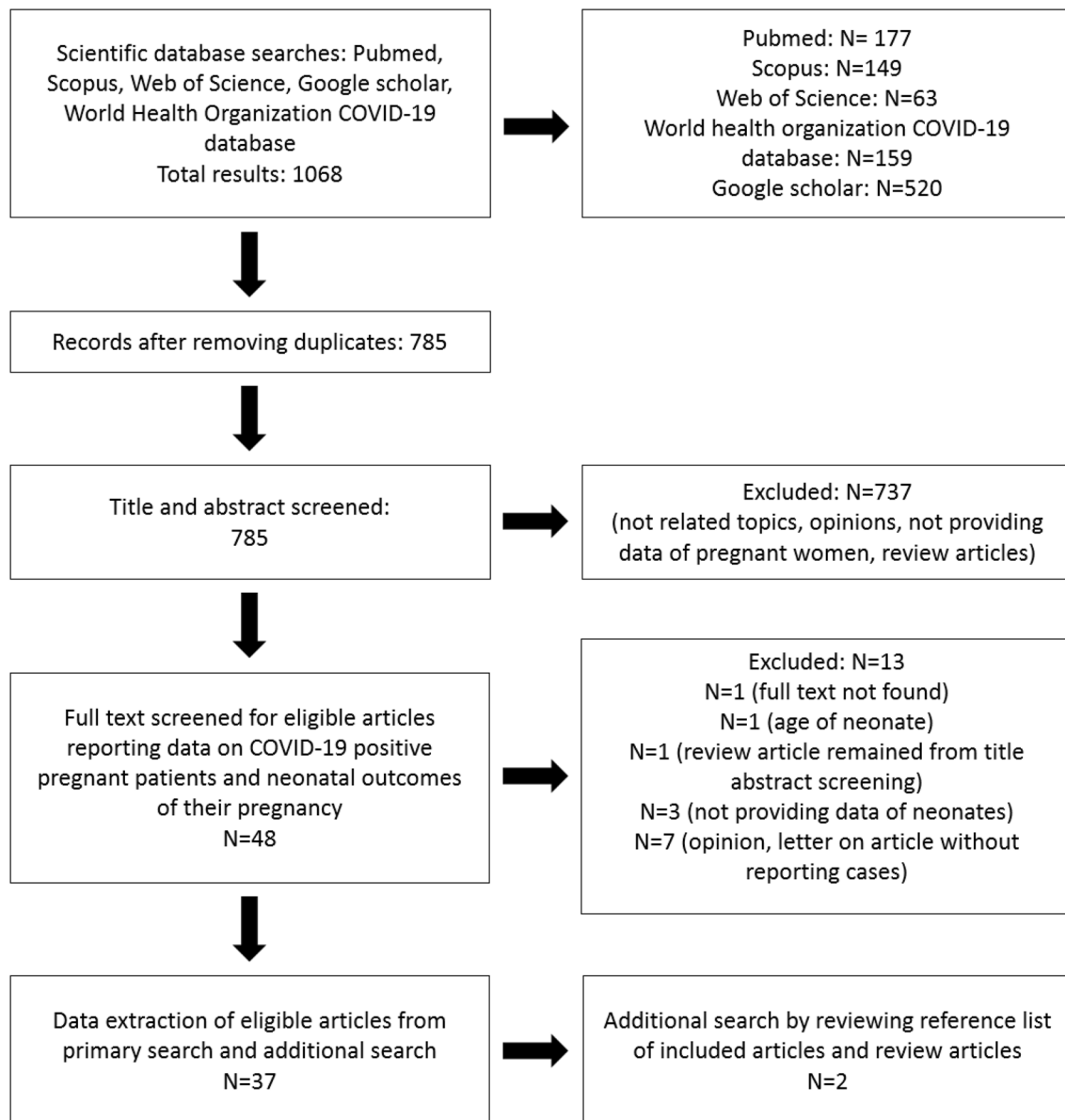


Fig. 1 PRISMA flowchart of the literature search

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

Table 1 Characteristics of pregnant women with COVID-19 included in the systematic review

Article title	Author	Study type	Country	Number of patients	Clinical features of the disease in pregnant patients (=N)	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

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 manifestations and outcome of SARS-CoV-2 infection during pregnancy	Liu et al.	Case Study	China	13	Fever (=10) Dyspnea (=3) Fatigue (=2) Cough (=2) Sore throat (=1) No symptoms (=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 One case still in the hospital
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 Cured and discharged (=8)

Table 1 (continued)

Article title	Author	Study type	Country	Number of patients	Clinical features of the disease in pregnant patients (=N)	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)

Table 1 (continued)

Article title	Author	Study type	Country	Number of patients	Clinical features of the disease in pregnant patients (=N)	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

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
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

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 characteristics of 19 neonates born to mothers with COVID-19	Liu et al.	Retrospective study	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

Table 1 (continued)

Article title	Author	Study type	Country	Number of patients	Clinical features of the disease in pregnant patients (=N)	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 (=N)	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) Cough (=2) A decrease in appetite (=1) Oil intolerance (=1)	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) Cough (=82) Chest tightness (=20) Fatigue (=19) Dyspnea (=8) Diarrhea (=8) Headache (=7) Asymptomatic (=6)	Third trimester (=75) First or second trimester (=43)	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) Vaginal delivery (=5) Spontaneous abortion (=3) Ectopic pregnancy (=2) Induced abortion (=4) Still pregnant (=41)	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
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
								Result	Diagnostic method		
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) Premature with LBW (=1)	No remarkable clinical problem was reported	No complications were reported	Negative	Neonatal throat swab nucleic acid testing	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	Neonatal throat swab nucleic acid testing	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	Neonatal throat swab nucleic acid testing	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	Neonatal throat swab nucleic acid testing and imaging study	Not reported	None of the neonates needed special treatment. No neonatal death

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
								Result	Diagnostic method		
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	Neonatal throat swab nucleic acid testing	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	Neonatal throat swab nucleic acid testing	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	Neonatal throat swab nucleic acid testing	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	Neonatal throat swab nucleic acid testing (36th-hour birth)	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 (=1) Low-grade Fever and diffuse haziness of lungs without patchy consolidation which cured with antibiotic	No complications were reported	Negative	Neonatal throat 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	Neonate test for nCoV-2019		Apgar score	Neonatal outcome
								Result	Diagnostic method		
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 (=5)	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

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
								Result	Diagnostic method		
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	Neonatal throat swab nucleic acid testing	Not reported	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****	5th min Apgar score: 9	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

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
								Result	Diagnostic method		
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 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	Neonate test for nCoV-2019		Apgar score	Neonatal outcome
								Result	Diagnostic method		
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

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
								Result	Diagnostic method		
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

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
								Result	Diagnostic method		
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	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) Preterm (=4)	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
								Result	Diagnostic method		
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	Negative	Neonatal throat swab nucleic acid testing	5th min Apgar score: 8-9	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)			Survived (=299) died (=3)

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 clarified 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

φ Nasopharyngeal swab was taken from 8 neonates

φφ Apgar 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
				Result	Method		
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	No further samples were examined
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	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)	No further samples were examined
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)	No further samples were examined
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	Not reported	Pre-eclampsia (=1) Gestational diabetes (=2)	Not reported

Table 3 (continued)

Article title	Author	Study type	Country	Placental test for nCoV-2019 nucleic acid		Pregnancy complications	Further information
				Result	Method		
Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn	Dong et al.	Case report	China	Not reported	Not reported	Not reported	Mother's vaginal discharge and breastmilk were negative for COVID-19 PCR test result
Lung ultrasound and computed tomographic findings in a pregnant woman with COVID-19	Kalafat et al.	Case report	Turkey	Negative	RT-PCR	Not reported	Breast milk and cord blood were negative
Coronavirus disease 2019 (COVID-19) during pregnancy: a case series	Liu et al.	Case series	China	Negative	RT-PCR	Gestational hypertension	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: a case-control study	Li et al.	Case-control	China	Not reported	Not reported	gestational diabetes mellitus (=3) PROM (=1) gestational hypertension (=3), hypothyroidism (=2), pre-eclampsia (=1) Sinus tachycardia (=1) Fetal distress (=2)	Not reported
A pregnant woman with COVID-19 in Central America	Zambrano et al.	Case report	United States, USA	Not reported	Not reported	gestational hypertension and hypothyroidism	Neonate's blood sample was negative
Pregnancy and perinatal outcomes of women with Coronavirus Disease (COVID-19) pneumonia: a preliminary analysis	Liu et al.	Cross-sectional	China	Not reported	Not reported	Placenta previa (=1)	Not 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	Not reported	Not reported	Uterine scarring (=3) Hypothyroidism (=1)	Not reported
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	Not reported	Not reported	PROM (=3)	Not reported

Table 3 (continued)

Article title	Author	Study type	Country	Placental test for nCoV-2019 nucleic acid		Pregnancy complications	Further information
				Result	Method		
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	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	Amniotic fluid, vaginal mucosa, cord blood, and breast milk were all negative
Severe COVID-19 during pregnancy and possible vertical transmission	Alzamora et al.	Case report	The United States, USA	Not reported	Not reported	Diabetes mellitus	Not reported
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	Cord blood was negative, but Amniotic fluid was positive
Vaginal delivery report of a healthy neonate born to a convalescent mother with COVID-19	Xiong et al.	Case report	China	Negative	RT-PCR	Not reported	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	Not 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	Not reported	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	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	Not reported

Table 3 (continued)

Article title	Author	Study type	Country	Placental test for nCoV-2019 nucleic acid		Pregnancy complications	Further information
				Result	Method		
Clinical features and outcomes of pregnant women suspected of Coronavirus Disease 2019	Yang et al.	Case-control	China	Not reported	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	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	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	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	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	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	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	Not reported
Clinical characteristics of pregnant women with Covid-19 in Wuhan, China	Chen et al.	Retrospective study	China	Not reported	Not reported	Not reported	Breast milk of three mothers were negative for the virus
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 be complicated during the COVID-19 outbreak, even if women do not get infected by the virus.

In this study, from 386 parturient women with COVID-19, 257 out of 299 patients gave birth by cesarean section, which means the cesarean section rate among these patients was about to 86%, which is very high. In a national cohort study reported by Knight et al., the cesarean rate in pregnant women with COVID-19 in the United Kingdom was about 59% [78]. In Germany, the CRONOS register

website established to gather comprehensive data on mothers with COVID-19 who give birth around this country reports cesarean rate as about 37.5% by the last of January 2021 [79]. These national reports come from two highly developed countries equipped with the best available strategies to control the COVID-19 and related stress. It may 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 studied 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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