The impact of COVID-19 on pregnancy and neonatal health: a systematic review

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Abstract

Background: In December 2019, a novel coronavirus disease (COVID-19) emerged in Wuhan, China. With an incredible rate of contagion, it has reached all over the world, with more than 2 million confirmed cases at the mid of April. However, the vertical transmission of COVID-19 is uncertain. This is a systematic review of published studies concerning pregnant women with confirmed COVID-19 and their neonates.

Methods: We performed a systematic search in Pubmed, Web of Sciences, Google Scholar, Scopus, and World Health Organization (WHO) COVID-19 database to find articles reporting clinical data of COVID-19-positive pregnant women and their neonates.

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 of which 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.
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. As of April 21, 2020, COVID-19 has reached all 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 [1]. Therefore, COVID-19 is, in general, a life-threatening condition.

COVID-19 mainly involves the respiratory system, where its involvement can cause a wide range of symptoms from a common cold to severe respiratory distress [2]. 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. However, as for other infectious conditions, immune dysregulation might increase the risk of severe illness and death from COVID-19.

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 [3]. It remained unclear whether or not this potentially fatal virus can vertically be transmitted and what are the possible effects of disease on the pregnancy outcomes.

Methods

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)).

**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 [4-10], three studies lacked data on neonates or vertical transmission [11-13], one study reported a 17-day neonate who had exposure to parents complaining of fever and cough [14], one study was not original research [15], and the full-text was not available for one article [16]. Also, we carried out an additional search through reviewing reference lists of 35 included articles from systematic search and
Tables 1–3 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 [18, 19]. 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 included myalgia, diarrhea, dyspnea, headache, and chest tightness. There were two women with specific presentations: one with Cholecystitis [26] and another with oil intolerance [44].

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 [26, 29, 31].

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) [17, 19, 29, 34, 36, 40, 42, 50, 51]. Two of these ten patients died from severe pneumonia and multiple organ dysfunction [42, 50].

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 [19, 36]. Chen et al. reported that 38 of 63 cases who underwent cesarean sections claimed to have a fear of COVID-19 [29]. 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 [29].

**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 [18, 33]. 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 [42]. 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 [26]. 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 [34]. 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 [51]. 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 two days. This neonate had an Apgar score of 3, 4, and 4 at the first, fifth, and tenth minute after delivery and required resuscitation [43]. 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-minute 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 [23]. This neonate had early close contact with COVID-19 positive mother, and the specimen was collected 36 hours 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 [32]. This specimen was collected 36 hours 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 [43]. 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 [50]. Also, the other four COVID-19 positive neonates did not develop any complications and survived [21]. 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 [50]. 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) [54].

**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 163097 deaths out of 2.4 million confirmed cases, corresponding to the mortality rate of about 7% [55]. 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 [50]. Interestingly, two studies reported high IgM levels in neonates who tested negative for SARS-CoV2 [18, 46]. 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.

Conclusion
In conclusion, 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 the 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.

Declarations

Ethics approval and consent to participate
Not applicable

Consent for publication
Availability of data and materials
Not applicable

Competing interests
The authors declare that they have no conflicts of interest.

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Authors' contributions
M.M. conceptualized the study, conducted database search, search results screening, detailed review, data extraction, and prepared the initial draft. N.R. supervised the project and critically appraised the manuscript. All authors have read and approved the manuscript.

Acknowledgments
Not applicable

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Tables

Table 1. recordings of pregnant patients with COVID-19

| Article Title | Author | Study type | Country | Number of patients | Clinical features of disease in pregnant patients |
|---------------|--------|------------|---------|--------------------|--------------------------------------------------|
| Pregnant women with new coronavirus infection: a clinical characteristics and placental pathological analysis of three cases | Chen S et. Al. | Case study | China | 3 | Fever (=3) |
| Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia | Zhu H et. Al. | Case study | China | 9 | Fever (=7)  
Cough (=4)  
Cholecystitis (=1)  
Diarrhea (=1) |
| Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. | Chen H et. Al. | Case study | China | 9 | Fever (=7)  
Cough (=4)  
Myalgia (=3)  
Sore throat (=2)  
Malaise (=2) |
| Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province | Zhang L et. Al. | case-control | China | 16 (45 Controls) | 15 moderate case and 1 severe case of pneumonia |
| Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy | Liu Y et. Al. | Case Study | China | 13 | Fever (=10) Dyspnea (=3) Fatigue (=2) Cough (=2) Sore throat (=1) No symptoms (=1) |
| Lack of Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, China | Li Y et. Al. | Case Report | China | 1 | Cough and temperature of 37.2°C |
| A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery | Wang X Et. al. | Case Report | China | 1 | Fever |
| A case report of neonatal COVID-19 infection in China | Wang S Et. al. | Case report | China | 1 | Fever |
| Perinatal Transmission of COVID-19 Associated SARS-CoV-2: Should We Worry? | Fan C et al. | Case report | China | 2 | Fever (=2) Nasal congestion (=2) Chill (=1) Sore throat (=1) Abdominal rush (=1) |
| Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia | Chen S et al. | Case series | China | 5 | Fever (=5) Coryza (=1) Sputum (=1) Cough (=1) |
| Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn | Dong L et al. | Case report | China | 1 | Fever and Nasal congestion |
| Lung ultrasound and computed tomographic findings in pregnant woman with COVID-19 | Kalafat E et al. | Case report | Turkey | 1 | Cough and Shortness of breath |
| Coronavirus disease 2019 (COVID-19) during pregnancy: a case series | Liu W et al. | Case series | China | 3 | Fever (=2) Cough (=1) |
| Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study | Li N et al. | Case-control | China | 16 | Fever (=12) |
| Study Title                                                                 | Authors            | Studies Type                      | Country | Total Cases | Symptoms                                                                                   |
|----------------------------------------------------------------------------|--------------------|----------------------------------|---------|-------------|-------------------------------------------------------------------------------------------|
| A pregnant woman with COVID-19 in Central America                          | Zambra no L et al. | Case report                      | America | 1           | Fever, headache, myalgia and cough                                                          |
| Pregnancy and Perinatal Outcomes of Women with Coronavirus Disease: (COVID-19) Pneumonia - A Preliminary Analysis | Liu D et al.       | Cross sectiona l                 | 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) |
| Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study | Yu N et al.        | Retrospective study              | China   | 7           | Fever (=6) Cough (=1) Dyspnea (=1) Diarrhea (=1)                                           |
| Neonatal Early-Onset Infection with SARS CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China | Zeng L et al.      | Cohort study                     | China   | 33          | Fever on admission (=8) Cough (=10) Post-partum fever (=5)                                  |
| Mortality of a pregnant patient diagnosed with COVID-19: A case report with clinical, radiological, and histopathological findings | Karami P et al     | Case report                      | Iran    | 1           | Fever Myalgia cough                                                                         |
| Unlikely SARS-CoV-2 vertical transmission from mother to child: A case report | Peng Z et al.      | Case report                      | China   | 1           | Fever Fatigue shortness of breath                                                          |
| Severe COVID-19 during Pregnancy and Possible Vertical Transmission         | Alzamor a M et al  | Case report                      | America | 1           | Fever (low grade) Shortness of breath malaise                                               |
| Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission | Zamani an M et al  | Case Report                      | Iran    | 1           | Fever Myalgia Nausea Cough Dyspnea Anorexia                                                |
| Vaginal Delivery Report of a Healthy Neonate Born to a Convalescent Mother with COVID-19 | Xiong X et al      | Case Report                      | China   | 1           | Fever Cough Shivering                                                                     |
| Study Title                                                                 | Authors          | Study Type      | Location | N   | Symptoms                                                                 |
|----------------------------------------------------------------------------|------------------|-----------------|----------|-----|--------------------------------------------------------------------------|
| Association of COVID-19 infection with pregnancy outcomes in healthcare     | Khan S et al.    | Case series     | China    | 17  | Cough (=6) Fever (=3) Diarrhea (=3) Nasal congestion (=2) Shortness of   |
| workers and general women                                                  |                  |                 |          |     | breath (=2) Sputum production (=1)                                       |
| Impact of COVID-19 infection on pregnancy outcomes and the risk of         | Khan S et al.    | Case report     | China    | 3   | Fever (=2) Cough (=3) Chest tightness (=1)                                |
| maternal-to-neonatal intrapartum transmission of COVID-19 during natural    |                  |                 |          |     | birth                                                      |
| delivery                                                                    |                  |                 |          |     |                                                                          |
| Clinical characteristics of 19 neonates born to mothers with COVID-19       | Liu W et al.     | Retrospective   | China    | 19  | Fever (=11) Cough (=5) Diarrhea (=2)                                      |
|                                                                              |                  | study          |          |     |                                                                          |
| COVID-19 infection among asymptomatic and symptomatic pregnant women:      | Breslin N et al. | Cohort study    | America  | 43  | No symptoms (=14) Fever (=14) Cough (=19) Myalgias or fatigue (=11)     |
| Two weeks of confirmed presentations to an affiliated pair of New York     |                  |                 |          |     | Dyspnea (=7) Chest pain (=5) Headache (=8)                                |
| City hospitals                                                             |                  |                 |          |     |                                                                          |
| Clinical Features and Outcomes of Pregnant Women Suspected of Coronavirus    | Yang H et al.    | Case-control    | China    | 13  | Prenatal Fever (=2) Postpartum Fever (=8) Cough (=2)                      |
| Disease 2019                                                               |                  |                 |          |     |                                                                          |
| Asymptomatic COVID-19 in pregnant woman with typical chest CT manifestation| Renbin Z et al.  | Case report     | China    | 1   | Asymptomatic                                                              |
| a case report                                                              |                  |                 |          |     |                                                                          |
| Chest CT Findings in a Pregnant Patient with 2019 Novel Coronavirus Disease| Liao X et al.    | Case report     | China    | 1   | Fatigue Cough                                                             |
| Infants Born to Mothers With a New Coronavirus (COVID-19)                  | Chen Y et al.    | Case report     | China    | 4   | Fever (=3) Cough (=2) Headache (=2)                                      |
|                                                                              |                  |                 |          |     |                                                                          |
| Anesthetic Management for Emergent Cesarean Delivery in a Parturient with   | Song L et al.    | Case report     | China    | 1   | Fever Cough Myalgia                                                      |
| Recent Diagnosis of Coronavirus Disease 2019 (COVID-19): A Case Report      |                  |                 |          |     |                                                                          |
| Study Title                                                                 | Authors                        | Study Type      | Location | Total Number of Cases | Symptoms Listed                           |
|---------------------------------------------------------------------------|-------------------------------|-----------------|----------|-----------------------|-------------------------------------------|
| Clinical characteristics and risk assessment of newborns born to mothers with COVID-19 | Yang P et al.                 | Case series     | China    | 7                     | (Fever =5, Cough =1, Diarrhea =1, Abdominal pain =1) |
| COVID-19 in pregnancy: early lessons                                      | Breslin N et al.              | Case series     | America  | 7                     | (Fever =2, Cough =3, Myalgia =3, Headache =2, Asymptomatic =2) |
| Antibodies in Infants Born to Mothers With COVID-19 Pneumonia            | Zeng H et al.                 | Case study      | China    | 6                     | Mild clinical presentations (=6)           |
| Novel Coronavirus Infection in Newborn Babies Under 28 Days in China      | Zhang Z et al.                | Case series     | China    | 4                     | (Fever =3, Cough =2, Decrease in appetite (=1), Oil intolerance (=1) |
| Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China  | Chen L et al.                 | Retrospective study | China    | 118                   | (Fever =84, Cough =82, Chest tightness =20, Fatigue =19, Dyspnea =8, Diarrhea =8, Headache =7, Asymptomatic =6) |
| 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) |

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. recordings of neonates born from patients with COVID-19

| Article Title                                                                 | Author          | Study type | Country | Number of neonates | Neonatal maturity (=N) | Neonatal Clinical presentations (=N) |
|-------------------------------------------------------------------------------|-----------------|------------|---------|--------------------|------------------------|-------------------------------------|
| Pregnant women with new coronavirus infection: a clinical characteristics and placental pathological analysis of three cases | Chen S et. Al.  | Case study | China   | 3                  | mature infants (=2) premature with LBW (=1) | No remarkable problem wa: |
| Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia    | Zhu H et. Al.   | Case study | China   | 10 (2 twins)      | 4 full terms, 6 premature (2 SGA AND 1 LGA) | Respiratory GI tract sym Fever (=2) Increased ht Vomiting (= |
| Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. | Chen H et. Al.  | Case study | China   | 9                  | Full term babies (=5), birth at 36th week of gestational age (=4*) | No remarkable problem wa: |
| Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province | Zhang L et. Al. | case-control | China   | 10                 | Full term babies (=9), Premature babies (=1) | 3 neonate d bacterial pn |
| Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy | Liu Y et. Al.   | Case Study | China   | 10                 | full term babies (=4), Premature babies (=6) | 9 neonates : no remarkable problem, 1 died due t MODS |
| Lack of Vertical Transmission of Severe Acute Respiratory                   | Li Y et. Al.    | Case Report | China   | 1                  | Premature baby in 35th | No remarkable problem wa: |
| Study Title | Authors | Publication Type | Country | GA Week(s) | Outcome(s) | Additional Information |
|-------------|---------|------------------|---------|-------------|------------|------------------------|
| A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery | Wang X et al. | Case report | China | 1 | Premature baby in 30th week of GA | No remarkable problem was reported |
| A case report of neonatal COVID-19 infection in China | Wang S et al. | Case report | China | 1 | Full term baby | COVID-19 Pneumonia |
| Perinatal Transmission of COVID-19 Associated SARS-CoV-2: Should We Worry? | Fan C et al. | Case report | China | 2 | Full term neonate (=1) 36th week and 5 days of GA (=1) | Mild neonatal and lymphopenia Low grade fever and diffuse haziness without patchy consolidation with antibiotics |
| Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia | Chen S et al. | Case series | China | 5 | Full term neonate (=5) | Fetal tachycardia |
| Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn | Dong L et al. | Case report | China | 1 | 34 weeks and 5 days | Elevated IgM |
| Lung ultrasound and computed tomographic findings in pregnant woman with COVID-19 | Kalafat E et al. | Case report | Turkey | 1 | 35 weeks and 3 days | No remarkable problem was reported |
| Title: Coronavirus disease 2019 (COVID-19) during pregnancy: a case series | Liu W et al. | Case series | China | 3 | Full term neonates (=3) | Chorioamnionic meconium syndrome (=1) |
| Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study | Li N et al | Case-control | China | 17 | Full term (=13) Premature (=4) LBW (=3) | Intrauterine growth restriction (=2) |
| A pregnant woman with COVID-19 in Central America | Zambrano L et al. | Case report | America | 1 | 32 weeks of GA | No remarkable problem was reported |
| Study Title                                                                 | Authors          | Study Design     | Country | Study Group   | Clinical Features/Outcomes                                                                 |
|---------------------------------------------------------------------------|------------------|------------------|---------|---------------|------------------------------------------------------------------------------------------|
| Pregnancy and Perinatal Outcomes of Women with Coronavirus Disease (COVID-19) Pneumonia A Preliminary Analysis | Liu D et al.     | Cross sectional  | China   | 11            | Full term (=8) Preterm delivery (=3) No remarkable problem was reported                   |
| Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study | Yu N et al.      | Retrospective    | China   | 7             | Full term (=7) Mild shortness of breath (=2)                                              |
| Neaternal Early-Onset Infection with SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China | Zeng L et al.    | Cohort study     | China   | 33            | Full term (=29) Preterm (=4) Fever (=2); 1 positive COVID-19                              |
| Mortality of a pregnant patient diagnosed with COVID-19: A case report with clinical, radiological, and histopathological findings | Karami P et al.  | Case report      | Iran    | 1             | Stillbirth                                                                               |
| Unlikely SARS-CoV-2 vertical transmission from mother to child: A case report | Peng Z et al.    | Case report      | China   | 1             | Preterm                                    Mild respiratory                            |
| Severe COVID-19 during Pregnancy and Possible Vertical Transmission         | Alzamora M et al| Case report      | America | 1             | Preterm                                    Mild respiratory And sporadic                        |
| Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission | Zamania M et al  | Case Report      | Iran    | 1             | Preterm                                    Fever                                      |
| Vaginal Delivery Report of a Healthy Neonate Born to a Convalescent Mother with COVID-19 | Xiong X et al.   | Case Report      | China   | 1             | Full term                                  No remarkable problem was reported           |
| Study Title                                                                 | Authors          | Study Type  | Country | N    | Gestation Status | Additional Information |
|---------------------------------------------------------------------------|------------------|-------------|---------|------|------------------|------------------------|
| Association of COVID-19 infection with pregnancy outcomes in healthcare workers and general women | Khan S et al.    | Case series | China   | 17   | Full term (14) Preterm (3) | Neonatal pneumonia 2 case of CC one of them pneumonia |
| Impact of COVID-19 infection on pregnancy outcomes and the risk of maternal-to-neonatal intrapartum transmission of COVID-19 during natural birth | Khan S et al.    | Case report | China   | 3    | Full term (2) Preterm (1) | No remarkable problem wa: |
| Clinical characteristics of 19 neonates born to mothers with COVID-19     | Liu W et al.     | Retrospective study | China   | 19   | Full term (17) Preterm (2) | No remarkable problem wa: |
| COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals | Breslin N et al. | Cohort study | America | 18   | Full term (17) Premature (1) | Respiratory One patient congenital d |
| Clinical Features and Outcomes of Pregnant Women Suspected of Coronavirus Disease 2019 | Yang H et al.    | Case-control | China   | 20   | Mean ± SD GA: 38.2±2.3 | Fever (1 fr positive mot |
| Asymptomatic COVID-19 in pregnant woman with typical chest CT manifestation: a case report | Renbin Z et al.  | Case report  | China   | 1    | Full term | No remarkable problem wa: |
| Chest CT Findings in a Pregnant Patient with 2019 Novel Coronavirus Disease | Liao X et al.    | Case report  | China   | 1    | Preterm | No remarkable problem wa: |
| Infants Born to Mothers With a New Coronavirus (COVID-19)                  | Chen Y et al.    | Case report  | China   | 4    | Full term (4) | No remarkable problem wa: |
| Anesthetic Management for Emergent Cesarean Delivery in a Parturient with Recent Diagnosis of Coronavirus Disease 2019 (COVID-19): A Case Report | Song L et al.    | Case report  | China   | 1    | Preterm | No remarkable problem wa: |
| Article Title                                                                 | Author            | Study type          | Country  | placental test for nCoV nucleic acid | Result         | Method  |
|------------------------------------------------------------------------------|-------------------|---------------------|----------|--------------------------------------|----------------|---------|
| Clinical characteristics and risk assessment of newborns born to mothers with COVID-19 | Yang P et al.     | Case series         | China    |                                      | Full term (=3) | Preterm (=4) | Mild respiratory syndrome (=2) | Vomiting and hypoglycemia |
| COVID-19 in pregnancy: early lessons                                          | Breslin N et al.  | Case series         | America  |                                      | Full term (=2) |          | No remarkable problem was reported |
| Antibodies in Infants Born to Mothers With COVID-19 Pneumonia                 | Zeng H et al.     | Case study          | China    |                                      | Not reported   |          | No remarkable problem was reported*** |
| Novel Coronavirus Infection in Newborn Babies Under 28 Days in China          | Zhang Z et al.    | Case series         | China    |                                      | Full term (=2) |          | Shortness of breath |
| Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China      | Chen L et al.     | Retrospective study | China    |                                      | Full term (=56) | Preterm (14) | No remarkable problem was reported |
| Total results                                                                 |                   |                     |          | Total number of neonates: 302         | Full term      | (=210/276) | Premature (=65/276) stillbirth (=1) |

Table 3. pregnancy outcomes of COVID-19
| Study Title                                                                 | Authors            | Study Type     | Country | Test Results | Methodology |
|----------------------------------------------------------------------------|--------------------|----------------|---------|--------------|-------------|
| Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records | Chen H et. Al.     | Case study     | China   | Not reported |            |
| Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province | Zhang L et. Al.    | case-control   | China   | Not reported |            |
| Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy | Liu Y et. Al.      | Case Study     | China   | Not reported |            |
| Lack of Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, China | Li Y et. Al.       | Case Report    | China   | Negative     | RT-PCR     |
| A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery | Wang X Et. al.     | Case report    | China   | Negative     | RT-PCR     |
| A case report of neonatal COVID-19 infection in China                        | Wang S Et. al.     | Case report    | China   | Negative     | RT-PCR     |
| Perinatal Transmission of COVID-19 Associated SARS-CoV-2: Should We Worry?  | Fan C et al.       | Case report    | China   | Negative     | RT-PCR     |
| Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia    | Chen S et al.      | Case series    | China   | Not reported |            |
| Possible Vertical Transmission of SARS-CoV-2 From an Infected Mother to Her Newborn | Dong L et al.     | Case report    | China   | Not reported |            |
| Lung ultrasound and computed tomographic findings in pregnant woman with COVID-19 | Kalafat E et al.  | Case report    | Turkey  | Negative     | RT-PCR     |
| Coronavirus disease 2019 (COVID-19) during pregnancy: a case series         | Liu W et al.       | Case series    | China   | Negative     | RT-PCR     |
| Study Title                                                                 | Authors            | Study Type          | Country   | Outcome reporting | Methodological details |
|---------------------------------------------------------------------------|--------------------|---------------------|-----------|-------------------|------------------------|
| Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study | Li N et al         | Case-control        | China     | Not reported      | Not reported           |
| A pregnant woman with COVID-19 in Central America                         | Zambrano L et al.  | Case report         | America   | Not reported      | Not reported           |
| Pregnancy and Perinatal Outcomes of Women with Coronavirus Disease (COVID-19) Pneumonia A Preliminary Analysis | Liu D et al.       | Cross sectional     | China     | Not reported      | Not reported           |
| Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study | Yu N et al.        | Retrospective study | China     | Not reported      | Not reported           |
| Neonatal Early-Onset Infection with SARS-CoV-2 in 33 Neonates Born to Mothers With COVID-19 in Wuhan, China | Zeng L et al.      | Cohort study        | China     | Not reported      | Not reported           |
| Mortality of a pregnant patient diagnosed with COVID-19: A case report with clinical, radiological, and histopathological findings | Karami P et al     | Case report         | Iran      | Not reported      | Not reported           |
| Unlikely SARS-CoV-2 vertical transmission from mother to child: A case report | Peng Z et al.      | Case report         | China     | Negative          | RT-PCR                 |
| Severe COVID-19 during Pregnancy and Possible Vertical Transmission        | Alzamora M et al.  | Case report         | America   | Not reported      | Not reported           |
| Preterm delivery in pregnant woman with critical COVID-19 pneumonia and vertical transmission | Zamanian M et al   | Case Report         | Iran      | Not reported      | Not reported           |
| Vaginal Delivery Report of a Healthy Neonate Born to a Convalescent Mother with COVID-19 | Xiong X et al      | Case Report         | China     | Negative          | RT-PCR                 |
| Association of COVID-19 infection with pregnancy outcomes in healthcare workers and general women | Khan S et al.      | Case series         | China     | Not reported      | 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 S et al       | Case report         | China     | Not reported      | Not reported           |
| Clinical characteristics of 19 neonates born to mothers with COVID-19       | Liu W et al        | Retrospective study | China     | Not reported      | Not reported           |
| Study Title                                                                 | Authors          | Study Design | Location | Data Availability | Summary |
|---------------------------------------------------------------------------|------------------|--------------|----------|-------------------|---------|
| COVID-19 infection among asymptomatic and symptomatic pregnant women: Two weeks of confirmed presentations to an affiliated pair of New York City hospitals | Breslin N et al. | Cohort study | America | Not reported | Not reported |
| Clinical Features and Outcomes of Pregnant Women Suspected of Coronavirus Disease 2019 | Yang H et al. | Case-control | China | Not reported | Not reported |
| Asymptomatic COVID-19 in pregnant woman with typical chest CT manifestation: a case report | Renbin Z et al. | Case report | China | Not reported | Not reported |
| Chest CT Findings in a Pregnant Patient with 2019 Novel Coronavirus Disease | Liao X et al. | Case report | China | Negative | RT-PCR |
| Infants Born to Mothers With a New Coronavirus (COVID-19)                 | Chen Y et al.    | Case report  | China | Not reported | Not reported |
| Anesthetic Management for Emergent Cesarean Delivery in a Parturient with Recent Diagnosis of Coronavirus Disease 2019 (COVID-19): A Case Report | Song L et al.    | Case report  | China | Not reported | Not reported |
| Clinical characteristics and risk assessment of newborns born to mothers with COVID-19 | Yang P et al. | Case series  | China | Not reported | Not reported |
| COVID-19 in pregnancy: early lessons                                    | Breslin N et al. | Case series  | America | Not reported | Not reported |
| Antibodies in Infants Born to Mothers With COVID-19 Pneumonia             | Zeng H et al.    | Case study   | China | Not reported | Not reported |
| Novel Coronavirus Infection in Newborn Babies Under 28 Days in China      | Zhang Z et al.   | Case series  | China | Not reported | Not reported |
| Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China  | Chen L et al.    | Retrospective study | China | Not reported | Not reported |
| Total results                                                             |                  |              |          | All samples examined were negative | RT-PCR |
RT-PCR: Reverse transcription polymerase chain reaction

PROM: Premature rupture of membranes

Figures

Scientific database searches: Pubmed, Scopus, Web of Science, Google scholar, World Health Organization COVID-19 database
Total results: 1068

Records after removing duplicates: 785

Title and abstract screened: 785

Full text screened for eligible articles reporting data on COVID-19 positive pregnant patients and neonatal outcomes of their pregnancy
N=48

Excluded: N=737
(not related topics, opinions, not providing data of pregnant women, review articles)

Excluded: N=13
N=1 (full text not found)
N=1 (age of neonate)
N=1 (review article remained from title abstract screening)
N=3 (not providing data of neonates)
N=7 (opinion, letter on article without reporting cases)

Data extraction of eligible articles from primary search and additional search
N=37

Additional search by reviewing reference list of included articles and review articles
N=2

Figure 1

PRISMA flowchart of the literature search