Abstract

**Background and Aims:** The outbreak of coronavirus disease 2019 (COVID-19) over the past year has affected public health worldwide. During pregnancy, the maternal immune system and inflammatory responses are widely suppressed. Pregnancy-related immune system suppression could make the mother vulnerable to infectious diseases like SARS-COV-2. However, current data suggest little to no possibility of COVID-19 transmission in pregnant women to the fetus during pregnancy or childbirth. This systematic review focused on the possible complications of COVID-19 infection in the fetus and newborn babies including the possibility and evidence of vertical transmission by reviewing articles published during the first year of the COVID-19 pandemic.

**Methods:** We conducted a systematic search using keywords on PubMed, Embase, and Scopus databases. The studies followed a title/abstract and a full-text screening process, and the eligible articles were included in the study.

**Results:** In total, 238 published papers were identified using a systematic search strategy (44 articles met the inclusion criteria and were included in the final review). In all studies, a total of 2375 women with signs and symptoms of COVID-19, who were in the second and third trimester of pregnancy, were assessed; mild to moderate pneumonia was one of the most common symptoms. Seventy-three percent of the women did not present any comorbidity, 19% had a fever, 17% had to cough as the most frequent clinical signs and symptoms, 7.5% had pulmonary changes with chest scans, 8% had increased C reactive protein, and 9.4% had decreased lymphocytes (lymphocytopenia). A total of 2716 newborns and fetal were assessed; the delivery method of 1725 of them was reported, 913 (53%) through C-section delivery, and 812 through normal vaginal delivery (47%). Of total newborns, 13 died (five died along with the mother), and 1965 were tested for SARS-CoV-2: 118 tested positive. In a study, vertical transmission in seven cases was reported in total of 145 cases assessed.
Conclusion: It appeared that most pregnant COVID patients were mildly ill, and there is currently no convincing evidence to support the vertical transmission of COVID-19 disease. Therefore, neonates do not represent any additional risk for adverse outcomes neither during the prenatal period nor after birth.

KEYWORDS
COVID-19, fetus, neonatal, newborn, prenatal, SARS-CoV-2

INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19) over the past year has affected public health worldwide and led to many deaths.1,2 As of January 8, 2021, a total of 86 436 449 clinically confirmed COVID-19 positive and 1 884 341 death reported globally.3 Mothers and newborns are at-risk populations and need special attention.4

During pregnancy, the maternal immune system and inflammatory responses are widely suppressed, and the fetus in the womb without the mother’s immune system attacking.5 Pregnancy-related immune system suppression could make the mother vulnerable to infectious diseases and increases the risk of being infected, including coronavirus-related diseases.6-9 Studies exploring the indirect adverse events of COVID-19 on the population have reported that pregnant women are at greater potential risk.8-10 Maternal death, stillbirth, ruptured ectopic pregnancy, and maternal depression have had significant increase during the pandemic.11 albeit the symptoms and severity of COVID-19 are as mild in most pregnant women as in the general population.12-15 Moreover, the findings of a study showed asymptomatic infection in one-third of pregnant women.16 The most common symptoms reported in COVID-19-positive pregnant women are fever, shortness of breath, diarrhea, and cough. In some severe cases, mechanical ventilation was performed17-22 and maternal deaths were reported.23-25 In a systematic review of the effects of COVID-19 on perinatal and maternal outcomes, the findings of studies from high-income countries (HICs) and low-income and middle-income countries (LMICs) showed a significant heterogeneity in the incidence of pregnancy complications; meaning that the adverse outcomes were much higher in LMICs. It also found that lack of immediate healthcare response in LMICs was responsible for heterogeneity of most of the outcomes rather than the stringent lockdown measures. The COVID-19 pandemic has manifested several lacunae in healthcare systems around the world, widening the gap between HICs and LMICs.11

There are still many challenges related to SARS-CoV-2 infection in newborns and approaching the respiratory involvement in the case of infection.26 However, the possibility of COVID-19 transmission from pregnant women to the fetus during pregnancy or childbirth is still unknown.27,28 The consequences of pregnancy-related diseases could be detrimental to both mother and fetus.29,30 Although most studies considered the vertical transmission unlikely,31-37 a recent case report of a newborn with a positive early test indicated the possibility of vertical transfer in the uterus.38 Additionally, four births with COVID-19 have been reported in recent studies.24,39,40 Several clinical symptoms such as fever,24,31 disseminated intravascular coagulation, feeding intolerance, bleeding, cyanosis,31 birthing problems,31,35 rash, edema, dyspnea,31,41 and pneumonia39 have been reported in neonates born from mothers infected with COVID-19.

One of the World Health Organization (WHO) millennium development goals is to preserve pregnant mother’s and babies’ lives; therefore, knowing how coronavirus affects maternal and fetal health can help to prevent complications. This systematic review focused on the possible complications of COVID-19 infection in the fetus and newborns by reviewing articles published during the SARS-CoV-2 pandemic in the past year.

METHODS

2.1 Design

We conducted a systematic search using keywords on PubMed, Embase, and Scopus databases. The identified records were screened by title/abstract to meet the inclusion criteria. Following this step, the full text of the included studies were evaluated based on the parameters mentioned in Section 2.2. Two researchers then extracted the data of the retrieved articles for drafting this systematic review.

2.2 Search strategy

We utilized the following search strategy using the approach mentioned in [C].

A. [Neonatal*] OR [Newborn*] OR [Maternal*] OR [Prenatal*] OR [Fetus*] OR [Fetal*] OR [Embryo*] (Title/Abstract)
B. [Covid-19] OR [SARS-CoV-2] OR [SARS-CoV2] OR [Novel coronavirus] OR [2019-nCoV] (Title/Abstract)
C. [A] AND [B]

2.3 Eligibility criteria

We performed the systematic search and included the original studies cohering to the aim of our study from December 2019 to August 2021.
| ID | Study          | Country | Maternal age (years) | GA on admission (weeks) | Symptoms                                      | Other symptoms                                                                                           |
|----|----------------|---------|----------------------|-------------------------|-----------------------------------------------|----------------------------------------------------------------------------------------------------------|
| 1  | Zheng et al.44 | China   | 33, 29               | 36 + 3, 39 + 4          | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Diarrhea, GI symptoms, Malaise | Limb asthenia, fetal distress                                                                           |
| 2  | Zamanian et al.24 | Iran    | 22                   | 32                      | —                                              | Myalgia, anorexia, nausea (maternal death)                                                              |
| 3  | Yu et al.45     | China   | 30–34                | 37–41 + 2               | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 4  | Wu et al.46     | China   | 29, 59               | 35–36, 37–38, 39–41     | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Diarrhea, GI symptoms, Malaise, Vomiting, PROM | Fetal intrauterine hypoxia—Nasal obstruction, PROM, Threatened abortion                                  |
| 5  | Wu X47          | China   | 24–37                | 6–40                    | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Diarrhea, GI symptoms, Malaise, Vomiting, PROM | Fetal intrauterine hypoxia—Nasal obstruction, PROM, Threatened abortion                                  |
| 6  | Spencer et al.48 | USA     | 33                   | 39                      | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 7  | Santana-Cabrera49 | Spain   | 44                   | 29 + 2                  | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 8  | Salvatore et al.50 | USA      | NR                   | Median 38 (27–41)       | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 9  | Pirjani et al.51 | Iran    | 30.97                | 36.57                   | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 10 | Oncel et al.52  | Turkey   | NR                   | 37, 35                  | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 11 | Liu et al.53    | China    | 26–38                | 35 + 2–41 + 2           | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 12 | Liu et al.54    | China    | 32                   | 37.41                   | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 13 | Lowe and Bopp55 | Australia | 31                   | 40 + 2                  | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 14 | Martinez-Perez et al.56 | Spain | 35 (19–43), 33 (19–48) | 39 + 1, 38 + 3 | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 15 | Khan et al.23   | China    | 27–34                | 31–39                   | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 16 | Koumoutsea et al.57 | Canada   | 40, 23               | 35 + 3, 35 + 2          | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 17 | Khan et al.39   | China    | 28, 33, 27           | 34 + 6, 39 + 1, 38 + 2  | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 18 | Juusela et al.58 | USA      | 26, 45               | 39 + 2, 33 + 6          | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| 19 | Hantoushzadeh et al.23 | Iran | 25–49               | 24–38                   | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough, Fever, Liver function abnormality, Myalgia, anorexia, nausea (maternal death) | Liver function abnormality                                                                              |
| ID  | Study                  | Country              | Maternal age (years) | GA on admission (weeks) | Symptoms                                                                 |
|-----|------------------------|----------------------|----------------------|-------------------------|--------------------------------------------------------------------------|
| 20  | Griffin et al.         | USA                  | —                    | 39.0 ± 1.4              | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough               |
| 21  | Ferrazzi et al.        | Italy                | 21–44                | 34–37<                  | Fatigue, Shortness of breath, Dyspnea, Sore throat, Cough               |
| 22  | Dos Santos Bezzo et al.| Brazil               | —                    | 33 4/7–38 4/7           | Fever, Viral pneumonia, acute hypoxemia, end-organ failure             |
| 23  | Antoun et al.          | UK                   | 29.3 ± 2.9           | 38.7 ± 1.4              | Chest pain, abdominal pain                                             |
| 24  | Buonsenso et al.       | Italy                | —                    | 17-38                   | Ageusia, anosmia                                                       |
| 25  | Abasse et al.          | France               | 36                   | 33                      | Bronchiectasis                                                         |
| 26  | Alonso Díaz et al.     | Spain                | 41                   | 38 + 4                  | Pneumonia                                                              |
| 27  | Alzamora et al.        | Peru                 | 41                   | 33                      | Chills                                                                  |
| 28  | Coronado Munoz et al.  | USA                  | 21                   | 36                      | Tachycardia, tachypnea, lymphopenia, mild elevation of liver enzymes,  |
| 29  | Iqbal et al.           | USA                  | 34                   | 39                      | UTI                                                                     |
| 30  | Kalafat et al.         | Turkey               | 32                   | 35 ± 3                  | Pneumonia                                                              |
| 31  | Kulkarni et al.        | India                | 24                   | 38 + 2                  | Body ache                                                              |
| 32  | Kelly et al.           | USA                  | —                    | 33                      | Tachycardia, tachypnea, lymphopenia, mild elevation of liver enzymes,  |
| 33  | Villar et al.          | UK                   | 30.2 ± 6.1           | 37.9 ± 3.3              | Infection requiring antibiotics, 1.6% death, ICU admission             |
| 34  | Al-Matary et al.       | Saudi Arabia         | 32                   | 38                      | Premature birth, preeclampsia, leukopenia, neutropenia, thrombocytopenia, |
| 35  | Angelidou et al.       | USA                  | 30.4 ± 6.3           | 37.9 ± 2.6              | Myalgia                                                                |
| 36  | Rabiei et al.          | Iran                 | 38                   | 29 + 2                  | Myalgia                                                                |
| 37  | Puneet et al.          | India                | 24.7 ± 2.4           | 36.6 ± 3.3              |                                                                         |
The exclusion criteria were the following:

- Reviews and other nonoriginal studies
- Ongoing studies and clinical trials
- Laboratory and animal studies
- Abstracts, conference abstracts, and articles not possessing an available full-text

### RESULTS

In total, 238 documents were identified using a systematic search strategy. After the initial review of the retrieved articles, duplicates were removed and the title and abstract of the remaining sources were reviewed. Based on the selection criteria, 44 articles were eventually included in the final review (Tables 1 and 2).

Tables 1 and 2 describe the characteristics of pregnant women and newborns associated with COVID-19. A total of 2716 newborns and fetuses were assessed. Also, 2375 women in their second and third trimester, admitted with signs and symptoms of COVID-19; in several studies, the condition of the mothers was not assessed. In women, the most common manifestation was mild to moderate pneumonia. Near three in four women did not present with any comorbidities (73%). The most frequent clinical symptoms were fever (19%) and cough (17%). In terms of the imaging findings, chest CT scans were reported in some studies, which revealed pulmonary changes in 7.5% of women; the most common change was bilateral or unilateral ground-glass opacities (98%). Laboratory examinations revealed increased C reactive protein (8%) and decreased lymphocytes (lymphocytopenia) (9.4%). Of the 2716 infants, the delivery method of 1725 of them was reported, 913 (53%) through Cesarean-section delivery and 812 through normal vaginal delivery (NVD) (47%). Of the total newborns, 13 died; five died along the mother. Also, 10 fetal death occurred before birth. A total of 1965 newborns were tested for SARS-CoV-2, of which 118 (6%) tested positive. In a study, vertical transmission in seven cases were reported in the total 145 assessed cases.43

### DISCUSSION

The SARS-CoV-2 virus caused the COVID-19 pandemic that started in Wuhan, China, in December 2019.81,82 Mothers and neonates have been one the most vulnerable population in the pandemic situations due to the weakened immune system of the expectant mother.5 This maternal immune reaction is to prevent the fetus from being rejected as a foreign body by the mother’s immune system. Therefore, the maternal inflammatory responses are diminished to prevent fetal rejection.6,7 Although these responses are essential for a normal reaction to infections, in the case of COVID-19, it can be hypothesized that their decline might help by lowering the severity of the disease symptoms caused by inflammatory reactions. However, pregnant women might carry higher risks for severe COVID-19 compared to
| ID  | Study                        | Birth weight           | Neonatal medical complication                                                                 |
|-----|------------------------------|------------------------|------------------------------------------------------------------------------------------------|
| 1   | Zheng et al.                 | 2520, 3520             | Pneumonia √, Shortness of breath, Dyspnea, Respiratory tract symptoms √, Cough, Fever, Vomiting √, Other complication: Congenital talipes equinovarus, club foot myocardial injury |
| 2   | Zamanian et al.              | 2350                   | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 3   | Yu et al.                    | 3200–3500              | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 4   | Wu et al.                    | 2760–3570              | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 5   | Wu et al.                    | NR                     | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 6   | Spencer et al.               | 3320                   | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 7   | Santana-Cabrera              | NR                     | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 8   | Salvatore et al.             | 3110, 3410             | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 9   | Pirjani et al.               | NR                     | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 10  | Oncel et al.                 | 3140, 2465             | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 11  | Liu et al.                   | 2500–4120              | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 12  | Liu et al.                   | 3001                   | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 13  | Lowe and Bopp               | 3.93, 2.54             | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 14  | Martínez-Perez et al.        | 360, 3210              | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 15  | Khan et al.                  | 2940–3300              | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 16  | Koumoutsea et al.            | 2.93, 2.54             | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 17  | Khan et al.                  | 2.900, 3.500, 3.730    | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 18  | Juusela et al.               | 2.890                   | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 19  | Hantoush Zadeh et al.        | 1180–3200              | Neonatal pneumonia, Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 20  | Griffin et al.               | 3.348 ± 474            | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| 21  | Ferrazzi et al.              | 840–4040               | Pneumonia, Shortness of breath, Dyspnea, Respiratory tract symptoms, Cough, Fever, Vomiting    |
| ID  | Study                                      | Birth weight | Neonatal medical complication                                                                 | Respiratory tract symptoms | Cough | Fever | Vomiting | Other complication                                                                 | Neonatal mortality |
|-----|-------------------------------------------|--------------|------------------------------------------------------------------------------------------------|---------------------------|-------|-------|----------|----------------------------------------------------------------------------------|-------------------|
| 22  | Dos Santos Beozzo et al.61                | 2980, 2130, 3600 | Pneumonia —                                              Dyspnea √                | —                          | —     | —     | —        | Respiratory distress, The head grade II intraventricular hemorrhage, bleeding in the stool, and anemia | —                 |
|     |                                           | –            | Shortness of breath —                                    |                           |       |       |          | Nasal congestion and a runny nose                                                | –                 |
| 23  | Antoun et al.62                          | 3139 g ± 437  | Bacterial pneumonia                                       | —                          | —     | —     | —        | Sinus bradycardia, hypocalcemia                                                  | —                 |
| 24  | Buonsenso et al.63                       | –            | —                                                            | —                          | —     | —     | —        | Intermittent hyperpnea with mild intercostal retractions                         | —                 |
| 25  | Abasse et al.64                          | 1830         | √                                                            | √                          | √     | √     | —        | Hypotension, tachycardia, hypothermia, tachypnea, and reduced feeding             | —                 |
| 26  | Alonso Díaz et al.65                     | 2500         | —                                                            | √                          | √     | √     | —        | Lymphopenia, neutropenia, thrombocytopenia, low hemoglobin level, hyperbilirubinemia, fetal death | —                 |
| 27  | Alzamora et al.17                        | 2970         | —                                                            | √                          | √     | √     | √        | —                                                                              | —                 |
| 28  | Coronado Munoz et al.66                  | –            | –                                                            | √                          | √     | √     | —        | —                                                                              | —                 |
| 29  | Iqbal et al.34                           | –            | –                                                            | —                          | —     | —     | —        | —                                                                              | —                 |
| 30  | Kalafat et al.67                         | –            | –                                                            | —                          | —     | —     | —        | —                                                                              | —                 |
| 31  | Kulkarni et al.68                        | 3200         | —                                                            | —                          | —     | —     | √        | Thrombocytopenia and elevated inflammatory markers (CRP/procalcitonin/ ferritin), elevated d-dimers | —                 |
| 32  | Kelly et al.69                           | –            | –                                                            | —                          | —     | —     | —        | —                                                                              | —                 |
| 33  | Villar et al.70                          | 2960 ± 700   | √                                                            | √                          | —     | —     | —        | Low birth weight                                                                | √                 |
| 34  | Al-Matary et al.71                       | –            | √                                                            | √                          | √     | √     | —        | Lymphopenia, neutropenia, thrombocytopenia, low hemoglobin level, hyperbilirubinemia, fetal death | —                 |
| 35  | Angelidou et al.72                       | 31 116.3 ± 655.6 | Yes                                      | √                          | √     | √     | √        | Hypotonia                                                                         | √                 |
| 36  | Rabiei et al.73                          | 1390         | –                                                            | —                          | —     | —     | —        | NICU admission                                                                    | —                 |
| 37  | Puneet et al.74                          | 2600 ± 600   | –                                                            | —                          | —     | —     | —        | NICU admission, Fetal distress                                                  | —                 |
| 38  | Oncel et al.75                           | 2465         | –                                                            | √                          | √     | —     | —        | NICU admission                                                                    | —                 |
| 39  | Mullins et al.76                         | –            | –                                                            | —                          | —     | —     | —        | —                                                                              | —                 |
nonpregnant patients. The results from the present review indicate that one-third of pregnant women who tested positive for COVID-19 were asymptomatic that is approximately similar to the general population.

In the present review, women were often in their second and third trimesters of pregnancy. Besides, the available data do not show any clear relation between GAI (general admission 1) and infection in mothers or neonates. Likewise, there was no association between maternal age and neonatal complications. Birth weights mostly ranged between 2000 and 4000 g, and Villar et al. demonstrated low birth weight as a complication of COVID-19 in the neonates.

According to findings, cough and fever were the most common symptoms in mothers. Other relatively common symptoms included dyspnea, diarrhea, and cardiac symptoms such as tachycardia. However, fever and respiratory tract symptoms such as cough and dyspnea were the most common symptoms in neonates. But one of the most important and noticeable findings were cardiovascular problems, particularly tachycardia and hypotension.

Neonatal pulmonary changes in chest CT scans were mostly unilateral or bilateral ground-glass opacities. The most common laboratory findings were the increase of C-reactive protein and decrease of lymphocytes (lymphocytopenia). Although less than half of neonatal patients had comorbidities (12%), fetal distress was the most common. Five neonatal death occurred along with the mother. However, other neonatal deaths did not involve maternal death (n = 8). Pneumonia was also one of the most common neonatal complications of COVID-19 disease reported in other reviews.

This study comes with limitations. Some of the included studies lacked information related to the severity of the complications in the neonates. Some also did not report the final status of the newborns and whether they were cured or not, or had short- or long-term sequels. Also it will be useful if the studies mention the long-term outcomes of the patients and the impact of the disease and its possible complications in longer periods. On the other hand, there were also some limitations related to the data about the mothers in a portion of the studies, for example, the starting date of COVID-19 and the duration of the disease. We also did not perform a statistical analysis. Nevertheless, this study provided some important information related to perinatal and neonatal complications of COVID-19 and future well-designed meta-analyses can increase our awareness of this disease more.

**5 | CONCLUSION**

Evidence suggests that vertical transmission in the uterus is responsible for COVID-19 in neonates that makes neonatal infection through the umbilical cord unlikely. In addition, parental infection is less severe due to the suppression of immune system during pregnancy. Neonates do not present any additional risk for COVID-19 complications during the prenatal period. However, further epidemiological studies are recommended to explore the possibility of mother-to-child...
(vertical) transmission of COVID-19 and determine the potential perinatal complications.

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CONFLICT OF INTEREST
The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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TRANSPARENCY STATEMENT
Esmaeil Mehraeen affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

AVAILABILITY OF DATA AND MATERIAL
The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE
Not applicable.

CONSENT TO PUBLICATION
Not applicable.

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