

Effects of Corona Pandemic on Maternal-Neonatal Outcomes and Vaccination of Pregnant Women: A Narrative Review Study

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Abstract

Aims: Corona is a highly contagious respiratory disease. Pregnant women are more susceptible to viral respiratory infections. On the other hand, there is limited information on vaccination of pregnant women, so this review was conducted to investigate the relationship between maternal-neonatal outcomes and vaccination of pregnant women.

Information & Methods: A present narrative review study was performed from late 2019 to September 2021 by collecting information from Magiran, SID, Library Cochrane, Science Direct, Scopus, PubMed and, Google scholar Web of Science databases, and using the English and Persian keywords "Delivery", "Pregnancy", "Vaccine", "SARS-COV-2", "COVID-19", "Neonatal", "Outcomes", and "New-born". Finally, 28 studies were included in the study with inclusion criteria.

Findings: Adverse obstetric and neonatal outcomes increase in sufferers in the second half of pregnancy. Common maternal consequences include cesarean section, premature birth, abortion, tachycardia, and premature rupture of the amniotic sac, and common neonatal consequences include effects on fetal brain development, increased risk of autism, and neurological problems. Also, maternal vaccination by transferring antibodies from the placenta to the fetus makes the baby immune.

Conclusion: Although pregnancy is not known as a factor in corona disease, with the focus on the consequences for both mother and neonate, self-care education is important. If possible, vaccination programs should target pregnant women early in pregnancy or before fertilization.

Keywords

COVID-19 [<https://www.ncbi.nlm.nih.gov/mesh/2052179>];

Pregnancy [<https://www.ncbi.nlm.nih.gov/mesh/68011247>];

Pregnancy Outcomes [<https://www.ncbi.nlm.nih.gov/mesh/68011256>];

Delivery [<https://www.ncbi.nlm.nih.gov/mesh/68036861>];

Newborn [<https://www.ncbi.nlm.nih.gov/mesh/68007231>];

Vaccination [<https://www.ncbi.nlm.nih.gov/mesh/68014611>]

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Introduction

In late 2019, a new virus, COVID-19, was identified in Wuhan, China, in people with pneumonia of unknown cause. This virus is from the family of corona viruses that can cause a wide range of respiratory diseases from mild to severe [1]. Corona virus is transmitted through respiratory droplets and aerosols [2]. Common symptoms include shortness of breath, fever, cough, fatigue, increased heart rate and headache [3], and even some affected people may have neurological symptoms [4].

Among the people who are exposed to the COVID-19 virus, pregnant women may be more sensitive to the virus or experience the disease more severely due to the immune and physiological changes created during pregnancy [5]. Changes during pregnancy, including increased heart rate, changes in ACE2 receptor expression, oxygen consumption, respiratory tract edema, decreased lung capacity, increased risk of thromboembolic disease, and changes in immune system function, expose pregnant women to a higher risk in epidemics [6]. Some studies indicate that infected and symptomatic pregnant women show more severe symptoms than non-pregnant women and are more likely to be admitted to the intensive care unit, and also have a higher mortality rate than non-pregnant women. These data suggest that pregnant women should be counseled regarding the possible increased risk of severe disease, including death [7].

In another study conducted on 262 symptomatic women infected with the coronavirus, they concluded that symptomatic pregnant women are significantly more at risk of severe coronavirus disease compared to non-pregnant women (who used both World Health Organization scales for clinical improvement); Therefore, pregnancy significantly increases the risk of severe coronavirus disease [8].

On the other hand, if pregnant mothers are infected, we may see harmful effects on their fetuses and babies [9]. Articles published since the outbreak of the virus have reported the effect of the virus on pregnancy and attempted to determine adverse neonatal and delivery outcomes following infection. Meanwhile, mother-to-child transmission of the virus has been established, and the World Health Organization (WHO) has identified the virus as part of the TORCH (Toxoplasma, Rubella virus, Cytomegalovirus [CMV] and Herpes simplex Virus [HSV]) family of infections [10].

Initial reports based on limited data from China did not show increased maternal or infant mortality. However, some more recent studies evaluating pregnant and non-pregnant women have provided more information on the incidence and associated morbidity and mortality [7, 11, 12]. Some reports have shown an increased rate of preterm delivery and cesarean section, while others have reported a close

association between SARS-CoV-2 infection and pre-eclampsia or pre-eclampsia-like syndromes [10].

Similar to outbreaks of other infectious diseases such as human immunodeficiency virus, Ebola virus, and Zika virus, vaccination is a power reduction strategy followed by an attack against the disease agent [13]. Maternal vaccination can protect the mother, the fetus and the newborn, so a single intervention provides powerful protection for two susceptible individuals who are more at risk of contracting the disease and its consequences, but considering the specific physiologies and sensitivities of pregnancy, the answer to vaccination may differ from the general population [14].

Since pregnant mothers have been excluded from the initial trials of vaccination against COVID-19, there is very limited information in this field [15]. Therefore, considering the importance of the health of pregnant women and newborns as two vulnerable groups against SARS-COV-2, as well as the unknown consequences of this disease during pregnancy and the effects of vaccines on the health of mothers and babies, this review study was conducted with the aim of investigating the effects of the corona epidemic during pregnancy, maternal and infant outcomes, and the effects of vaccination of pregnant mothers.

Information and Methods

The present narrative review was based on the information obtained from the search of Internet resources in Magiran, SID, Library, Cochrane, PubMed, Science Direct, Google Scholar, Web of Science, and Scopus databases.

In this search, the keywords "Delivery", "Pregnancy", "Vaccine", "SARS-COV-2", "COVID-19", "Neonatal", "Outcomes", and "New-born" with "And" and "OR" operators were used in English and Persian.

The criteria for including articles in the study were as follows:

1. Original research articles or case reports
2. The target population includes pregnant women with COVID-19 or vaccinated pregnant women or babies born to infected mothers.
3. Consequences of the disease during pregnancy or childbirth and in the fetus and newborn have been mentioned.
4. Complications and consequences of vaccination of pregnant mothers are mentioned.

Exclusion criteria also included:

1. Studies in laboratory conditions or on animals
- 2- Examination of the virus or vaccination in the non-pregnant population
3. Letter to the editor, conference and abstract
4. Lack of access to the full text of the article after sending 2 emails to the responsible author

The overall search included 4639 articles, and finally 28 articles were included in the study (Figure 1).

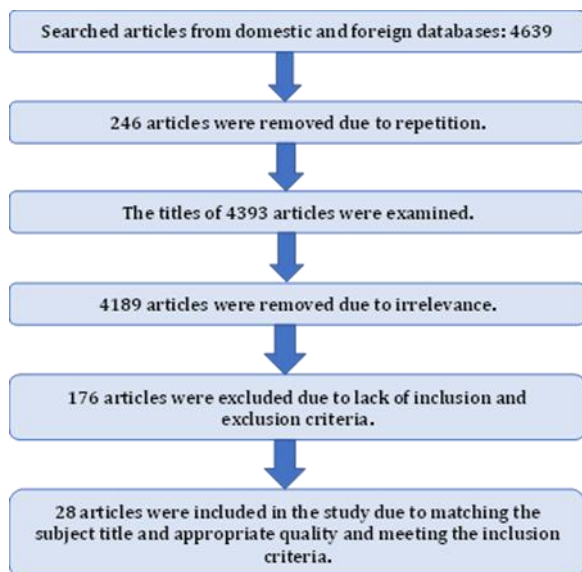


Figure 1) Flowchart of selecting articles

Findings

In this study, 28 articles were examined. Among these, 20 articles investigated the physical and psychological consequences of contracting the disease of COVID-19 and its clinical and laboratory findings. 3 studies investigated placental membrane swap samples of newborn and placentas of affected pregnant women. Also, in 5 studies, the consequences of vaccination in pregnant and lactating mothers and the transmission of antibodies from mother to fetus and newborn were investigated.

Among the reviewed articles, 14 studies were conducted in China, 4 studies in the United States, 2 studies in Israel, 2 studies in France, 5 studies in Iran and one study in Spain. A total of 7 maternal deaths, 3 neonatal deaths and 5 IUFD (Intrauterine Fetal Demise) cases were reported. 10 infants tested positive for COVID-19 but survived, and 3 placental membrane swaps were positive for SARS-COV-2. Antibodies produced by the vaccine were found in the umbilical cord blood sample of women who were vaccinated during pregnancy (Table 1).

In the context of examining psychological symptoms, the results of Karimi et al.'s study showed a high level of anxiety caused by the COVID-19 pandemic, which was directly related to perceived social support (wife, family, and friends); So that pregnant women who had weak social support experienced more intense anxiety [38]. Also, the results of Abedzadeh et al.'s study showed that the level of anxiety and stress of pregnant women during the COVID-19 pandemic was high and women had a lot of worries about their infection and their baby's infection or going to prenatal care [39].

The effect of the COVID-19 virus on the fetus: At the beginning of the pandemic, reports indicated that there is no possibility of intrauterine

transmission in COVID-19, but later reports showed positive umbilical cord blood and venous blood serology tests in a number of babies, which caused concerns. Examining the tissue of 3 placentas did not show the presence of infection or inflammation, but the deposition of fibrin strands and infarcted points were observed in and around the villi, which may be related to pregnancy problems such as preeclampsia [44]. Later, the presence of intrauterine transmission was clearly confirmed in some studies, and chronic and acute intervillitis was reported in the placenta examination, which indicates that the baby's viremia is due to infection [33]. There is another report that the tests of vaginal secretions and mother's feces are positive, which raises the hypothesis of intrauterine transmission [45]. Between 6-14 weeks of pregnancy, the level of ACE 2 is very low, so the possibility of virus transmission to the fetus in the first trimester is very low, however, respiratory failure and hypoxia caused by the destruction of the uterine-placental barrier in the mother may cause abortion.

In one baby, an increase in IgM and IgG antibodies was reported about 2 hours after delivery, but PT-PCR of his oral-pharyngeal secretions at the time of birth was negative [21]. The serological results of 2 out of 6 babies born to infected mothers suggested the hypothesis of intrauterine transmission. The mother's IgM antibody does not cross the placental barrier and the presence of this antibody in the blood is a sign of intrauterine infection, but it should be noted that the IgM test usually has false positive results [21]. In a baby after birth, the oral pharyngeal swab sample was negative for the COVID-19 virus, but the baby's IgM, Interleukin 6 (IL-6), and IgG were high [31].

Fetal control of people with COVID-19 should be done monthly. If preterm delivery is predicted based on the mother's conditions, according to the guidelines, corticosteroids can be started to accelerate fetal maturation [46]. There is little evidence of intrauterine transmission of COVID-19, but even if the virus is not present in the placenta, the mother's response to the infection causes an increased fetal inflammatory response, called Fetal Inflammatory Response Syndrome (FIRS). This syndrome actually occurs with the increase of placenta inflammatory cytokines such as IL-6, IL-8 and TNF- α (Tumor Necrosis Factor-alpha). These cytokines affect the fetal brain and increase the risk of autism, schizophrenia, neurological problems and psychosis [47]. The mother's illness may later cause complications in the newborn, such as the effect on brain development; For this reason, it is necessary to be aware and take care of the condition of mother and fetus with careful management and monitoring. Unfortunately, there is no information about the onset of the disease in the first and second trimesters and its consequences, also, the studies were retrospective and with a small sample size, and some samples may have been included in the study

several times, therefore, care must be taken when interpreting the findings. Also, we cannot definitively state that the consequences mentioned in mothers and their fetuses are related to the corona virus. Because in most of these studies there was no control group of non-infected women at the same time and the stress of the COVID-19 situation may have led to these results.

The effect of the COVID-19 vaccine on pregnant mothers and their babies: Although the side effects of pregnant women receiving the SARS-COV-2 vaccine were not significantly different from those of non-pregnant women, the relatively high

incidence of fever has raised concerns about the possible effects of fever on the fetus. On the other hand, among the specific complications of vaccination in pregnancy reported to VEARS (Vaccine Adverse Event Reporting System), abortion was the most common case. This is similar to what happened during the H1N1 A influenza vaccination in 2009; Therefore, when considering vaccination in pregnancy, the evidence related to the benefits of the vaccine and possible harm to the mother and the fetus should be carefully weighed [20].

Table 1) Articles obtained about investigating maternal-newborn outcomes and the role of vaccination

Researcher/year/country	Title/type of article	Sample size	Tools	Results
Chen et al./2020/China [16]	Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women/Retrospective review	9 pregnant women	- CTscan - Nasopharyngeal swab test for baby and mother - Amniotic fluid, umbilical cord blood and breast milk sample test	1. The average gestational age was 36-39 weeks. 2. All mothers underwent cesarean section. 3. Fetal distress was reported in two cases, premature rupture of membranes in two cases, lymphopenia in five cases, and increased aminotransferase concentration in three cases. 4. Clinical symptoms of infected mothers were similar to non-pregnant infected mothers. 2. In all 9 babies, the Apgar score of the first minute was 8-9 and the Apgar score of the fifth minute was 9-10. 5. The umbilical cord blood, amniotic fluid and pharyngeal swab samples of these babies were negative for COVID-19. 6. No evidence of intrauterine transmission was found.
Chen et al./2020/China [17]	Pregnancy with new coronavirus infection: clinical characteristics and placental pathological analysis of three cases/Retrospective	3 placentas of affected mothers	- CTscan - Placenta examination - Maternal blood test and nCoV-2019 nucleic acid detection	1. All three women underwent emergency cesarean section in the third trimester. 2. Different degrees of fibrin deposition inside the villi were reported in all three placentas, chorionic hemangioma in one placenta, and placental infarction in one case. 3. Throat swab samples were negative for COVID-19 in all three babies. 4. No morphological changes related to placental infection and no pathological changes and chorioamnionitis were observed.
Wang et al./2020/China [18]	A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery/ Case Report	A case of an infected pregnant mother	- CT scan - Nasopharyngeal swab test for baby and mother - Blood test and clinical examination	1. A 28-year-old mother with a gestational age of 30 weeks was admitted to the hospital with symptoms of intermittent fever. 2. Tomography scan of the chest showed patchy subpleural fixation on the left side and ground glass opacity on the right side. 3. On the third day of hospitalization, fetal movements and heart rate monitoring changes were not detected, and an emergency caesarean section was performed under combined epidural spinal anesthesia. 4. A preterm male infant weighing 1.83 kg was delivered uneventfully, with Apgar scores of 9 and 10 at 1 and 5 minutes, respectively. 5. The sample of amniotic fluid, placenta, umbilical cord blood, gastric juice and throat swab of the baby during delivery were negative.
Zhu et al./2020/China [19]	Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia/Retrospective	10 babies born to infected mothers	- CT scan of the mother - X ray of the baby - Clinical signs	1. Ten premature births and 2 vaginal births. 2. Common symptoms included fever, headache, and cough. 3. No cases of asphyxia were reported. 4. Ten babies tested negative for COVID-19.
Yu et al./2020/China [20]	Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19/Retrospective	7 infected pregnant mothers and their babies	- CT scan - X ray - Laboratory and clinical results	1. Clinical symptoms were similar to non-pregnant affected women. 2. All patients had an average gestational age of 39 weeks±2d. 3. Three babies were tested for COVID-19 and the throat swab sample of one baby was positive 26 hours later and he was discharged two weeks later. 4. Maternal, fetal and neonatal outcomes of those pregnant women who were infected with the COVID-19 virus at the end of pregnancy seemed to be better.

Yang et al./2020/China [21]	Novel coronavirus infection and pregnancy/Retrospective	41 infected pregnant women	- CTscan - Nucleic acid detection test for COVID-19 Clinical signs	<ol style="list-style-type: none"> 1. Clinical symptoms in pregnant women were similar to non-pregnant affected women. 2. No evidence of vertical transmission from mother to baby was reported. 3. No case of maternal death was reported.
Qiancheng et al./2020/China [22]	Coronavirus disease 2019 in pregnancy/Retrospective	28 non-affected pregnant women and 54 affected non-pregnant women	- Blood test - Clinical signs	<ol style="list-style-type: none"> 1. There was no relationship between pregnancy and disease severity. 2. The result of PT-PCR test was negative for all babies. 3. 22 cases of cesarean section, 5 cases of vaginal delivery, one case of premature delivery 4. Maternal and infant deaths were not reported.
Shanes et al./2020/USA [23]	Placental pathology in COVID-19/Retrospective	16 placentas of affected mothers	Laboratory findings	<ol style="list-style-type: none"> 1. Five placentas were small for gestational age and one placenta was slightly large for gestational age. 2. No pathognomonic features were identified. 3. The nasopharyngeal swab sample of newborns was negative for COVID-19. 4. Placentas of infected women did not show a significant increase in acute or chronic inflammatory pathology.
Hantoushadeh et al./2020/Iran [24]	Maternal death due to COVID-19/Retrospective	9 infected pregnant women and 11 of their babies	Nucleic acid detection test	<ol style="list-style-type: none"> 1. Out of 9 pregnant women, 7 died due to heart, lung and kidney problems. 2. Six mothers underwent cesarean section and 3 mothers had vaginal delivery. 3. Five cases of IUFD and 3 neonatal deaths were reported. 4. A baby tested positive for COVID-19 on the 7th day of life and was intubated due to respiratory failure, but eventually survived.
Penfield et al./2020/USA [25]	Detection of severe acute respiratory syndrome coronavirus 2 in placental and fetal membrane samples/Retrospective	11 babies born to infected mothers	- Nasopharyngeal swap test - PCR test - Placental or membrane swap of the baby	<ol style="list-style-type: none"> 1. Of 11 placental or membrane swaps, three were positive for COVID-19 (all of these were in women with severe to critical illness). 2. There were no clinical signs of vertical transmission and the findings indicate the possibility of exposure of affected infants to the COVID-19 virus during delivery.
Diaz et al./2020/Spain [26]	First case of neonatal infection due to SARS-CoV-2 in Spain/Case report	A baby born to an infected mother	- Clinical signs - Laboratory results	<ol style="list-style-type: none"> 1. The mother was hospitalized with severe pre-eclampsia and symptoms of COVID-19 and underwent cesarean section at 38±4 weeks. 2. The pregnancy was IVF and the mother had a history of hypothyroidism. 3. The baby was born with low weight and the Apgar score was 7 in the first minute and 9 in the fifth minute. 4. The initial test for COVID-19 in this baby was negative, but the subsequent tests were positive. 5. Due to respiratory discomfort, the baby was put on respiratory support.
Qiao/2020/China [27]	Risks of COVID-19 infection in pregnant women/Retrospective	10 infected women	- Clinical signs - Laboratory results	<ol style="list-style-type: none"> 1. Pregnant women are susceptible to respiratory diseases, especially if they have underlying diseases. 2. Common symptoms included fever, cough, headache and nausea.
Fan et al./2021/China [28]	Perinatal transmission of 2019 Coronavirus disease-associated severe acute respiratory syndrome coronavirus 2: Should we worry?/ Cohort	2 affected mothers	- Newborn nasopharyngeal swap test - Complete examination of the umbilical cord sample, amniotic fluid, placenta tissue and mother's vaginal sample	<ol style="list-style-type: none"> 1. Both mothers successfully underwent cesarean section and the baby was immediately separated from the mother. 2. Umbilical cord blood, amniotic fluid, placenta tissue and throat swap sample of newborns were negative for COVID-19.
Zeng et al./2020/China [29]	Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with	33 babies born to infected mothers	- PCR - Clinical signs	<ol style="list-style-type: none"> 1. Out of 33 babies, 3 babies were infected with COVID-19 and showed severe symptoms. 2. Although the samples of amniotic fluid, umbilical cord blood and breast milk were negative for vertical transmission of the disease, vertical transmission cannot be ruled out in this group.

	COVID-19/Cohort			
Zhang et al./2020/China [30]	Analysis of the pregnancy outcomes in pregnant women with COVID-19/Retrospective	16 infected pregnant women and 45 non-infected pregnant women and 10 babies	- X ray - Corona virus nucleic acid	<ol style="list-style-type: none"> 1. There were no cases of COVID-19 infection in pregnant women. 2. No significant difference was reported in terms of delivery type, gestational age, birth weight, premature delivery, meconium excretion, fetal disturbance and asphyxia. 3. Timely termination of pregnancy in critical conditions does not increase the risk of infant asphyxia.
Dong et al./2020/China [31]	Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn/Case report	An infected mother and her baby	- Clinical signs - CT Scan - PP-PCR	<ol style="list-style-type: none"> 1. PT – PCR was repeatedly negative. 2. Antibody and cytokinin test results 2 hours after birth were abnormal. 3. Mother's vaginal secretions and breast milk were negative.
Li et al./2020/China [32]	Lack of vertical transmission of severe acute respiratory syndrome coronavirus 2/Case report	13 infected women and their babies	- Swab samples - Clinical signs	<ol style="list-style-type: none"> 1. No evidence of intrauterine transmission was confirmed. 2. Premature rupture of the amniotic sac, fetal disturbance, premature delivery and stillbirth were not reported. 3. No case of neonatal asphyxia, infant death or abortion was reported.
Badr et al./2020/France [10]	Severe acute respiratory syndrome coronavirus 2 and pregnancy outcomes according to gestational age at time of infection/Cohort	393 infected pregnant mothers	- Nasopharyngeal swab samples - Clinical signs	<ol style="list-style-type: none"> 1. Out of 393 patients, 196 were symptomatic (8 critical, 12 severe, 34 moderate, 135 mild, and 7 not classified. Of these, 46 patients had pneumonia and 16 had acute respiratory distress syndrome. 2. COVID-19 infection was associated with an increase in pre-eclampsia, eclampsia and HELLP syndrome. 3. Pregnant women were more susceptible to infection side effects in the late second trimester and early third trimester.
Vivanti et al./2020/France [33]	Transplacental transmission of SARS-CoV-2 infection/Case report	An infected pregnant mother and her baby	- Nasopharyngeal, vaginal and rectal swab samples - Organ functional tests - Clinical signs	<ol style="list-style-type: none"> 1. Mother's age was 23 years and mother's gestational age was 35±2 weeks. 2. Mother's symptoms included severe cough, fever of 38.6 and a lot of sputum. 3. PT_PCR was positive in blood and nasopharyngeal and vaginal swabs. 4. Amniotic fluid was positive for both S and E genes of SARS-COV-2 virus. 5. Apgar score of the baby was 4 (heart rate = 1, breathing = 1, skin color = 1, muscle tone = 1 and the rest were scored zero). 6. Analysis of umbilical cord gas showed normal pH and lactate levels. 7. The baby's nasopharyngeal and rectal swabs were positive one hour later and on days 3 and 18 for both SARS-COV-2 genes. 8. Routine tests (troponin and kidney and liver function) that were repeated on the second day of life were normal.
Shimabukuro et al./2021/China [15]	Preliminary findings of mRNA COVID-19 vaccine safety in pregnant persons/Retropective	35691 pregnant women	- Clinical signs	<ol style="list-style-type: none"> 1. Injection site pain was reported more in pregnant women than in non-pregnant women, while systemic reactions including headache, myalgia, chills and fever were less. 2. Out of 827 pregnant participants, 712 live births, 104 spontaneous abortions, one stillbirth and other complications in 10 cases were reported. 3. Out of 104 abortions, 96 cases were before 13 weeks. 4. Out of 712 live births, 700 cases received the first dose of qualified vaccine in the third trimester of pregnancy. 5. Premature birth was reported in 60 cases out of 639 people who were vaccinated before 37 weeks. 6. Small size for gestational age was seen in 23 cases out of 724 cases that reported unfavorable results. 7. Major congenital anomalies were seen in 16 of the 724 cases reported in VAERS. 8. No infant deaths were reported.
Gray et al./2020/USA [34]	Coronavirus disease 2019 vaccine response in pregnant and lactating women/Cohort	131 vaccine recipients in reproductive age (84 pregnant	- Umbilical cord test of vaccinated mothers - Antibody test	<ol style="list-style-type: none"> 1. There was no significant difference in vaccine-induced antibody titer in pregnant and lactating women compared to non-pregnant women. 2. The titers of all antibodies produced by the vaccine were significantly higher than those induced by the acute respiratory syndrome of COVID-19 in pregnancy. 3. 13 participants gave birth during the study period (3 cesarean section, 10 vaginal delivery)

	t	women, 31 lactating women and 16 non-pregnant women)		4. The antibodies produced by the vaccine were present in all cord blood and breast milk samples.
Prabhu et al./2020/USA [35]	Antibody response to Coronavirus Disease 2019 (COVID-19) messenger RNA vaccination in pregnant women and transplacental passage into cord blood/Cohort	122 pregnant women and their babies	- Antibody test	<ol style="list-style-type: none"> 1. Until delivery, 55 pregnant women had received one dose of mRNA vaccine and 67 women had received both doses of vaccine. 2. IgG response was reported in 87 pregnant women and IgM and IgG response in 19 cases, and no specific antibody response was reported in 16 women. 3. The first detection of antibody in women was 5 days after receiving a dose of a vaccine. 4. The first detection of antibody in cord blood was 16 days after receiving a vaccine dose. 5. In two cases of umbilical cord blood samples, antibody transfer to the baby was not detected. 6. IgG was detected in 44% of cord blood samples of women who received only one dose of vaccine. 7. IgG was detected in 99% of cord blood samples of mothers who received both doses of the vaccine.
Wainstock et al./2021/Israel [36]	Prenatal maternal COVID-19 vaccination and pregnancy outcomes/Cohort	4399 pregnant women	- Observation of clinical symptoms	<ol style="list-style-type: none"> 1. As compared to the unvaccinated women, vaccinated women were older, more likely to conceive following fertility treatments, to have sufficient prenatal care, and of higher socioeconomic position. 2. The mean time interval between first vaccination and delivery was 7.5 weeks and the range was <1–21 weeks. 3. The mean time interval between second vaccination and delivery was 5.4 weeks and the range was <1–18 weeks. 4. No differences were observed between the groups in vaccine complications and outcomes. 5. Women who received the 2-dose vaccination delivered at slightly higher gestational age and birthweight. 6. No relationship was found between vaccination status and pregnancy and childbirth and the characteristics and complications of the newborn.
Bookstein et al./2021/Israel [37]	Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine/Case-control	390 pregnant women and 260 non-pregnant women	- Clinical signs	<ol style="list-style-type: none"> 1. Pain, myalgia, arthralgia and headache were significantly less among pregnant women compared to the control group after the first and second doses. 2. Local pain or swelling during pregnancy was significantly less only after the first dose and axillary lymphadenopathy was observed more. 3. Paraesthesia was more common in pregnant women compared to the control group after the second dose. 4. Fever above 38 degrees was observed in 1.5% of pregnant women after the first dose and 9% after the second dose of vaccine, but only 0.8% of fever above 39 degrees was observed in pregnant women after the second dose. 5. Uterine contractions occurred in 5 patients after the first dose and in 25 patients after the second dose of the vaccine, and in 15 of these 25 cases, the contractions occurred after the 34th week and did not lead to premature delivery. 6. Vaginal bleeding was reported in only one pregnant woman after the first dose and in 6 pregnant women after the second dose. 7. No PROM was reported within 7 days after the first dose, while three cases experienced PROM after the second dose at 36±3, 36±4, and 37±1 weeks. 8. Ninety-one cases gave birth during the study period, the average gestational age at the time of delivery was 39.5 weeks and the average birth weight was 3269±410.
Karimi et al./2021/Iran [38]	Relationship between social support and anxiety caused by COVID-19 in pregnant women/Cross-sectional description	200 pregnant women	- Demographic and midwifery information checklist - Social Support Family Scale (PSS-Fa) - Anxiety questionnaire of pregnant women due to the COVID-19 epidemic	<ol style="list-style-type: none"> 1. There was a significant difference in the level of anxiety caused by the COVID-19 epidemic in the subgroups of weak, moderate and strong social support ($p < 0.0001$). 2. There was an inverse and significant correlation between the amount of anxiety caused by the epidemic and the amount of social support received in pregnant women. In other words, with the increase in the amount of social support from the family, the level of anxiety in pregnant women due to the COVID-19 epidemic decreased significantly.
Abedzadeh et al./	Anxiety and perceived	360 pregnant	- Demographic	<ol style="list-style-type: none"> 1. The total anxiety score of pregnant women related to the corona virus disease was 18.71 ± 12.48 and the perceived stress score was 24.57 ± 7.00. The results showed that women's perceived stress is high during the pandemic

2021/Iran [39]	stress of pregnant women towards COVID-19 disease and its related factors in Kashan/Cross-sectional description	women	c and midwifery information questionnaire - Corona virus anxiety scale - Cohen's Perceived Stress scale	and women's anxiety scores are higher in the psychological dimension than in the physical dimension. 2. Based on the results of the linear regression test, a person's job, problems during pregnancy, history of childbirth, family members being infected with corona and worry about the consequences of the disease for themselves and the baby were predictors of the perceived stress score, and variables of family infection with corona and the presence of worry about the infection of oneself and the baby, worry about receiving pregnancy care and the presence of problems during pregnancy were predictors of anxiety score in pregnant women.
Eshraghi et al./2021/Iran [40]	A pregnant woman with uncommon symptoms and complications of COVID-19/Case report	A pregnant mother	- Clinical and laboratory findings	1. The patient, a 24-year-old woman with a gestational age of 8 weeks and 4 days, presented with a complaint of diffuse abdominal pain and bloating. Symptoms of epigastric pain and transmitted to the hypogastric region were observed. 2. In his tests, sodium = 127 milliequivalents/liter, potassium = 2.3 milliequivalents/liter, and blood sugar was 324 mg/dL, which clearly had hypernatremia and hyperglycemia. In the physical examination, the abdomen was soft and rebound tenderness was not found, only on deep palpation of the abdomen, there was slight tenderness. 3. Abdominal and pelvic ultrasound showed an enlarged and unperforated appendix, so the mother underwent surgery. 4. After 20 hours, the patient developed a fever and tested positive for COVID-19 with a nasopharyngeal swab. But the mother did not have respiratory symptoms such as dry cough and shortness of breath. 5. Gastrointestinal symptoms should be observed as symptoms of COVID-19.
Moaya et al./2020/Iran [41]	Maternal and neonatal outcomes of pregnant women with COVID-19 in Amir-al-momenin hospital during March to May 2020/Cross-sectional description	7 pregnant mothers and their babies	- Clinical and laboratory findings	1. The most common disease symptom in 7 women was fever. 2. Only two women needed nasal oxygen after delivery. 3. All patients showed high CRP and pulmonary involvement in lung CT scan. 4. Five babies were born naturally. 5. One preterm baby and one baby weighing less than 2500 were born. 6. A baby boy had asphyxiation. 7. A baby boy died after 5 hours of birth. 8. Two infants were admitted after birth with symptoms of COVID-19, although their PCR tests were negative.

Adverse pregnancy and neonatal outcomes among women who received mRNA vaccines were similar to those reported in other studies of prepandemic pregnant women [6]. Based on the currently available data, mRNA vaccines seem safe for pregnant women. Oxford-Astrazeneca and Johnson/Janssen adenovirus vaccines have been associated with serious coagulation disorders and thrombosis with thrombocytopenia syndrome in recipients younger than 50 years of age [6]. However, these adverse effects are very rare and the incidence varies from one in every 26,000 to one in every 127,000 doses [6]. Also, two-dose vaccination (mRNA vaccines) appears to be associated with longer gestation and increased birth weight compared to a single dose. On the other hand, vaccination has caused humoral immunity in all vaccinated pregnant women. Although SARS-COV-2 IgG levels were lower in pregnant women compared to non-pregnant women, these levels were much higher than in recovered patients with COVID-19 [37]. The IgG produced by the vaccine crosses the placenta and provides immunity to the baby. Also, the increase in maternal IgG level with the passage of time after receiving the vaccine and its relationship with the increase in transfer of placental IgG shows that the

time between vaccination and delivery may be an important factor for considering the vaccination strategy of pregnant women [48].

Discussion

This review study was conducted with the aim of investigating the effects of the corona epidemic during pregnancy, maternal and infant outcomes, and the effects of vaccination of pregnant mothers.

The findings from 28 studies investigated indicate that the symptoms of infection are not much different between infected pregnant women and non-pregnant women, but infected pregnant women in the late second trimester or early third trimester are more susceptible to side effects of SARS-COV-2 infection [10].

Pregnant women are susceptible to respiratory diseases, so that during the SARS and MERS epidemics, approximately one third pregnant women were infected with these diseases [48]. Physiological changes in the cardiovascular and immune systems of pregnant women make them susceptible to infection and hypoxia. Approximately one fifth of pregnant women suffer from congestion and runny nose in late pregnancy due to swelling of mucous membranes of the pharynx and nose, which

cover the symptoms of COVID-19 and make them carriers of the disease. In pregnant women, inhalation and exhalation of the lungs are not performed well, and due to the pressure of the uterus, the functional residual volume and exhalation capacity decrease. Also, the increased need for oxygen due to high metabolism, anemia during pregnancy and oxygen consumption by the fetus causes physiological dyspnea in the mother, which should be diagnosed from pathological dyspnea. At the end of pregnancy, the decrease in the number and activity of Natural Killer (NK) cells and T-cells makes the mother susceptible to infection. ACE 2 is the main and important way for the coronavirus to enter the lungs, and the ACE2 receptor increases in pregnant women, so the sensitivity of pregnant mothers to the virus increases [49].

Weakening of the immune system along with changes in hormones (progesterone and prostaglandin) increases the risk of viral diseases in pregnant women [13]. On the other hand, the increase of anti-inflammatory cytokines (interleukins 4 and 10) and other unknown mechanisms reduce the severity of the disease in pregnant women [48]. Therefore, it can be said that during pregnancy, some factors can reduce the symptoms of the disease and others can aggravate the disease.

One of the strong points of the study is the use of new articles whose content may not yet be included in the reference books. One of the weak points of the study is the lack of access to the full text of some articles related to the research topic, as a result of which the authors could not use those materials in writing the article.

One of the main limitations of the research was the lack of studies related to the vaccination of pregnant women in Iran with the available vaccines; Therefore, a large number of related studies and articles were not available in the desired field.

Conclusion

Although pregnancy has not been proven as a risk factor for the disease, pregnant women are among the risk groups. The results of the studies indicate that adverse obstetric and neonatal outcomes increase in sufferers in the second half of pregnancy. Common maternal consequences include cesarean section, premature birth, abortion, tachycardia, and premature rupture of the amniotic sac, and common neonatal consequences include effects on fetal brain development, increased risk of autism, and neurological problems.

Also, studies show that maternal vaccination by transferring antibodies from the placenta to the fetus makes the baby immune, and since there are few safe treatment methods during pregnancy, the priority is to deal with and prevent the disease. On

the other hand, little information about the possible consequences of vaccination on the mother and fetus does not make it possible to draw definitive conclusions, and the harmful effects of the disease should be considered compared to the possible consequences of vaccination; Therefore, it is suggested to carry out more studies in the field of vaccination of pregnant mothers, comparing different types of corona vaccines in pregnancy and its effects on the mother and the fetus.

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