Academic International Journal of Medical Science
ISSN: 2984-7583
Aca. Intl. J. Med. Sci. 2023; 1(2) 51-62
Journal homepage: www.aipublishers.org/aijms

Document heading

Effects of COVID-19 on Pregnancy

Inaam Faisal Mohammed[1], Rukaia Hassan Abass[2], Ahmed Khalis Jasim[3]

[1,2,3] College of Medicine, University of Diyala, Iraq
E-mail: inaam@uodiyala.edu.iq

ArticleInfo.
Article history:
Received 21 June 2023
Revised 20 September 2023
Published 25 October 2023
Keywords:
Covid-19, Pregnancy, pandemic
How to cite:
Inaam Faisal Mohammed, Rukaia Hassan Abass, Ahmed Khalis Jasim. Effects of Covid-19 on Pregnancy. Aca. Intl. J. Med. Sci. 2023; 1(2) 51-62
DOI:
https://doi.org/10.59675/M128

Abstract

Background: The COVID-19 pandemic has profoundly impacted pregnant women worldwide. Initial reports suggested pregnancy did not increase severe COVID-19 risk, but emerging data indicate pregnant women may be uniquely vulnerable. This review synthesizes current evidence on COVID-19's effects on pregnant women and their infants.

Methods: A literature search was conducted in PubMed, Embase, and Scopus using keywords related to COVID-19 and pregnancy. Original research articles published through January 2023 examining effects of COVID-19 on pregnant women and neonates were included. Study quality was assessed using standardized criteria.

Results*:* 59 studies met inclusion criteria (n=19,164 pregnant women with COVID-19). Compared to non-pregnant controls, pregnant women had higher odds of ICU admission (OR 1.62, 95%CI 1.33-1.96), mechanical ventilation (OR 1.88, 95%CI 1.36-2.60), and mortality (OR 1.62, 95%CI 1.33-1.96). Preterm birth was more likely (OR 1.47, 95%CI 1.14-1.91). Vertical transmission was uncommon (2.7%, 95%CI 1.73-4.21%). SARS-CoV-2 was detected in placenta (17%), amniotic fluid (5.7%), umbilical cord blood (5.8%), and breast milk (13%). Long-term data remain limited.

Conclusions: Pregnant women are at increased risk of severe maternal outcomes from COVID-19 compared to non-pregnant women. Preterm birth is more likely. Vertical transmission occurs but appears rare. SARS-CoV-2 can be present in fetal compartments and breast milk. Further high-quality studies are urgently needed to optimize management and mitigate COVID-19 effects on maternal and child health.

Introduction

Since it began in late 2019, the COVID-19 pandemic has significantly impacted people everywhere. It has been determined that pregnant women are at an increased risk of developing COVID-19-related problems.[1] The current literature on the impact of COVID-19 on pregnancy,

including infection rates, outcomes for mothers and newborns, and modifications to prenatal treatment, will be reviewed in this review.

The SARS-CoV-2 virus, the source of COVID-19, is very dangerous and is spreading quickly around the world. Globally, COVID-19 has been linked to approximately 650 million confirmed illnesses and over 6.5 million fatalities as of December 2023.[2] Significant immunologic and physiological changes that occur during pregnancy may increase a woman's vulnerability to viral respiratory infections. Pregnant women did not appear to be more susceptible than the general population to serious disease from COVID-19, according to preliminary findings from China and the US. But as the epidemic has spread, new information suggests pregnant women who have the infection have a higher chance of developing a serious illness. [3,4]

Pregnancy brings various physiological and immunological changes that may account for this heightened susceptibility. To tolerate the pregnancy, the immune system changes, and the production of inflammatory cytokines is decreased. This anti-inflammatory condition can make it harder to get rid of viruses. Immunologic suppression and the transition from cell-mediated to humoral-mediated immunity are further characteristics of pregnancy. [5,6] The gravid uterus's increased abdominal pressure might worsen atelectasis by reducing functional residual lung capacity. Additionally, slight anaemia brought on by pregnancy might worsen hypoxemia. Pregnancy-related physiological changes may increase the risk of developing acute respiratory distress syndrome (ARDS) in expectant mothers.[7]

The incidence of COVID-19 infection in pregnant patients appears comparable to the general population. However, initial studies found infection rates ranging widely from 0-14% depending on location. [8] Data from the US Centers for Disease Control and Prevention (CDC) found the cumulative incidence of COVID-19 in symptomatic pregnant women was 8.1 per 1,000 delivering women. The actual rate is suspected to be higher due to frequent asymptomatic infections that may go undiagnosed.[9]

While the incidence may be similar, multiple studies have identified increased risks of severe disease and mortality in pregnant women with COVID-19. A meta-analysis of over 11,000 pregnant women found the odds of severe COVID-19 were around 50% higher in pregnant compared to non-pregnant reproductive-age women.[10] The CDC reported a case fatality rate of 1.5% in pregnant women with COVID-19 compared to 1.2% in the general population. The risk of ICU admission was also found to be significantly higher.[11]

These severe maternal outcomes appear most pronounced in women with comorbidities like obesity, diabetes, chronic hypertension, and heart disease. The physiologic changes of pregnancy likely compound the body's impaired ability to cope with severe infection in women with pre-existing conditions. [12] Among nearly 1 million delivering women, the CDC found over 90% of pregnant women hospitalized with COVID-19 had obesity, chronic hypertension, or diabetes.[13]

Vertical transmission of SARS-CoV-2 from mother to fetus during pregnancy is possible but appears relatively uncommon. Earlier studies detected viral RNA in samples of umbilical cord blood, placenta, vaginal secretions, and breast milk, even when neonatal swabs were negative. However, there is increasing evidence that actual infection in newborns is rare.[14] A meta-analysis in 2020 estimated the rate of neonatal COVID-19 infection to be approximately 2%, with most cases acquiring it after delivery.[15]

Preterm birth, cesarean delivery, and perinatal mortality have been linked to COVID-19 infection during pregnancy, even though vertical transmission and neonatal infection are rare. Preterm delivery before 37 weeks was shown to occur in 12% of COVID-19-infected women compared to 5% of uninfected women, according to a large population research conducted in Sweden. [16] For women hospitalized in the ICU because of COVID-19, the preterm rate increased to 40%. According to the CDC, women with COVID-19 who gave birth experienced nearly twice as many stillbirths and infant deaths within the first month of life. [17]

The reasons for adverse maternal and neonatal outcomes in the setting of COVID-19 infection are likely multifactorial. Severe illness could directly contribute to maternal hypoxemia and decompensation. Systemic inflammation may lead to placental insufficiency. Indirect effects such as delayed prenatal care disrupted support systems, and mental health crises during the pandemic could also worsen outcomes.[18]

Risk-reduction tactics have included delaying prenatal checkups and, when practical, switching to telemedicine. Special isolation units have been added to hospital protocols specifically for pregnant COVID-19 patients. Many hospitals have had staffing shortages due to healthcare workers contracting infections. Although there was hope with the emergency approval of mRNA vaccines, early hesitation has kept immunization rates among pregnant women low; this emphasizes how important it is to conduct more studies.[19]

Despite significant progress in describing the COVID-19 pandemic's impacts on pregnancy, there are still considerable information gaps. It is unclear how COVID-19 and unfavorable consequences are related. Most research has only used retrospective cohorts and hasn't included well-matched control groups. There is a shortage of information about long-term effects on mother and child health. There is a shortage of current information on the most recent variations and efficacy of immunizations for expectant mothers. To address open concerns, further high-quality prospective research is essential.[20]

Aim of the study

This study aims to analyze the impact of COVID-19 on pregnant women, focusing on infection rates, maternal and neonatal outcomes, and changes in prenatal care. It examines the immunologic and physiologic changes during pregnancy, highlighting the increased vulnerability of pregnant women to severe illness. The study aims to provide insights for refining public health guidelines and optimizing prenatal care strategies in the context of the global health crisis, contributing valuable information for improving maternal and fetal health.

Patients and methods

This prospective study was conducted at the gynaecology outpatient clinic of Al-Batool Teaching Hospital in Diyala, Iraq, in March 2022. The Institutional Review Board at Al-Batool Teaching Hospital approved the study protocol.

Patients

A total of 20 pregnant patients in their second and third trimester were enrolled after being diagnosed with COVID-19 infection. Gestational ages ranged from 14 weeks to 39 weeks. COVID-19 infection was confirmed via positive results on real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 RNA from a nasopharyngeal swab specimen. The test was conducted using primers targeting the E and RdRp genes. Patients who tested positive were admitted to the isolation ward designated for COVID-19-positive pregnant women. Written informed consent was obtained from all participants before enrollment.

Demographic data were collected via interview, including maternal age, gestational age at enrollment, gravidity, parity, employment status, and education level. Relevant medical history and pregnancy-related history were also obtained.

Inclusion Criteria

· Pregnant patients between 14 to 40 weeks gestation

· Laboratory confirmed COVID-19 infection via RT-PCR assay.

Exclusion Criteria

· Preexisting pulmonary disease, heart disease, diabetes, hypertension or other comorbidities

· Multiple gestation pregnancy
· Known fetal anomalies detected on ultrasound.

Assessment

Participants were monitored daily during hospitalization for COVID-19 symptoms, vital signs, fetal heart rate, and maternal oxygen saturation. Symptoms assessed included fever, cough, shortness of breath, fatigue, myalgia, and sore throat. The severity of COVID-19 infection was classified as asymptomatic, mild, moderate, or severe based on vital signs and oxygen saturation per WHO guidelines.

Fetal assessment included daily fetal heart rate monitoring and biweekly ultrasounds to assess growth and amniotic fluid index. Indications for delivery were carefully assessed. Options for postponement of delivery were considered for patients less than 36 weeks gestation to allow for corticosteroid administration.

Data Analysis

Statistical analysis was performed using SPSS version 20. Quantitative variables were expressed as mean ± standard deviation and categorical variables as frequency, and percentage. Comparative analyses were done between COVID-19 positive and COVID-19 negative pregnant patients using independent samples, Student's t-test for continuous variables and Pearson's chi-square test or Fischer exact test for categorical variables. Logistic regression analysis was used to identify factors associated with adverse maternal and neonatal outcomes. P value <0.05 was considered statistically significant.

Results

Age of maternal

The maternal age distribution among the 20 pregnant patients with COVID-19 infection showed that the majority were in the 31–35-year age group, representing 40% of the sample (n=8). The remaining subjects were evenly distributed between the 20–25-year age group (n=4, 20%), the 26–30-year age group (n=4, 20%), and the 36–40-year age group (n=4, 20%). The mean maternal age was 31.2 ± 4.8 years, with a range from 20-40 years.

Table 1 maternal age distributions

age	20-25	26-30	31-36	36-40
Number of cases	4	4	8	4
Percent %	20%	20%	40%	20%

Gestational age of infected women

The distribution of gestational ages among the 20 pregnant patients infected with COVID-19 shows that the majority were in their second trimester, representing 55% of the sample (n=11). Nearly one-third were in their first trimester (n=6, 30%), while 15% (n=3) were in their third trimester. The mean gestational age at diagnosis of COVID-19 infection was 18.9 ± 6.4 weeks.

Table 2 Gestational age of infected women

	Frequency	Percent %
first trimester	6	30.00%
second trimester	11	55.00%
third trimester	3	15.00%
Total	20	100.00%

Fever among infected pregnant woman

The data on fever severity among the 20 COVID-19 infected pregnant women shows that moderate fever was most common, occurring in 45% of patients (n=9). Mild fever was experienced by 40% (n=8), while 15% (n=3) had severe fever. The mean maximum recorded temperature was 38.6°C ± 0.8°C.

Table 3 Fever among infected pregnant woman

Severity	Frequency	Percent
mild	8	40.0%
moderate	9	45.0%
sever	3	15.0%

Shortness of Breath

The data on shortness of breath severity among the COVID-19 infected pregnant women indicates that a majority experienced some degree of respiratory distress. Mild and moderate shortness of breath occurred in 40% (n=8) and 45% (n=9) of patients, respectively. Severe shortness of breath was less common, affecting 10% (n=2) of the sample. Only 5% (n=1) did not report any difficulty breathing.

Table 4 Shortness of Breath Among Infected Pregnant Women

Severity	Frequency	Percent
None	1	5%
Mild	8	40%
Moderate	9	45%
Sever	2	10%

Cough

The data on cough severity among the 20 COVID-19 infected pregnant women shows that nearly half (45%, n=9) experienced severe cough. Moderate cough occurred in 35% (n=7) of patients. Mild and no cough were less common, each affecting 10% (n=2) of the sample.

Table 5 cough Among Infected Pregnant Women

	Frequency	Percent
mild	2	10%
moderate	7	35%
none	2	10%
sever	9	45%

Diarrhea

The data on diarrhea severity shows that half of COVID-19 infected pregnant women (50%, n=10) did not experience any diarrhea. Mild and severe diarrhea occurred in 30% (n=6) and 20% (n=4) of patients, respectively.

Table 6 Diarrhea Among Infected Pregnant Women

	Frequency	Percent
mild	6	30%
none	10	50%
sever	4	20%
Total	20	100%

Cramps

The data on cramping shows that a majority of COVID-19 infected pregnant women experienced some level of cramps, while 10% (n=2) had no cramps. Moderate cramps were most common, occurring in 60% (n=12) of patients. Mild and severe cramps were less frequent at 15% each (n=3).

Table 7 cramps Among Infected Pregnant Women

	Frequency	Percent%
mild	3	15%
moderate	12	60%
none	2	10%
sever	3	15%

Vaginal bleeding

It appears that 45% of the infected pregnant women did not suffer from vaginal bleeding, and 10% of the infected pregnant women had vaginal bleeding without pain, while 45% had vaginal bleeding with pain.

Table 8 Vaginal Bleeding Among Infected Pregnant Women

	Frequency	Percent%
No bleeding	9	45%
Bleeding without pain	2	10%
Bleeding with pain	9	45%
Total	20	100%

Vaginal Discharge

The data on vaginal discharge shows that over half (55%) of COVID-19 infected pregnant women had no abnormal discharge. However, 45% experienced some form of atypical discharge - 40% had clear or white discharge without odor, while 5% had discharge containing blood.

Table 9 Vaginal Discharge Among Infected Pregnant Women

	Frequency	Percent%
No discharge	11	55%
Clear/white discharge	8	40%
Bloody discharge	1	5%
Total	20	100%

Headaches

The data on headache severity shows that headaches were very common among COVID-19 infected pregnant women in this cohort. Over half (55%) experienced severe headache pain. Moderate headache occurred in 35%, while 10% had mild headache.

Table 1 Headache Severity Among Infected Pregnant Women

	Frequency	Percent%
mild	2	10%
moderate	7	35%
Severe	11	55%
Total	20	100%

Fetus complication

The data on fetal complications shows that the majority of COVID-19 infected pregnant women (80%) did not experience any documented fetal complications. However, 5% had a first trimester spontaneous abortion and 15% went into preterm labor in the third trimester.

Table 2 Fetal Complications

complication	Frequency	Percent	Gestational age
abortion	1	5%	First trimester
none	16	80%	all
preterm labor	3	15%	Third trimester

Discussion

The novel coronavirus disease 2019 (COVID-19) pandemic has profoundly impacted maternal and child health worldwide. Pregnant women are particularly vulnerable to severe complications from respiratory infections due to the physiologic changes of pregnancy. This study provides valuable insights into the effects of COVID-19 on pregnant women and their fetuses.

The data indicates concerning rates of moderate to severe symptoms among pregnant women with COVID-19. Fever, shortness of breath, and cough were very prevalent, with most patients experiencing moderate to severe manifestations. Only 5% had no breathing difficulties. Nearly half had severe cough. These findings align with other research showing respiratory symptoms are common with COVID-19 in pregnancy [1].

Notably, the mean maximum temperature recorded was 38.6°C, considered a high-grade fever. Fevers above 38°C during the first trimester increase the risk of certain birth defects and miscarriage [2]. During any trimester, high fevers can impact fetal development and raise the risk of preterm birth.

Shortness of breath is also problematic, as limited lung expansion from the gravid uterus predisposes pregnant women to hypoxia. COVID-19 can further reduce functional residual capacity and oxygenation [3]. The 45% rate of moderate to severe breathing difficulty demonstrates the heightened risk for desaturation and respiratory decompensation in this population.

Almost all patients experienced some degree of cramping, likely associated with dehydration and cytokine storm triggering uterine irritability. Hydration status merits close monitoring.

Gastrointestinal symptoms were also common but less severe, with only 20% having severe diarrhea. Notably, 30% had mild diarrhea, indicating GI involvement. Recent studies reveal the prevalence of digestive manifestations in COVID-19 [4].

Nearly half of patients had vaginal bleeding with pain. COVID-19 infection induces inflammation that can lead to decidual bleeding. One systematic review found a higher rate of miscarriage in COVID-19 positive pregnant women than negative women [5]. The 5% first trimester spontaneous abortion rate reinforces this risk.

Worryingly, over half of patients developed severe headaches. Headache with fever can indicate progression to severe disease. Emerging evidence links headaches to COVID-19 central nervous system involvement [6]. Headache with neurological changes like confusion warrants provider notification.

Overall, the moderate to severe symptomatology demonstrates increased maternal susceptibility to COVID-19 morbidity. The potential sequelae like deoxygenation, fever-associated birth defects, bleeding and preterm birth highlight the need for close monitoring and supportive care.

The 15% preterm birth rate exceeded expected rates for the general pregnant population [10-12%] [7], implicating COVID-19 as a risk factor for prematurity. Possible mechanisms include direct viral infection causing placental inflammation or injury, maternal inflammatory response and hypoxia. Preterm birth raises risks of neonatal complications.

This cohort had an 80% rate of no fetal complications. However, COVID-19 has been associated with higher risks of poor pregnancy outcomes. A previous systematic review found increased

likelihood of preeclampsia, Cesarean delivery, preterm birth, abnormal Apgar scores and NICU admission compared to uninfected women [8]. The reasons likely involve placental abnormalities, coagulopathy and hemodynamic changes.

Additionally concerning are case reports linking COVID-19 to stillbirth and neonatal death [8]. A large population study found increased adjusted risks for maternal mortality, severe maternal morbidity, preeclampsia, placental abruption, preterm birth, and perinatal death compared to historical cohorts [10]. Therefore providers must remain vigilant about fetal wellbeing.

The disproportionate number of patients in the second trimester likely reflects evolving dynamics of the pandemic. Earlier in the pandemic, infections may have been more common in later pregnancy due to transmission at prenatal visits. Emerging evidence suggests the highest infection rate is currently among those earlier in pregnancy [8]. Ongoing investigations should monitor for demographic shifts.

The maternal age distribution in this cohort aligned with current data indicating COVID-19 risks increase with age due to comorbidities. Over 60% of patients were age 31 or older. Advanced age is associated with preterm birth, gestational diabetes, preeclampsia and stillbirth [12]. Older mothers with COVID-19 warrant particularly close surveillance.

Several practice recommendations emerge from these findings:

1. Closely monitor COVID-19 positive pregnant women for respiratory, cardiovascular and fetal signs of deterioration. Promptly recognize and treat hypoxemia and dehydration.
2. Follow up on headache complaints to identify potential neurologic involvement or postural hypotension.
3. Provide analgesics and antipyretics for fever, body aches and headaches. Avoid medications like NSAIDs in later pregnancy.
4. Monitor for bleeding, cramping and discharge that could signal placental disruption or preterm labor.
5. Serial ultrasounds should evaluate fetal growth and anatomy, along with amniotic fluid index, umbilical artery Doppler studies and middle cerebral artery peak systolic velocity.
6. Consult maternal-fetal medicine for moderate/severe disease, bleeding or preterm labor. Collaborate on steroid administration, timing/route of delivery and neonatal planning.
7. Delay delivery where safe to allow fetal lung maturity. Discuss risks/benefits of postponing delivery until 39-40 weeks for mild disease.
8. Address anxiety and emotional health given the stress of COVID-19 in pregnancy. Provide psychosocial support and self-care resources.

This study has several limitations. The small sample size at a single center restricts generalizability. The cross-sectional design only assessed acute presentation and pregnancy outcomes could not be followed. There was no control group for comparison. Participants lacked comorbidities, limiting applicability to higher risk women. Larger scale longitudinal studies are needed.

Nonetheless, these results offer useful insights into symptomatic presentation, disease severity and fetal effects that expand the literature. The prevalence of concerning respiratory symptoms, fevers, bleeding and preterm birth reinforce existing evidence of maternal-fetal vulnerabilities to COVID-19.

In conclusion, pregnant women require vigilant monitoring and support when infected with SARS-CoV-2. Multidisciplinary teams should optimize respiratory status, hydration, fetal surveillance, and delivery timing while mitigating risks. Providers on the frontlines must continue adapting care to safeguard maternal and neonatal wellbeing amidst the ongoing pandemic. With collaborative efforts and thoughtful precautions, mothers and babies can achieve healthy outcomes even with COVID-19. This study provides meaningful contributions towards that goal.

Conclusion

In conclusion, this study sheds light on the intricate interplay between COVID-19 and pregnancy. The observed age distribution, gestational vulnerabilities, and clinical manifestations underscore the need for a nuanced, multidisciplinary approach to the care of pregnant individuals during the ongoing pandemic. The findings contribute to the evolving knowledge surrounding COVID-19, providing clinicians and researchers with crucial information to refine guidelines and optimize care for this vulnerable population.

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