



Current Aspects in the Management of SARS-CoV-2 Infection in Pregnancy

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ABSTRACT

Because clinical studies on diagnosis, management, prevention, and many other aspects of pregnancy and breastfeeding during COVID-19 have improved significantly since the beginning of the pandemic, a substantial amount of prior knowledge has changed, and previous publications may no longer be applicable. In addition, to reduce maternal, fetal, and neonatal morbidity and mortality in the event of future pandemics, vaccination recommendations in pregnancy must be made early. This review of the literature seeks to offer a comprehensive update on the mutual effects of pregnancy and COVID-19 infection, debate current issues based on the most recent discoveries, and identify existing knowledge gaps. Emerging studies indicate significant risks associated with SARS-CoV-2 infection during pregnancy, including preeclampsia, intrauterine growth restriction, preterm birth, and the risk of birth malformations. Vaccination against COVID-19 is advised for women who are pregnant, trying to become pregnant, breastfeeding, or who may become pregnant in the future. Vaccination during pregnancy is associated with the transmission of SARS-CoV-2 antibodies to the fetus. Additional clinical trials should investigate long-term consequences, results, the safety of vaccinations, and the influence of the pandemic on the health of pregnant women.

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1. Introduction

Because clinical studies on diagnosis, management, prevention, and many other aspects of pregnancy and breastfeeding during COVID-19 have improved significantly since the beginning of the pandemic, a substantial amount of prior knowledge has changed, and previous publications may no longer be applicable. As the COVID-19 pandemic moves into its third year, new research shows that being infected with SARS-CoV-2 during pregnancy increases the risk of preeclampsia, intrauterine growth restriction, premature birth, and congenital abnormalities.

There are still a lot of questions about how COVID-19 affects pregnancy and how it affects the fetus in the long run [1]. Aside from making people socially isolated because they have to stay in quarantine, the pandemic has caused several unique stresses for pregnant people. To stop the spread of COVID-19, healthcare providers have changed prenatal and pregnancy care models, visitor policies, and infection prevention policies. They have also made suggestions about how important social distance is [2]. Getting vaccinated or getting a booster shot for COVID-19 while pregnant is safe. Also, the information we have shows that getting vaccinated during pregnancy is linked to passing SARS-CoV-2 antibodies to the fetus. High levels of SARS-CoV-2 antibodies are found in the breast milk of women who have been vaccinated and are breastfeeding. According to data on vaccine coverage, pregnant women have been less likely to receive the COVID-19 vaccine despite their increased risk for severe disease and the risks of adverse pregnancy and neonatal outcomes if infected.

This review of the literature seeks to offer a comprehensive update on the mutual effects of pregnancy and COVID-19 infection, debate current issues based on the most recent discoveries, and identify existing knowledge gaps.

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2. How does COVID-19 affect pregnancy?

The Coronavirus disease 2019 (COVID-19) is still a big problem all over the world. As of June 2022, about 500 million cases and 6 million deaths were documented [3]. Along with the emergence of the COVID-19 pandemic, there have been more reports of COVID-19 in pregnant women [4,5].

As a state of altered physiological and immunological function, pregnancy offers a higher risk of contracting the virus. Adaptive alterations in the respiratory system, such as a reduction in respiratory volumes, an increase in oxygen consumption, an elevated diaphragm, and edema of the respiratory tract, contribute to the diminution of hypoxia intolerance. In addition, a prothrombotic state makes pregnant women more vulnerable to serious diseases [6]. The current understanding of the entire impact of COVID-19 infection on pregnant women is incomplete, mostly because the evidence is continually collected.

In pregnancy, factors such as older maternal age, a high body mass index, and pre-existing comorbidities tend to affect the prognosis for COVID-19 [7]. Given that SARS-CoV-2 infection is associated with severe pulmonary manifestations, such as pneumonia (the most prevalent nonobstetric condition in pregnancy [8]), acute respiratory distress syndrome, pervasive microemboli, and coagulation perturbations [9], higher morbidity and mortality were anticipated among pregnant women. Moreover, pregnancy is linked with normal maternal physiological changes such as hypercoagulability, altered cell-mediated immunity [10] and modifications in pulmonary function that result in decreased total lung capacity and difficulty adequately removing pulmonary secretions [11]. These modifications are anticipated to increase the possibility of clinically severe pneumonia in pregnant women who get COVID-19.

All kinds of pneumonia have been linked to early labor, premature rupture of the membranes, slow growth of the fetus, and death of the fetus, as well as the death of the newborn. According to CDC data, pregnant women are 2–3 times more likely to be admitted to an intensive care unit (ICU) (10.5 vs. 3.9 per 1,000), 2.9 times more likely to need invasive ventilation (2.9 vs. 1.1 per 1,000 cases), 2.4 times more likely to need extracorporeal membrane oxygenation (0.7 vs. 0.3 per 1,000 cases), and 1.7 times more likely to die (1.5 vs. 1.2 per 1,000 cases). Pregnant women are also more likely to end up in the hospital, need oxygen therapy or endotracheal intubation, and have a higher case-fatality rate than women of the same age who are not pregnant [12–14].

When pregnant women with SARS-CoV-2 infection are compared to those who do not have SARS-CoV-2 infection, they have an increased risk of preeclampsia, premature birth, gestational diabetes, low birth weight, and stillbirth [15–18]. According to data from the United Kingdom and the United States System, black race, older age, and underlying medical conditions such as obesity, chronic lung disease, chronic hypertension, pregestational diabetes mellitus, and being overweight or obese were risk factors for hospitalization among pregnant women [19,20].

Evaluation of every pregnant woman is not required but is favored [21]. The most prevalent symptom among pregnant COVID-19 patients is fever [22]. During the first trimester of pregnancy, fever and hyperthermia might negatively impact organogenesis [23,24]. It could potentially cause neural tube abnormalities and miscarriage [25]. Additionally, maternal fever may impact brain development as well as heart and tooth health [26]. According to studies, even a modest fever exposure during the pre-implantation phase can result in an abortion [27]. Acetaminophen may be used properly to prevent problems, however, recent research suggests that Ibuprofen may exacerbate the condition and so should not be administered to COVID-19 patients [28–30]. In addition to shortness of breath, fatigue, dry cough, sore throat, headache, weakness, myalgia, nasal congestion, and gastrointestinal indications, such as nausea and vomiting, are also typical [31–34].

Recent studies have shown that COVID-19-positive moms have a higher risk of miscarriage, premature birth, preeclampsia, and cesarean section than the general population. In addition, their newborns are more likely to die prematurely and be hospitalized in a neonatal intensive care unit (NICU) [35–37]. Moreover, as COVID-19 infection is usually associated with atypical symptoms in newborns, such as the multisystem inflammatory syndrome in children (MIS-C), infants must be monitored more carefully to detect abnormal symptoms [38,39].

Although it does happen occasionally, the intrauterine viral transmission of COVID-19 from the mother to the fetus before delivery is rare [40,41]. There may be more than one reason why it seems like transmission is rare. For intrauterine transmission of a viral pathogen to happen, the pathogen must reach and cross the placenta, which SARS-CoV-2 infection does not do [42,43]. Also, the placenta may not have high levels of the main factors that help SARS-CoV-2 get into cells, such as angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2), although the data on the expression of these factors are not always the same [44,46].

A systematic review also found no link between breastfeeding and late postnatal transmission, which is defined as happening after 72 hours of life. But it was seen that the risk of late postnatal transmission was higher when the babies were not taken away from their infected mothers [47]. This possible increased risk needs to be weighed against the known benefits of bonding between mother and child and the low risk of a serious illness in the infant. Most guidelines say that an infected mother and her baby should stay in the same room, especially if the mother is not sick and has no fever [48,49]. The American Association of Pediatrics

(AAP) says that mothers and newborns can stay in the same room as usual. The mother should wear a mask and wash her hands, and healthcare providers should wear gowns, gloves, N95 respirators, and eye protection when caring for healthy infants in the room when the mother has COVID-19. Breastfeeding is also encouraged with the same precautions [50].

3. COVID-19 vaccination in pregnant and lactating persons

Since the start of the COVID-19 epidemic, pregnant women have been identified as a population at high risk for serious consequences. Observational studies demonstrated that SARS-CoV-2 infection in pregnant women is related to an increased risk of hospitalization, intensive care unit admission, and invasive ventilation compared to nonpregnant women [7,12,51].

Since December 2020, vaccination against COVID-19 has been available and is the most effective way to minimize maternal and fetal problems associated with SARS-CoV-2 infection. Vaccination of a pregnant mother protects against maternal morbidity and mortality, as well as infant protection [52,53]. Professional organizations were first reticent to suggest the vaccination for pregnant women. Pregnant women have not been included in any of the trials for US and UK-approved vaccines, despite their increased risk status. Due to the fact that pregnancy is already considered an immunosuppressed condition, excluding this population from SARS-CoV-2 vaccine trials significantly limits the safety data that may influence a pregnant woman's decision to receive a COVID-19 vaccine [54].

Although pregnant and lactating women were omitted from the first clinical trials that resulted in the approval of three COVID-19 vaccines in the United States, despite the huge number of pregnant and lactating women who have been vaccinated, no safety concerns have been raised. The significantly reduced vaccine acceptance rate among pregnant women resulted in a substantial rise in maternal mortality by the end of 2021. This decreased vaccine acceptance rate is consistent with physician reluctance to suggest immunization during pregnancy, as well as a large lag in vaccine recommendations during pregnancy by professional organizations. To avoid maternal, fetal, and neonatal morbidity and death in the event of future pandemics, vaccine recommendations for pregnant women must be provided as soon as possible.

The Centers for Disease Control and Prevention (CDC) specifies that any of the currently permitted vaccines may be delivered to pregnant or breastfeeding women, regardless of vaccine type [55]. The American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal-Fetal Medicine (SMFM), and the Centers for Disease Control and Prevention (CDC) promote vaccination for pregnant and breastfeeding women. The ACOG also emphasizes that pregnant women should be encouraged to discuss their immunization plan with their obstetrician and ask any questions they may have. This should not, however, be a prerequisite for vaccination, as it could act as a barrier. Patients who deny immunization should be offered it again and informed of the necessity of maintaining other preventative measures, such as wearing a mask and maintaining physical distance [56].

Additionally, maternal immunoglobulin G antibodies cross the placenta effectively, resulting in relatively high titers in the fetus (Jamieson, AJOG 2-2022). There are no known or theorized hazards associated with vaccinating breastfeeding mothers, and there are no immunization restrictions. Women should be reassured that COVID-19 vaccines do not affect fertility, that COVID-19 vaccines cannot cause COVID-19 because none of them contain the live virus, that COVID-19 vaccines do not interact with or alter genetic material, and that the vaccines do not contain controversial ingredients [57]. ACOG advice also does not specify a preferred vaccine type or vaccination timing during pregnancy [56]. The Royal College of Obstetricians and Gynecologists in the United Kingdom recommends an mRNA vaccine for pregnant women because there is more safety data available for mRNA vaccines than adenoviral vaccines [58].

4. Mental health: impact of isolation measures on pregnancy outcome during the COVID-19 pandemic

Numerous issues remain unresolved regarding the effects of COVID-19 on pregnancy and its long-term effects on the fetus [1]. In addition to the social isolation caused by quarantine, the pandemic has introduced some novel stressors for pregnant women [2].

Anxiety is a prevalent mental health issue in pregnancy [59]. Moreover, the COVID-19 epidemic concerns the mental health of nearly everyone [60]. In general, it has been demonstrated that females are more susceptible to psychological effects and are associated with more stress, anxiety, and sadness [61]. In addition to conventional issues such as infection and quarantine, pregnant women have additional concerns, such as worry of possible vertical transmission and teratogenic effects of the virus [62]. Psychiatric disorders are associated with an increased risk of preeclampsia, nausea and vomiting, preterm labor, low birth weight, and low neonatal APGAR score during pregnancy [63].

During the pandemic, a comprehensive multicenter survey of more than 9000 pregnant and breastfeeding women revealed elevated levels of sadness and anxiety [64]. In addition, studies have identified race, social and familial support, being underweight during pregnancy, employment, primigravida, being younger than 35, education, and low physical activity as potential risk factors for anxiety connected to pandemics [65-68]. Anxiety rates ranged from 3.8% to 17.5% among pregnant women in Asian countries and from 23.9% to 72.0% in Western countries, according to a meta-analysis. This study also found a 5.2% to

40% depression rate [69]. In addition, prior research [70] has found a higher prevalence of anxiety during the first trimester of pregnancy compared to the second and third.

Consequently, women remain susceptible to mental health difficulties even after giving birth. People with coronavirus are quarantined in the hospital. Also, after the possible delivery, the infant may be separated from the mother for safety purposes. This separation could result in anxiety and depression [71].

In addition, the widespread anxiety and dread of the pandemic have influenced the healthcare staff, which could add to the difficulty of providing maternal care. When caring for pregnant COVID-19 patients, additional activities should be explored, including the implementation of psychological support services for both health professionals and pregnant women [72-74].

Consequently, management includes increasing clinician awareness of the elevated risk for these mental health problems, providing health care professionals with the appropriate tools to assess for perinatal depression and anxiety, and ensuring that these assessments include inquiries about social supports and evaluation of/coping with the pandemic. In addition, healthcare professionals must have clear evidence-based standards for either treating individuals or referring them to other experts, and, in the event of transfer, ensure that patients are aided with service navigation [75].

Cognitive-Behavioral Therapy (CBT) and mindfulness-based methods are beneficial in lowering depression and anxiety in perinatal women, according to substantial evidence. CBT is a manualized intervention that may be administered by a variety of primary health care specialists. With these increased rates of sadness and anxiety the management should include more primary health care professionals to develop skills to provide CBT and to ensure that family health teams have mental health professionals that can provide counselling. Implementing extensive public health and clinical interventions in the setting of the pandemic can be difficult, but there is evidence that electronic interventions can effectively address mental health issues [75-77]. For instance, the management in Ontario, the Canadian Mental Health Association (CMHA) has developed a self-guided manualized intervention called Bounceback, which involves a skill-building program that individuals can access over the phone with a coach and via online videos [78]. Given the increased prevalence of mental health issues, electronic therapies should be studied further.

The management of psychological distress may involve educating the workforce about mental health difficulties, offering training and motivating sessions to create constructive coping strategies, and developing resilience. Additionally, it is essential to search for potential resilience traits that may protect against prenatal stress. It has been demonstrated that social support can attenuate the effects of prenatal anxiety and depression symptoms on the mother and baby stress response systems. Teaching them relaxation techniques such as yoga or meditation can also aid in their good stress management. Physical activity is also connected with a decrease in depressed and anxious symptoms in pregnant women, and so may serve as an additional component in resilience. Regular online connection with family members is a good approach to build their support system, particularly for those who work away from home or are quarantined [79-81].

The management for reducing mental health problems experienced by pregnant people and preventing adverse developmental and health outcomes for their unborn children is systemically targeting specific COVID-related experiences (e.g., social isolation, relationship conflict) and the associated mental health difficulties through governmental, public health, and mental health initiatives.

5. Conclusions and future perspectives

This review of specialized studies proposes to provide current, effective, and efficient management regarding the importance of vaccination during pregnancy, preventing the negative effects of the pandemic on the mental health of pregnant women, and implicitly limiting their long-term complications.

There is currently substantial evidence that SARS-CoV-2 infection during pregnancy increases the risk of adverse maternal, fetal, and newborn health outcomes. Additional clinical trials should investigate long-term consequences, results, the safety of vaccinations, and the influence of the pandemic on the health of pregnant women. Understanding the impact of the COVID-19 epidemic on the mental health of pregnant women is becoming increasingly urgent. Vaccination against COVID-19 is advised for women who are pregnant, trying to become pregnant, breastfeeding, or who may become pregnant in the future. To better cope with the severity of the disease, it is necessary to continue vaccine development that includes pregnant persons in clinical trials and research the pathophysiology of SARS-CoV-2 in pregnant individuals.

Therefore, it is suggested that we optimize the lessons acquired from the COVID-19 pandemic in order to apply them to future planning and response to new illnesses.

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