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COMMENTARY

Impact of COVID-19 in pregnant and lactating women and the implications for their offspring

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Abstract
This commentary briefly discusses COVID-19 in pregnant and lactating women, the mother to child transmission risk, vaccination in pregnant and lactating women and transplacental antibody transfer after COVID-19 vaccination in pregnancy.

Introduction

The coronavirus disease 2019 outbreak is the first pandemic of the century, which has led to major impacts on health systems, society mobility and the economy. In December 2020 the Centers for Diseases Control and Prevention (CDC) included pregnancy as one of the high- risk medical conditions in phase 1c of their COVID-19 vaccine allocations, along with cancer, chronic kidney disease, diabetes, chronic obstructive pulmonary disease, heart disease, immunosuppression, and obesity. Increasing numbers of pregnant women with COVID-19 are being reported globally, with more than 73,600 infections and 80 maternal deaths in the United States alone as of 1 March 2021.[1] Pregnant women and their neonates are considered vulnerable populations for COVID-19

infection, with significantly greater morbidity and mortality risks.[2] Although pregnant women do not seem to contract this infection more frequently than the general population, they are at risk factor for severe COVID-19 disease. Data from large studies have demonstrated that approximately 8–11% of pregnant women with COVID-19 require hospitalization and between 2–4% require admission to an intensive care unit.[3]

Mother to child transmission

Less than 2% of neonates born to SARS-CoV-2-infected women test SARS-CoV-2 positive within 24 hours of birth. Postnatal transmission appears to be responsible for most of the SARS-CoV-2 infections documented in neonates. Mother-to-foetus (in utero or transplacental) transmission is a rare event.[4] Routes and mechanisms of transmission that have been reported are:

In utero transmission: possible, but rare and more likely to occur with severe maternal disease. The angiotensin converting enzyme type 2 receptors required for SARS- CoV-2 cellular entry have been identified on placental cells. These receptors are also found in foetal lung and tissues enabling foetal infection. SARS-CoV-2 causes vascular damage and placenta findings of infected mothers show vascular malperfusion and ischemic injury.

Intrapartum transmission: SARS-CoV-2 is more frequently detected in faeces than vaginal swabs of infected women. Faecal contamination of the vaginal canal during labour can cause transmission during vaginal birth.

Post-natal transmission: is responsible for the majority of neonatal infections through exposure to an infected mother or caregiver. SARS-CoV2 has not been detected in breast milk. Thus, breastfeeding should be promoted as studies have found that SARS-CoV-2 IgG, IgM, IgA can be detected in breast milk.[5,6]

The World Health Organization (WHO) recently convened an expert consultation at which consensus definitions were developed for (i) *in utero* transmission, (ii) *in utero* transmission with foetal demise, (iii) intrapartum transmission and (iv) early postnatal (>48 hours to 28 days) transmission. This is an important guide for neonatologists, paediatricians, and paediatric infectious diseases sub- specialists as it should assist us in investigating and classifying neonatal SARSCoV-2 infections that we encounter in clinical practice.[7]

Impact of COVID-19 on pregnancy and newborn health

The CDC, American College of Obstetricians and Gynecologists (ACOG), the Society for Maternal-Fetal Medicine (SMFM), and other women's health organizations have acknowledged and included pregnancy as a risk factor for severe COVID-19 illness.

A systematic review published in March 2021 demonstrated that SARS-CoV-2 infection in pregnant women compared to their non pregnant counterparts was associated with an increased risk of pre-eclampsia, ICU admission, ventilation, emergency c/s-and prolonged hospital stay for the mom and increased risk of preterm birth, still birth, low birth weight, NICU admission for the neonate.[8] Pregnant patients with co-morbidities such as obesity and diabetes are at increased risk of severe disease associated with perinatal morbidity and mortality compared to the general population.[9,10] Findings from a national cohort study published in England demonstrated an increased risk of adverse maternal and perinatal outcomes in women who tested positive at the time of birth and they were twice as likely to have foetal death and preterm delivery.[9]

Vaccination in pregnant and lactating women

Initial guidance from governments and professional organizations, advised against the COVID-19 vaccination for pregnant and breastfeeding woman. This, combined with the exclusion of pregnant

and lactating women from clinical trials, has led to reluctance of pregnant and lactating women to take up the vaccine offer. Although this advice has been refuted, it has left its mark among these women and has not yet been replaced by the latest recommendations. [3]The ACOG recommends that pregnant and lactating individuals have access to COVID-19 vaccines. Furthermore, prior advice circulated shortly after the start of the COVID-19 outbreak including: 1) that pregnancy should be avoided for 2–3 months after vaccination, 2) that pregnant women should not be vaccinated until the end of pregnancy, and 3) that women should avoid vaccination during lactation has been refuted by recent research findings.[11]

On the 29 January 2021 the WHO stated that there was no specific reason to believe that COVID-19 vaccines expose pregnant women to more risks than benefits.[12]

The ACOG recommended in December 2020 that 1) COVID-19 vaccination should not be withheld from pregnant women meeting criteria for vaccination, (2) pregnant women should be free to make their own decision and (3) access of pregnant women to vaccination should be facilitated by removing unnecessary barriers.[11]

The International Federation of Gynaecology and Obstetrics (FIGO) published its position in early March 2021 stating that there are no risks that outweigh the potential benefits of vaccination for pregnant women. Therefore, FIGO supports offering COVID-19 vaccination to pregnant and breastfeeding women.[3] Data collected from the VSAFE pregnancy registry from 14 December 2020 to 28 February 2021 showed similar incidences of adverse pregnancy and neonatal outcomes when compared to the pregnant population prior to COVID-19.[13]

The WHO recommends exclusive breastfeeding for the first 6 months of life, followed by continued breastfeeding with appropriate complementary foods until or beyond the age of 2 years. Breastfeeding should always be promoted and supported unless exceptional circumstances are present. Breast is best, even in the presence of maternal SARS- CoV-2 infection and the associated risk of infection to the newborn, is not a reason to discontinue breastfeeding. Recent studies have shown that SARS-CoV-2 antibodies cross into breastmilk after maternal COVID-19 vaccination with the possibility of passive immunity and protection to breastfed infants.[6]

The theoretical risks regarding the vaccination's safety does not outweigh the potential benefits of receiving the vaccine. For this reason, all the guidance currently agrees that COVID-19 vaccination is recommended for pregnant and breastfeeding women who meet the criteria for vaccination. The ACOG recommends mRNA vaccines (manufactured by Pfizer or Moderna) for pregnant and postpartum women.[3]

Antibody transfer and neonatal protection

With many women asking whether the vaccine will protect their unborn children, recent studies have reported that the transfer of anti–SARS-CoV-2 antibodies to the foetus is significantly impaired during the third trimester, however a large cohort of patients infected between 15 and 30 weeks of gestation generated both maternal and cord blood anti– COVID-19 antibodies. These observations suggest that there is a lag in antibody transfer across the placenta in late gestation.

Furthermore, a study undertaken in Israel found that the Pfizer-BioNTech COVID-19 mRNA vaccine elicits a rapid rise in IgG titres and results in effective transfer across the placenta, exceeding the titres observed in pregnant women with third trimester SARS-CoV-2 infection.

These data support the effectiveness of COVID-19 mRNA vaccines during pregnancy.

In addition to transplacental acquired defence, specific anti- SARS-CoV-2 antibodies cross into maternal breastmilk, potentially building another line of defence for breastfed infants. Antenatal immunization therefore provides maternal and neonatal protection at highly vulnerable life stages.[2]

Conclusion

To date there is no evidence that contraindicates COVID-19 vaccination in pregnant and lactating women. While ongoing studies and trials address the knowledge gaps about COVID-19 in pregnancy and lactation, pregnant and lactating women should be encouraged and supported to protect themselves and their offspring through vaccination, as current evidence shows that the unvaccinated pregnant and lactating women remain at heightened risk of severe COVID-19 with associated maternal, foetal and neonatal risks. Clinicians need to be aware of these adverse outcomes and adopt effective strategies to reduce maternal and foetal risks.

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