Editorial: Maternal SARS-CoV-2 Infection and Pregnancy Outcomes from Current Global Study Data

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Abstract

During the global COVID-19 pandemic, data from clinical studies, systematic review, and population registry data have shown that when compared with non-pregnant women, SARS-CoV-2 infection in pregnancy is associated with a small increase in risk to the mother. Large cohort studies and registry data collected from 2020 have included the US Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET), COVI-PREG, the UK and Global Pregnancy and Neonatal Outcomes in COVID-19 (PAN-COVID) study, the American Academy of Pediatrics (AAP) Section on Neonatal-Perinatal Medicine (SONPM) National Perinatal COVID-19 Registry, the Swedish Pregnancy Register, and the Canadian Surveillance of COVID-19 in Pregnancy (CANCovid-Preg) registry. Recently published data have shown that most maternal infections with SARS-CoV-2 occur during the third trimester and result in a small increase in hospital admission, admission to the intensive care unit (ICU), mechanical ventilation, preterm birth, and increased cesarean sections in mothers infected with SARS-CoV-2. However, currently approved vaccines given in pregnancy result in an immune response to current SARS-CoV-2 variants. Transplacental transmission of SARS-CoV-2 to the fetus can occur, but the immediate and long-term effects on the newborn infant remain unclear. Therefore, women who are pregnant or planning a pregnancy should be managed according to current clinical guidelines with timely vaccination to prevent infection with SARS-CoV-2. This Editorial summarizes what is currently known about maternal SARS-CoV-2 infection and pregnancy outcomes from multinational studies.

Keywords: Editorial • COVID-19 • Treatment Outcome

Since the beginning of the SARS-CoV-2 pandemic in early 2020, there have been concerns that pregnant women may have more severe COVID-19 symptoms and negative effects on pregnancy outcomes and that SARS-CoV-2 may be transmitted from the mother to the fetus or newborn infant. A year ago, in July 2020, a systematic review of the literature on SARS-CoV-2 infection in pregnancy concluded that the risk of preterm birth and cesarean delivery increased but that maternal morbidity and mortality were similar to non-infected pregnant women [1]. It was believed that vertical transmission of SARS-CoV-2 ‘probably’ occurred, but only in a small proportion of cases [1]. By September 2020, studies from Italy that examined placental tissue confirmed maternal-fetal transmission of SARS-CoV-2, by recruiting maternal inflammatory cells in the placenta, but without villitis [2,3]. Although vertical transmission of SARS-CoV-2 is rare, it most commonly occurs in the third trimester of pregnancy [2,3].

In April 2021, the findings from the multinational INTERCOVID study were published [4]. This cohort study analyzed data from March to October 2020 from 43 institutions in 18 countries to compare pregnancy outcomes in women infected with SARS-CoV-2 with non-infected pregnant women who received the same level of maternal care [4]. Pregnant women with COVID-19 had an increased risk for preeclampsia/eclampsia, infections, ICU admission, maternal mortality, and preterm birth [4]. In May 2021, a review of the published literature from April to August 2020 showed that 11% of pregnant women with COVID-19 required admission to the intensive care unit (ICU), 8% required mechanical ventilation, and most maternal infections occurred in the third trimester of pregnancy [5]. Also, this literature review identified that for women with COVID-19 who gave birth, 28% had a preterm birth, and 57% had a cesarean section [5].

Recent studies from population registries have been of particular value in evaluating the epidemiology of SARS-CoV-2 infection in pregnant women. Population registries can provide continuous epidemiological and clinical information on emerging and developing diseases and have previously been a valuable resource for information on maternal and infant disease to improve public health [6]. Several international registries have been established to monitor the effects of COVID-19 in pregnancy. Between March and October 2020, US public health
The UK and Global Pregnancy and Neonatal Outcomes in COVID-19 (PAN-COVID) study included a dataset of outcome data that focused on the effect of SARS-CoV-2 infection on the risk of fetal growth restriction (FGR), miscarriage, stillbirth, preterm delivery, vertical transmission, and early-onset symptomatic neonatal SARS-CoV-2 infection [10]. The American Academy of Pediatrics (AAP) Section on Neonatal-Perinatal Medicine (SONPM) National Perinatal COVID-19 Registry includes data for pregnant women who have tested positive for SARS-CoV-2 in samples taken from 14 days before delivery to three days after delivery [10]. In April 2021, Mullins et al. reported the findings from the 2020 UK PAN-COVID registry, which included pregnancies with maternal SARS-CoV-2 infection and the US AAP-SONPM National Perinatal COVID-19 registry which included data on SARS-CoV-2-pregnancies and maternal, fetal, perinatal, and neonatal outcomes [11]. The findings from 4,005 pregnant women with SARS-CoV-2 infection, 1,606 cases from PAN-COVID, and 2,399 cases from AAP-SONPM showed a maternal mortality rate of 0.2-0.5%, early neonatal death in between 0.2-0.3%, and stillbirth in 0.4-0.6% of births, with preterm delivery at <37 weeks gestation in between 12.0-15.7% and extreme preterm delivery at <27 weeks gestation in between 0.3-0.5% [11]. Neonatal SARS-CoV-2 infection was reported in between 0.9-1.8% of all deliveries, and the rates of neonatal small for gestational age (SGA) were between 8.2-9.7% [11]. The high concordance in the findings from the two registries from the UK and US, PAN-COVID and AAP-SONPM, supports the need for public health guidelines to prevent SARS-CoV-2 infection and to promote vaccination of pregnant women and women who are planning a pregnancy.

In May 2021, the findings from national registry data from a prospective cohort study from Sweden were published to determine the outcomes for infants born to mothers who tested positive for SARS-CoV-2 infection [12]. The investigators linked and analyzed the Swedish Pregnancy Register, the Register for Communicable Diseases, and the Neonatal Quality Register that contained 92% of all live births in Sweden between March, 2020 and January, 2021 [12]. However, the authors regarded the findings as exploratory only, as maternal SARS-CoV-2 infection in pregnancy was only significantly associated with a small increase in some neonatal morbidities [12]. Of the 88,159 infants born during the study period, 2,323 (1.6%) were delivered to mothers who were SARS-CoV-2-positive [12]. The mean gestational age of infants born to SARS-CoV-2-positive mothers was 39.2 weeks compared with 39.6 weeks for infants born to non-infected mothers [12]. After matching for maternal characteristics, there was an increase in admissions to NICU (11.7% versus 8.4%), neonatal respiratory distress syndrome (1.2% versus 0.5%), and hyperbilirubinemia (3.6% versus 2.5%) [12]. Neonatal mortality of infants born to SARS-CoV-2-positive mothers was 0.30% compared with 0.12% for infants born to non-infected mothers [12]. Only 21 infants (0.90%) of SARS-CoV-2-positive mothers had positive tests for SARS-CoV-2 in the neonatal period, 12 infants had no neonatal morbidity, and none had congenital pneumonia [12].

On June 3rd, 2021, data were published from the Canadian Surveillance of COVID-19 in Pregnancy (CANCICOVID-Preg) registry from five provinces in Canada, including British Columbia, Ontario, Manitoba, Quebec, and Alberta [13,14]. There were 4,805 pregnant women included in the CANCICOVID-Preg registry as of March 31st, 2021 [13,14]. Data from this registry showed that 37.5% of SARS-CoV-2-positive pregnant women were between 30-34 years of age, 40.1% were diagnosed at between 14-27 weeks gestation, and 43.7% of cases had community-acquired SARS-CoV-2 infections [13,14]. Obesity was the most common co-morbidity in 12.9%, followed by diabetes in 11.2%, and cardiovascular disease in 3.3% [14]. The most common symptoms of COVID-19 in pregnancy were cough (38.5%), fever (27.1%), and headache (25.6%), but 8% were asymptomatic [14]. This study showed that 7.1% of women were hospitalized, and 2.8% required admission to the ICU [14]. Comparison with non-pregnant women of between 18-45 years with COVID-19 showed that pregnant women with COVID-19 were at increased risk of hospitalization (RR 4.26; 95% CI, 3.45-5.10), and admission to the ICU (RR 2.68; 95% CI, 2.02-3.40) [14]. The pregnancy outcomes included 97.4% of SARS-CoV-2-positive mothers had positive tests for SARS-CoV-2 in the neonatal period, 12 infants had no neonatal morbidity, and none had congenital pneumonia [12].
of SARS-CoV-2 have more severe effects on the mother, fetus, and newborn infant. However, early studies have shown that approved vaccines for SARS-CoV-2 effectively prevent infection due to the current main variants of concern of SARS-CoV-2 [16]. A recent exploratory study showed that mRNA vaccines were immunogenic in pregnant women and that antibodies were transported to the infant cord blood and were present in maternal breast milk [17]. Also, pregnant women and non-pregnant women vaccinated with approved mRNA vaccines developed cross-reactive antibody responses and T-cell responses against current SARS-CoV-2 variants of concern [17].

Conclusions

Data from clinical studies, systematic review, and population registry data have shown a small increase in risk to the mother from SARS-CoV-2 infection. Transplacental transmission of SARS-CoV-2 from the mother to the fetus can occur, but the immediate and long-term effects on the newborn infant remain unclear. The increased risk of hospitalization and ICU admission in pregnant women infected with SARS-CoV-2 may be due to the immunosuppressive effects of pregnancy or increased caution by healthcare providers during the COVID-19 pandemic. Women who are pregnant or planning a pregnancy should be managed according to current clinical guidelines with timely vaccination to prevent infection with SARS-CoV-2.

References:

1. Khalil A, Kalafat E, Benlioglu C, et al. SARS-CoV-2 infection in pregnancy: A systematic review and meta-analysis of clinical features and pregnancy outcomes. EClinicalMedicine. 2020;25:100446
2. Facchetti F, Bugatti M, Drea E, et al. SARS-CoV2 vertical transmission with adverse effects on the newborn revealed through integrated immunohistochemical, electron microscopy and molecular analyses of Placenta. EBioMedicine. 2020;59:102951
3. Vivanti AJ, Vauloup-Fellous C, Prevot S, et al. Transplacental transmission of SARS-CoV-2 infection. Nat Commun. 2020;11:3572
4. Villar J, Arrif S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: The INTERCOVD Multinational Cohort Study. JAMA Pediatr. 2021;22:e211050
5. Mark EG, McAleese S, Golden WC, et al. Coronavirus disease 2019 in pregnancy and outcomes among pregnant women and neonates: A literature review. Pediatr Infect Dis J. 2021;40(5):473-78
6. Parums DV. Editorial: Registries and population databases in clinical research and practice. Med Sci Monit 2021;27:e933554
7. Woodworth KR, Olsen EO, Neelam V, et al; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team; COVID-19 Pregnancy and Infant Linked Outcomes Team (PILOT). Birth and infant outcomes following laboratory-confirmed SARS-CoV-2 infection in pregnancy – SET-NE, 16 Jurisdictions, March 29–October 14, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(44):1635-40
8. Panchaud A, Favre G, Pomar L, et al. An international registry for emergent pathogens and pregnancy. Lancet. 2020;395(10235):1483-84
9. Pregnancy and COVID-19 associated coagulopathy registry (COV-PREG-COAG). https://redcap.isth.org/surveys/?s=4IPX9W98BH
10. Banerjee J, Mullins E, Townsend J, et al. Pregnancy and neonatal outcomes in COVID-19: study protocol for a global registry of women with suspected or confirmed SARS-CoV-2 infection in pregnancy and their neonates, understanding natural history to guide treatment and prevention. BMJ Open 2021;11:e041247
11. Mullins E, Hudak ML, Banerjee J, et al; PAN-COVID investigators and the National Perinatal COVID-19 Registry Study Group. Pregnancy and neonatal outcomes of COVID-19: Co-reporting of common outcomes from PAN-COVID and AAP-SONPM registries. Ultrasound Obstet Gynecol. 2021;57(4):573-81
12. Norman M, Navèr L, Söderling J, et al. Association of maternal SARS-CoV-2 infection in pregnancy with neonatal outcomes. JAMA. 2021;325(20):2076-86
13. Money D. Canadian surveillance of COVID-19 in pregnancy: Epidemiology, maternal and infant outcomes. Report #4. Released June 3rd, 2021. Maternal and infant outcomes (March 1, 2020 to March 31, 2021) from five Canadian provinces. http://med-fom-rrdprogram.sites.otl.ubc.ca/files/2021/06/CANCovid_Preg-Report-4-ON-BC-QC-MB-AB_FINAL.pdf
14. McClymont E, Abenhaim H, Albert A, et al. Canadian surveillance of COVID-19 in pregnancy: Co-reporting of common outcomes from PAN-COVID. J Obstet Gynaecol Can. 2021;43(2):165-66
15. Parums DV. Editorial: Revised World Health Organization (WHO) terminology for variants of concern and variants of interest of SARS-CoV-2. Med Sci Monit. 2021;27:e933622
16. Krause PR, Fleming TR, Longini IM, et al. SARS-CoV-2 variants and vaccines. EBioMedicine. 2020;59:102951
17. Collier AY, McMahan K, Yu J, et al. Immunogenicity of COVID-19 mRNA vaccines in pregnant and lactating women. JAMA. 2021;325(23):2370-80