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COVID-19 infection in pregnancy: a Spanish perspective of spontaneous and in vitro fertilization pregnancies



As we continue to learn more about the adverse effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection on perinatal outcomes, it is important to understand whether specific groups of pregnant women, including those who conceive using assisted reproductive technology (ART), are more vulnerable to these consequences. Patients who conceive after in vitro fertilization (IVF) are known to be at a relative increased risk of adverse perinatal outcomes, including hypertensive disorders of pregnancy, low-birth-weight delivery, gestational diabetes mellitus, as well as preterm and operative delivery. Although the absolute risk of these adverse outcomes remains low, it is essential to educate patients about the potential additional risks of conception and subsequent pregnancy complicated by SARS-CoV-2 infection amidst an ongoing global pandemic.

In a prospective, multicenter, observational study by Calvo et al. (1), the investigators aimed to describe the perinatal and maternal outcomes of pregnancies in symptomatic and asymptomatic women infected with SARS-CoV-2. They classified pregnancies based on the method of conception (spontaneous vs. IVF) and oocyte source (autologous vs. donor) in patients who conceived after IVF. During the study period, 1,347 pregnant women found to be positive for SARS-CoV-2, as detected using polymerase chain reaction testing, were identified and registered. Seventy-four (5.5%) of these patients conceived by IVF. The investigators found no difference in disease severity based on the mode of conception. The rate of cesarean delivery in IVF-conceived pregnancies was 55.4%, most commonly due to an induction failure. Using multivariable regression analysis and controlling for maternal age and the clinical presentation of the infection, the investigators found a higher rate of cesarean delivery in the IVF group. Moreover, infected women who conceived by IVF had a higher rate of intensive care unit admission, which was attributed to a higher rate of hypertensive disorders of pregnancy.

This study is strengthened by its size; it includes a large group of pregnant women who underwent IVF and were infected with SARS-CoV-2 and appropriately stratifies them based on the method of conception and oocyte source. The prospective nature of this study allowed for robust data collection, and the tables aptly describe the cohort's baseline characteristics and perinatal outcomes.

The investigators highlighted the differences in IVF and spontaneously conceived pregnancies, specifically the rate of cesarean delivery and hypertensive disorders of pregnancy (2). Although the reported rate of cesarean delivery rate in IVF-conceived pregnancies in this study was well above the stated World Health Organization's ideal rate of 10%–15%, the investigators did not report the

baseline cesarean delivery rate in this population before the pandemic or the rate of cesarean delivery among patients not infected with SARS-CoV-2 who delivered during this time period, thereby limiting conclusions (3). The inclusion of only symptomatic patients without universal screening also introduces a significant risk of a selection bias. Additionally, the investigators used logistic regression but controlled only for maternal age and the clinical presentation of the infection. It is important to consider additional confounders when comparing spontaneous and ART pregnancies, including race, rate of multiple gestation, and gestational age, among others.

The ideal study investigating perinatal outcomes in SARS-CoV-2-positive patients would not only identify patients at the time of infection and track perinatal outcomes but also follow uninfected matched controls who experience pregnancy and delivery in the same clinical context and environment to better understand the correlations between infection and pregnancy outcomes. Furthermore, it is important to test patients for SARS-CoV-2 infection at different stages of reproduction, including preconception, early pregnancy, peripartum, and postpartum.

We have much more to learn about the effect of coronavirus disease 2019 (COVID-19) on the health and wellbeing of pregnant women, including those who conceive by IVF. We must acknowledge the limitations of our current data and strive to better understand more about how COVID-19 can modify pregnancy outcomes at all stages of reproduction so that we can protect our patients and be informed advocates for systemic vaccination in this population. Data regarding the implications of the infection during pregnancy may also inform future scenarios in which preconception and pregnant patients are faced with another coronavirus infection. As we continue to strive for the safe provision of ART, we look forward to more prospective research that can enhance our knowledge and guide our practice, including published peer-reviewed studies from ongoing pregnancy registries and vaccine surveillance systems, such as the University of California San Francisco Assessing the Safety of Pregnancy In the CoRonavirus PandEmic (ASPIRE) study as well as the Centers for Disease Control and Prevention COVID-19 Pregnancy and V-safe registries.

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