Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy

Elyse O. Kharbanda, MD, MPH1; Jacob Haapala, MPH1; Malini DeSilva, MD, MPH1; et al

COVID-19 infection during pregnancy can be associated with severe maternal morbidity.[1] In the United States, 1 COVID-19 vaccine has been approved and 2 have been authorized for use for pregnant women. To date, data on maternal COVID-19 vaccine safety come primarily from passive surveillance, and studies lack an unvaccinated comparison group.[2,3] Spontaneous abortion has been identified as a priority outcome in studies of maternal vaccine safety,[4] and concerns regarding risks of spontaneous abortion may be a barrier to vaccination during pregnancy. We present findings from case-control surveillance of COVID-19 vaccination during pregnancy and spontaneous abortion.

The Vaccine Safety Datalink is a collaboration between the Centers for Disease Control and Prevention and 9 health systems, representing approximately 3% of the US population.[5] We applied a validated pregnancy algorithm, which incorporates diagnostic and procedure codes and electronic health record (EHR) data, to identify and assign gestational ages for spontaneous abortions and ongoing pregnancies.[6] Data from 8 health systems (Kaiser Permanente: Washington, Northwest, Northern California, Southern California, and Colorado; Denver Health; HealthPartners; and Marshfield Clinic, Wisconsin) over seven 4-week surveillance periods from December 15, 2020, through June 28, 2021, were included. Ongoing pregnancies between 6 and 19 weeks' gestation were identified on the last day of each 4-week surveillance period (index date) and contributed data to 1 or more surveillance periods. Spontaneous abortions were assigned to a 4-week surveillance period based on their outcome date; these spontaneous abortions could have been included in the ongoing pregnancy categories during prior periods (eFigure in the Supplement). Vaccination data came from EHRs, medical and pharmacy claims, and regional or state immunization information systems.

We analyzed the odds of receiving a COVID-19 vaccine in the 28 days prior to spontaneous abortion compared with the odds of receiving a COVID-19 vaccine in the 28 days prior to index dates for ongoing pregnancies. Both spontaneous abortions and ongoing pregnancies were assigned to gestational age groups (6-8, 9-13, and 14-19 weeks), surveillance periods, site, maternal age groups (16-24, 25-34, and 35-49 years), number of antenatal visits (≤1 or ≥2), and race and ethnicity. Generalized estimating equations with binomial distribution and logit link were used to account for repeated ongoing pregnancies across surveillance periods. Analyses by manufacturer and gestational age group were also conducted. Analysis was performed using SAS/STAT software version 9.4 (SAS Institute Inc).

This surveillance was approved by the institutional review boards of all participating sites with a waiver of informed consent.

Of 105 446 unique pregnancies, 13 160 spontaneous abortions and 92 286 ongoing pregnancies were identified. Overall, 7.8% of women received 1 or more BNT162b2 (Pfizer-BioNTech) vaccines; 6.0% received 1 or more mRNA-1273 (Moderna) vaccines; and 0.5% received an Ad26.COV.2.S (Janssen) vaccine during pregnancy and before 20 weeks' gestation. The proportion of women aged 35 through 49 years with spontaneous abortions was higher (38.7%) than with ongoing pregnancies (22.3%). A COVID-19 vaccine was received within 28 days prior to an index date among 8.0% of ongoing pregnancy periods vs 8.6% of spontaneous abortions (Table 1). Spontaneous abortions did not have an increased odds of exposure to a COVID-19 vaccination in the prior 28 days compared with ongoing pregnancies (adjusted odds ratio, 1.02; 95% CI, 0.96-1.08). Results were consistent for mRNA-1273 and BNT162b2 and by gestational age group (Table 2).

Among women with spontaneous abortions, the odds of COVID-19 vaccine exposure were not increased in the prior 28 days compared with women with ongoing pregnancies. Strengths of this surveillance include the availability of a multisite diverse population with robust data capture. Several limitations should be noted. First, gestational age of spontaneous abortions and ongoing pregnancies were not chart confirmed; pregnancy dating may be inaccurate early in pregnancy. Second, although vaccination status was identified using multiple data sources, the COVID-19 vaccine rollout has been complex and some vaccines may have been missed, potentially biasing findings to the null. Third, data on important confounders, such as prior pregnancy history, were not available. Fourth, it was not possible to assess risks specific to the Ad26.COV.2.S vaccine given the small number of exposures. Despite limitations, these data can be used to inform vaccine recommendations and to counsel patients.

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Article Information

Corresponding Author: Elyse O. Kharbanda, MD, MPH, HealthPartners Institute, 8170 33rd Ave S, Mail Stop 23301A, Minneapolis, MN 55408 (elyse.o.kharbanda@healthpartners.com).

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