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SYNOPSIS

Review of "Preliminary Findings of mRNA COVID-19 Vaccine Safety in Pregnant Persons"

04/27/2021

Article citation: Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary findings of mRNA covid-19 vaccine safety in pregnant persons. N Engl J Med. 2021 Apr 21 [Epub ahead of print]. Available from: https://doi.org/10.1056/nejmoa2104983

One-minute summary

- This study evaluated pregnancy registry data and vaccine adverse event reporting to describe the safety of mRNA COVID-19 vaccines BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) in pregnant persons in the United States (US). The study included 35,691 pregnant participants, ages 16 to 54 years, from December 14, 2020 to February 28, 2021. The authors compared the incidence of adverse pregnancy outcomes, adverse neonatal outcomes, and general adverse events following immunization in pregnant vaccine recipients to non-pregnant recipients. Rates of adverse events were also compared to historical published literature of pregnancy outcomes to assess for any safety signals.
    - The most commonly reported adverse events in pregnant participants were injection-site pain (91.9%), fatigue (71.5%), headache (55.4%), and myalgia (54.1%). Adverse events were more commonly reported after the second dose of mRNA vaccine.
    - The proportion of pregnant and non-pregnant patients reporting local and systemic side effects was similar with the exception of nausea and vomiting, which were slightly more common in pregnant recipients after the second vaccine dose (nausea: 2.1% in pregnant, 1.6% in non-pregnant; vomiting 0.5% in pregnant, 0.3% in non-pregnant).
    - Pregnancy and neonatal outcomes in persons vaccinated against Coronavirus Disease 2019 (COVID-19) were comparable to those reported in the published literature before the COVID-19 pandemic:
        - **Spontaneous abortion (<20 weeks):**
            - Rate in study: 104 of 827 (12.6%)
            - Rate in published literature: 10-26%
        - **Stillbirth (≥ 20 weeks):**
            - Rate in study: 1 of 725 (0.1%)
            - Rate in published literature: <1%
        - **Pre-term birth (37 weeks):**
            - Rate in study: 60 of 636 (9.4%)
            - Rate in published literature: 8-15%
        - **Small size for gestational age:**
            - Rate in study: 23 of 724 (3.2%)

- Rate in published literature: 3.5%.

- **Major congenital anomalies:**
  - Rate in study: 16 of 724 (2.2%)
    - None of recipients reporting congenital anomalies had received vaccine during pre-conception period or 1st trimester
  - Rate in published literature: 3%

Additional information

- Data were captured from the v-safe surveillance system, a smartphone-based active surveillance system to monitor for adverse events and outcomes post-COVID-19 vaccination. If patients identified as pregnant, they were then offered enrollment in the v-safe pregnancy registry.

- To capture clinically significant maternal and neonatal adverse events, reports from the Vaccine Adverse Event Reporting System (VAERS), a passive surveillance system administered by the US Centers for Disease Control and Prevention and the Food and Drug Administration, were collected. During the study period, VAERS received 221 reports involving COVID-19 among pregnant persons, 66 (29.9%) of these involved pregnancy or neonatal specific adverse events (most commonly spontaneous abortion (n=46, 37 occurred in the first trimester), followed by stillbirth (n=3), premature rupture of membranes (n=3), and vaginal bleeding (n=3). No congenital anomalies were reported to VAERS.

- Of 35,691 pregnant v-safe participants, the registry call centre attempted to contact 5,230 by telephone and 3,958 were enrolled in the v-safe pregnancy registry. The vast majority of these participants (3,719, 94.0%) identified as health care personnel. Of the patients in the registry, 827 had a completed pregnancy. Of the completed pregnancies, 712/827 (86.1%) resulted in a live birth and 700/712 (98.3%) of these received their first vaccine dose in the third trimester.

- Timing of first dose of vaccine administration relative to pregnancy for registry participants was as follows:

  - Peri-conception period: 92 (2.3%)
  - First trimester: 1,132 (28.6%)
  - Second trimester: 1,714 (43.3%)
  - Third trimester: 1,019 (25.7%)

PHO reviewer's comments

- These data are limited by the 1) lack of representativeness of the non-health care worker population as the vast majority of participants in the cohort were health care personnel and 2) relatively low participation rate in the v-safe pregnancy registry. There is risk for bias that could compromise the generalizability of these findings to a broader pregnant population. Additionally, comparison of adverse outcomes in this population to published estimates is limited by differences between these two populations (e.g., age, demographics, and clinical characteristics).

- The v-safe registry data are preliminary, include a relatively small sample size, and describe neonatal outcomes mostly from patients vaccinated in the third trimester. This limits the evaluation of outcomes associated with vaccine exposures earlier in pregnancy.

- Additional follow up using a more broadly representative, larger sample size and more longitudinal data will be helpful to better understand the association between COVID-19 mRNA vaccination and pregnancy outcomes.
- VAERS data does not provide information on the number of vaccines administered to pregnant patients, which may limit any evaluation of adverse events associated with number of doses received.
- Despite these limitations, these findings provide mounting evidence indicating safety of mRNA vaccines in pregnant patients and may help to support risk vs. benefit discussions between pregnant patients and their health care providers.

Citation

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