

# COVID-19 vaccination and pregnancy: What's the latest?

Although COVID-19 infection has clearly documented risks for maternal and fetal health, the number of vaccinated pregnant individuals remains low. The author summarizes the safety profile and efficacy of COVID-19 vaccinations and outlines data that may reassure and convince pregnant patients to obtain vaccinations.

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**C** COVID-19 vaccination is recommended for all reproductive-aged women, regardless of pregnancy status.<sup>1</sup> Yet, national vaccination rates in pregnancy remain woefully low—lower than vaccine coverage rates for other recommended vaccines during pregnancy.<sup>2,3</sup> COVID-19 infection has clearly documented risks for maternal and fetal health, and data continue to accumulate on the maternal and neonatal benefits of COVID-19 vaccination in pregnancy, as well as the safety of vaccination during pregnancy.

## Maternal and neonatal benefits of COVID-19 vaccination

**Does vaccination in pregnancy result in decreased rates of severe COVID-19 infection?** Results from a study from a Louisiana health system comparing maternal outcomes

between fully vaccinated (defined as 2 weeks after the final vaccine dose) and unvaccinated or partially vaccinated pregnant women during the delta variant—predominant COVID-19 surge clearly answer this question. Vaccination in pregnancy resulted in a 90% risk reduction in severe or critical COVID-19 infection and a 70% risk reduction in COVID-19 infection of any severity among fully vaccinated women. The study also provides some useful absolute numbers for patient counseling: Although none of the 1,332 vaccinated pregnant women in the study required supplemental oxygen or intensive care unit (ICU) admission, there was 1 maternal death, 5 ICU admissions, and 6 stillbirths among the 8,760 unvaccinated pregnant women.<sup>4</sup>

A larger population-based data set from Scotland and Israel demonstrated similar findings.<sup>5</sup> Most importantly, the Scotland data, with most patients having had an mRNA-based vaccine, showed that, while 77% of all COVID-19 infections occurred in unvaccinated pregnant women, 91% of all hospital admissions occurred in unvaccinated women, and 98% of all critical care admissions occurred in unvaccinated women. Furthermore, although 13% of all COVID-19 hospitalizations in pregnancy occurred among vaccinated women, only 2% of critical care admissions occurred among vaccinated women. The Israeli experience



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(which identified nearly 30,000 eligible pregnancies from 1 of 4 state-mandated health funds in the country), demonstrated that the efficacy of the Pfizer/BioNTech vaccine to prevent a SARS-CoV-2 infection of any severity once fully vaccinated is more than 80%.<sup>6</sup>

Breakthrough infections, which were more prevalent during the omicron surge, have caused some patients to question the utility of COVID-19 vaccination. Recent data from South Africa, where the omicron variant was

first identified, noted that efficacy of the Pfizer/BioNTech vaccine to prevent hospitalization with COVID-19 infection during an omicron-predominant period was 70%—versus 93% efficacy in a delta-predominant period.<sup>7</sup> These data, however, were in the absence of a booster dose, and in vitro studies suggest increased vaccine efficacy with a booster dose.<sup>8</sup>

**Counseling women on vaccination benefits and risks.** No matter the specific numeric rate of efficacy against a COVID-19

## Newborn protection from COVID-19 with maternal vaccination vs infection

Although the COVID-19 vaccine is currently approved by the US Food and Drug Administration for ages 5 and above, Pfizer-BioNTech has plans to submit for approval for their vaccine's use among kids as young as 6 months.<sup>1</sup> Assuming that this approval occurs, this will leave newborns as the only group without possible vaccination against COVID-19. But can vaccination during pregnancy protect these infants against infection, as vaccination with the flu vaccine during pregnancy confers protective benefit to newborns?<sup>2</sup>

In a recent research letter published in *Journal of the American Medical Association*, Shook and colleagues present their data on antibody levels against COVID-19 present in newborns of women who were either naturally infected with COVID-19 at 20 to 32 weeks' gestation (12 women) or who received mRNA vaccination during pregnancy at 20 to 32 weeks' gestation (77 women).<sup>3</sup> (They chose the 20- to 32-week timeframe during pregnancy because it had "demonstrated superior transplacental transfer of antibodies during this window.")

They found that COVID-19 antibody levels were higher in both maternal and cord blood at birth in the women who were vaccinated versus the women who had infection. At 6 months, 16 of the 28 infants from the vaccinated-mother group had detectable antibodies compared with 1 of 12 infants from the infected-mother group. The researchers pointed out that the "antibody titer known to be protective against COVID-19 in infants is unknown;" however, they say that their findings provide further supportive evidence for COVID-19 vaccination in pregnant women.<sup>3</sup>

### References

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2. Sakala IG, Honda-Okubo Y, Fung J, et al. Influenza immunization during pregnancy: benefits for mother and infant. *Hum Vaccin Immunother*. 2016;12:3065-3071. doi:10.1080/21645515.2016.1215392.
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infection, it is important to counsel women that the goal of vaccination is to prevent severe or critical COVID-19 infections, and these data all demonstrate that COVID-19 vaccination meets this goal. However, women may have additional questions regarding both fetal/neonatal benefits and safety with immunization in pregnancy.

Let us address the question of benefit first. In a large cohort of more than 1,300 women vaccinated during pregnancy and delivering at >34 weeks' gestation, a few observations are worth noting.<sup>9</sup> The first is that women who were fully vaccinated by the

time of delivery had detectable antibodies at birth, even with first trimester vaccination, and these antibodies did cross the placenta to the neonate. Although higher maternal and neonatal antibody levels are achieved with early third trimester vaccination, it is key that women interpret this finding in light of 2 important points:

1. women cannot know what gestational age they will deliver, thus waiting until the early third trimester for vaccination to optimize neonatal antibody levels could result in delivery prior to planned vaccination, with benefit for neither the woman nor the baby
2. partial vaccination in the early third trimester resulted in lower maternal and neonatal antibody levels than full vaccination in the first trimester.

In addition, while the data were limited, a booster dose in the third trimester results in the highest antibody levels at delivery. Given the recommendation to initiate a booster dose 5 months after the completion of the primary vaccine series,<sup>10</sup> many women will be eligible for a booster prior to delivery and thus can achieve the goals of high maternal and neonatal antibody levels simultaneously. One caveat to these data is that, while higher antibody levels seem comforting and may be better, we do not yet know the level of neonatal antibody necessary to decrease risks of COVID-19 infection in early newborn life.<sup>9</sup> Recent data from the Centers for Disease Control and Prevention provide real-world evidence that maternal vaccination decreases the risk of hospitalization from COVID-19 for infants aged <6 months, with vaccine efficacy estimated to be 61% during a period of both Delta and Omicron predominance.<sup>11</sup>

The evidence is clear—the time for COVID-19 vaccination is now. There is no "optimal" time of vaccination in pregnancy for neonatal benefit that would be worth risking any amount of time a woman is susceptible to COVID-19, especially given the promising data regarding maternal and neonatal antibody levels achieved after a booster dose.

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### Safety of COVID-19 vaccination: Current data

Risks for pregnancy loss, birth defects, and preterm delivery often are concerns of pregnant women considering a COVID-19 vaccination. Data from more than 2,400 women who submitted their information to the v-SAFE registry demonstrated a 14% risk for pregnancy loss between 6 and 20 weeks' gestation—well within the expected rate of pregnancy loss in this gestational age range.<sup>12</sup>

Data from more than 46,000 pregnancies included in the Vaccine Safety Datalink, which includes data from health care organizations in 6 states, demonstrated a preterm birth rate of 6.6% and a small-for-gestational-age rate of 8.2% among fully vaccinated women, rates that were no different among unvaccinated women. There were no differences in the outcomes by trimester of vaccination, and these rates are comparable to the expected rates of these outcomes.<sup>13</sup>

Women also worry about the risks of vaccine side effects, such as fever or rare adverse events. Although all adverse events (ie, Guillain-Barre syndrome, pericarditis/myocarditis, thrombosis with thrombocytopenia syndrome [TTS]) are very rare, the American College of Obstetricians and Gynecologists does recommend that women get an mRNA COVID-19 vaccine, as the Johnson & Johnson/Janssen vaccine is associated with TTS, which occurred more commonly (although still rare) in women of reproductive age.<sup>14</sup>

Two large studies of typical side effects experienced after COVID-19 vaccination

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*Common side effects reported after COVID-19 vaccination include injection site pain and fever (typically low grade)*

in pregnancy are incredibly reassuring. In the first, authors of a large study of more than 12,000 pregnant women enrolled in the v-SAFE registry reported that the most common side effect after each mRNA dose was injection site pain (88% after dose 1, 92% after dose 2).<sup>15</sup> Self-reported fever occurred in 4% of women after dose 1 and 35% after dose 2. Although this frequency may seem high, a fever of 38.0°C (100.4°F) or higher only occurred among 8% of all participants.

In another study of almost 8,000 women self-reporting side effects (some of whom also may have contributed data to the v-SAFE study), fever occurred in approximately 5% after dose 1 and in about 20% after dose 2.<sup>16</sup> In this study, the highest mean temperature was 38.1°C (100.6°F) after dose 1 and 38.2°C (100.7°F) after dose 2. Although it is a reasonable expectation for fever to follow COVID-19 vaccination, particularly after the

second dose, the typical fever is a low-grade temperature that will not harm a developing fetus and will be responsive to acetaminophen administration. Moreover, if the fever were the harbinger of harm, then it might stand to reason that an increased signal of preterm delivery may be observed, but data from nearly 10,000 pregnant women vaccinated during the second or third trimesters showed no association with preterm birth (adjusted hazard ratio, 0.91; 95% confidence interval, 0.82–1.01).<sup>13</sup>

### The bottom line

The data are clear. COVID-19 vaccination decreases the risks of severe infection in pregnancy, confers antibodies to neonates with at least some level of protection, and has no demonstrated harmful side effects in pregnancy. ●

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