

## EDITORIAL



## Covid-19 Vaccination during Pregnancy — Two for the Price of One

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The benefits of maternal vaccination to the infant through maternal antibody transfer across the placenta have long been recognized. In the 1870s, babies born to mothers who had received smallpox vaccination were unlikely to have smallpox early in life.<sup>1</sup> Tetanus toxoid vaccination during pregnancy, along with improved hygiene during delivery, has resulted in substantially reduced rates of neonatal tetanus in some developing countries.<sup>1</sup> Decreased risks of influenza and pertussis have been reported during the first few months of life among infants whose mothers had received the inactivated influenza vaccine and the combined tetanus–diphtheria–acellular pertussis (Tdap) vaccine, respectively. Both vaccines are routinely recommended during pregnancy in the United States; the influenza vaccine is recommended anytime during pregnancy, whereas the Tdap vaccine is recommended preferentially during the early part of gestational weeks 27 to 36 in order to maximize maternal antibody production, placental transfer, and antibody levels in the newborn.<sup>2</sup> Studies to evaluate whether maternal vaccination could prevent illness from other infections (e.g., respiratory syncytial virus infection or group B streptococcus infection) among infants are underway.<sup>1</sup>

At the time of authorization of the coronavirus disease 2019 (Covid-19) vaccines, information on their use during pregnancy was limited because pregnant women were excluded from the clinical trials. Since the time of authorization, safety data on vaccination during pregnancy have been accumulating rapidly.<sup>3,4</sup> The results of a retrospective cohort study now reported in the *Journal*<sup>5</sup> showed no association between maternal

vaccination and serious acute adverse events in the 42 days after vaccination. On the basis of the increased risk of severe disease and pregnancy complications associated with Covid-19 during pregnancy,<sup>6</sup> the reassuring safety data on the use of other vaccines during pregnancy, and the accumulating data on the safety of Covid-19 vaccination for the mother and fetus, the Centers for Disease Control and Prevention and professional organizations (e.g., the American College of Obstetricians and Gynecologists) have strongly recommended vaccination in pregnant women. A booster dose is also recommended after the completion of the initial vaccine series.

Given the experience with previous vaccines, maternal Covid-19 vaccination was expected to provide some level of infant protection. Maternal antibodies have been shown to be present in umbilical-cord blood, neonatal blood, and breast milk after maternal Covid-19 vaccination, but the correlation with infant protection from infection was unclear.<sup>6</sup>

Now in the *Journal*, Halasa and colleagues<sup>7</sup> report on the results of a large multicenter study in which a case–control, test-negative design was used to estimate the effectiveness of maternal vaccination against hospitalization for Covid-19 among infants younger than 6 months of age. In this study, 16% of the 537 infants hospitalized for Covid-19 (case infants) had been born to mothers who had been fully vaccinated against Covid-19 during pregnancy. In contrast, 29% of the 512 hospitalized infants who had a negative test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (control infants) had been born to mothers who had been fully vaccinated

during pregnancy. Maternal vaccine effectiveness against Covid-19–associated hospitalization among infants was 52%. Vaccine effectiveness against admission to an intensive care unit for Covid-19 was higher, at 70%. The current report extended earlier findings of this population<sup>8</sup> to include an additional 670 infants, many of whom were admitted to a hospital during circulation of the omicron variant. As expected, vaccine effectiveness was lower during circulation of the omicron variant than during the delta-predominant period (38% vs. 80%). In addition, vaccine effectiveness was higher when the second dose of Covid-19 vaccine was given after 20 weeks of pregnancy than when it was given earlier in pregnancy (during the first 20 weeks) (69% vs. 38%).

The results of the study by Halasa et al. provide compelling evidence that maternal vaccination is effective in reducing the risk of Covid-19–related hospitalization in infants younger than 6 months of age, a finding that further supports recommendations for Covid-19 vaccination during pregnancy. Such infants have a higher risk of severe illness and hospitalization than older children and cannot be vaccinated now or in the near future. Because vaccines are less likely to be effective in infants younger than 6 months of age,<sup>1</sup> the recently completed clinical trials of Covid-19 vaccines in young children have excluded that age group.

This study also raises the question of the appropriate timing of Covid-19 vaccination during pregnancy. Determining the appropriate timing is difficult because the benefits of maximizing infant protection must be balanced against the maternal risks of delaying vaccination, given the increased risk of severe Covid-19 during pregnancy. Further study is needed to assess whether an additional booster dose given in later pregnancy would increase infant protection.

Despite the increased risk of severe Covid-19 among pregnant women and the accumulating safety data regarding vaccines, only 71% of pregnant women in the United States were fully vaccinated as of May 14, 2022, with a markedly lower rate among non-Hispanic Black women (58%).<sup>9</sup> A recommendation from a health care

provider has been found to be associated with a higher likelihood of maternal vaccination, and data on vaccine safety and on protection of the infant through maternal vaccination have been shown to be important to a pregnant person's decision-making process.<sup>10</sup> Thus, this evidence that Covid-19 vaccines help to protect infants as well as mothers is highly relevant for patient counseling: a “two-for-one” deal may encourage more mothers to receive Covid-19 vaccination.

Disclosure forms provided by the authors are available with the full text of this editorial at NEJM.org.

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