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Editorials

Protecting infants through covid-19 vaccination during pregnancy

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Linked Research

Maternal mRNA covid-19 vaccination during pregnancy and delta or omicron infection or hospital admission in infants

Dana Danino, vice director pediatric ward[1], **Ilan Youngster, research professor**[2]

[1] *Faculty of Health Sciences, Ben-Gurion University; The Pediatric Infectious Disease Unit, Soroka University Medical Center, Beer-Sheva, Israel*

[2] *Sackler Faculty of Medicine, Tel Aviv University; Pediatric Infectious Disease Unit, Shamir Medical Center, Beer Yaakov, Israel*

Correspondence to: D Danino danadanino@hotmail.com

Evidence is reassuring, but needs to catch up with new subvariants and vaccines

By 23 January 2023, the global covid-19 pandemic had resulted in 664 873 023 confirmed cases, and 6 724 248 deaths according to the World Health Organization.**1** The initial burden of disease, in addition to marked social and economic effects, fuelled the rapid development of effective vaccines, with more than 13 billion doses administered worldwide to date.**1** In July 2022, the US Food and Drug Administration amended its emergency use authorisation of mRNA covid-19 vaccines to include children as young as six months of age,**2** followed by authorisation of newer bivalent mRNA vaccines for the same age group in December 2022.**3** Although this policy greatly expands possible vaccine coverage, infants six months or younger are still left unprotected. In a linked article, Jorgensen and colleagues (doi:10.1136/bmj-2022-074035) address this gap by evaluating the effectiveness of maternal vaccination by use of mRNA covid-19 vaccines in preventing SARS-CoV-2 infections and admission to hospital in young infants.**4**

Maternal vaccination is an established and effective way to protect young infants from preventable infections: influenza vaccines during the influenza season and pertussis vaccine between 27 and 36 weeks of gestation are routinely recommended. The cornerstone of successful protection of young infants through maternal immunisation is efficient transplacental transfer of IgG antibodies to the fetus, occurring primarily during the third trimester.[5] Early in the pandemic, several studies showed that SARS-CoV-2 specific antibodies cross the placenta after maternal infection or vaccination and that neonatal humoral responses (measured in cord blood after delivery) are positively associated with maternal titres.[6] Most infants born to vaccinated mothers still have SARS-CoV-2 maternal antibodies at six months of age,[7] but evidence for protection against neonatal covid-19 infection has been deficient.

Jorgensen and colleagues used multiple population based databases in Canada to conduct a test negative study, a case control design in a sample of infants tested for SARS-CoV-2, comparing the maternal vaccination histories of positive (case) and negative (control) infants. They reported that two doses of an mRNA vaccine given during pregnancy were 95% effective against infant infection and 97% effective against hospital admission with the delta variant. Effectiveness against the omicron variant was markedly lower (45% against infection and 53% against hospital admission) but increased when the second dose was given in the third trimester compared with earlier stages of pregnancy, increasing further after a third dose (73% against infection and 80% against hospital admission). Vaccine effectiveness in infants decreased substantially after eight weeks of life (from 57% effectiveness against omicron infection between birth and 8 weeks to 40% after 16 weeks).

These results concur with two previous test negative studies evaluating the effectiveness of maternal vaccination at preventing admission to hospital of infants who were symptomatic and positive for SARS-CoV-2.[8][9] Additionally, the results supported those of a Norwegian study of all live births, which reported a lower risk of a positive SARS-CoV-2 test result during the first four months of infants born to vaccinated mothers who received their second or third dose during the last two trimesters of pregnancy.[10] The consistency of all these findings is reassuring, given that the studies were conducted in four different countries on three continents with varying burdens of covid-19 and different national vaccination policies, non-pharmaceutical interventions, and testing behaviours.

The strengths of the new study lie in the robust data and large population level cohort on which the authors based their analyses. However, in the rapidly shifting landscape of SARS-CoV-2, even solid conclusions cannot provide definitive answers to many practical questions. Firstly, the dominant strains in this study were delta and omicron BA.1, BA.2, and BA.4. By December 2022, omicron BA.4 was no longer circulating, and even BA.5 accounted for fewer than 25% of circulating strains, having been partially replaced by more vaccine evasive strains, such as omicron BQ.1, BQ.1.1, BF.7, XBB, and XBB.1.[11] Whether the vaccine effectiveness reported in this and earlier studies still holds for these strains is unclear.

Secondly, a booster dose of a bivalent mRNA vaccine in people who had previously been vaccinated or boosted with the monovalent mRNA covid-19 vaccines increases protection only moderately against disease of any severity caused by current circulating omicron, although these boosters do confer significant protection against severe disease.[11][12] The protective effect for infants of maternal vaccination with a bivalent vaccine has yet to be evaluated.

Thirdly, the optimal timing of vaccination in pregnancy is not yet clear. Although the evidence shows better infant protection after a maternal booster given in the third trimester, this effect should be balanced against the potential harm to the mother and fetus associated with maternal covid-19 occurring before receipt of the vaccine.[13] Finally, at a time when a large proportion of women of childbearing age have received at least two doses of covid-19 vaccine before conception, the added benefit of another booster during pregnancy is yet to be determined.

Although Jorgensen and colleagues' study reinforces the value of maternal vaccination against covid-19 during pregnancy, more studies are needed to better inform vaccination recommendations in an evolving landscape of new SARS-CoV-2 strains and novel vaccines.

Footnotes

- Competing interests: The BMJ has judged that there are no disqualifying financial ties to commercial companies. We declare no competing interests.
- Provenance and peer review: Commissioned, not peer reviewed.

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Should covid-19 vaccines and drugs be “not for profit”?

- ○ Yes
- ○ No

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