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Impact of timing between Tdap and SARS-CoV-2 mRNA vaccinations during pregnancy on SARS-CoV-2 antibody levels at delivery

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Objective

Administration of the Tdap (tetanus, diphtheria, and acellular pertussis) and SARS-CoV-2 vaccines is recommended during pregnancy without any restriction on timing between vaccinations(1). We sought to study if timing between both vaccines interferes in the maternal SARS-CoV-2 antibody response(2).

Study Design

Patients admitted for delivery >=34 weeks between February 8, 2021 and September 27, 2021, and who received 2 doses of a SARS-CoV-2 mRNA vaccination (Pfizer-BioNTech or Moderna) at least 14 days prior to delivery were included in this study. Patients who also received Tdap vaccination between 27 and 36 weeks of gestation (Tdap) were compared to patients with confirmation of no receipt of Tdap during the pregnancy (no Tdap). Vaccination dates and obstetric data were abstracted from clinical records. Semi-quantitative maternal and umbilical cord blood anti-spike immunoglobulin G (anti-S IgG) antibody levels were analyzed at delivery(3). Differences in maternal IgG levels and placental transfer ratio to neonates between Tdap and no Tdap groups were studied using Wilcoxon rank sum test. Weeks elapsed between receipt of the Tdap vaccine and receipt of dose 2 of a SARS-CoV-2 vaccine were calculated irrespective of which vaccine was received first. The relationship between gestational age at

dose 2 of a SARS-CoV-2 vaccination and maternal IgG levels at delivery was studied using Spearman correlation and linear regression analysis in both Tdap and no Tdap groups. In the Tdap group, mixed ANOVA test was used to study whether weeks elapsed between the two vaccinations, as well as gestational age at SARS-CoV-2 vaccination, contributed to variance in the antibody data. This study was approved by the XXX IRB and is a secondary analysis of 473 out of 485 patients published previously(4,5).

Results

Of the 453 Tdap patients and 32 no Tdap patients, no patient had a known history of SARS-CoV-2 infection (no history of positive SARS-CoV-2 test, negative anti-nucleocapsid antibody test, and no clinical history of infection). There was no significant difference in anti-S IgG levels in the full cohort (p=0.14) (Figure 1A), or in a subcohort of patients who received Tdap vaccination within 2 weeks of SARS-CoV-2 vaccination (p=0.7) (Figure 1B). No differences were observed in the placental transfer ratio (Figure 1C) between groups. Maternal IgG levels were linearly associated with gestational age at dose 2 of a SARS-CoV-2 vaccination in both populations studied (no Tdap rho=0.64, P=8.1e-05; Tdap rho=0.52, P<2.2e-16) (Figure 1D). Mixed ANOVA analysis demonstrated that the time elapsed between SARS-CoV-2 vaccination and Tdap vaccination did not significantly contribute to variance in maternal IgG levels at delivery (p = 0.377), while gestational age at time of SARS-CoV-2 vaccination significantly influenced maternal IgG at delivery (p=8.681e-07) consistent with previous findings (3-5).

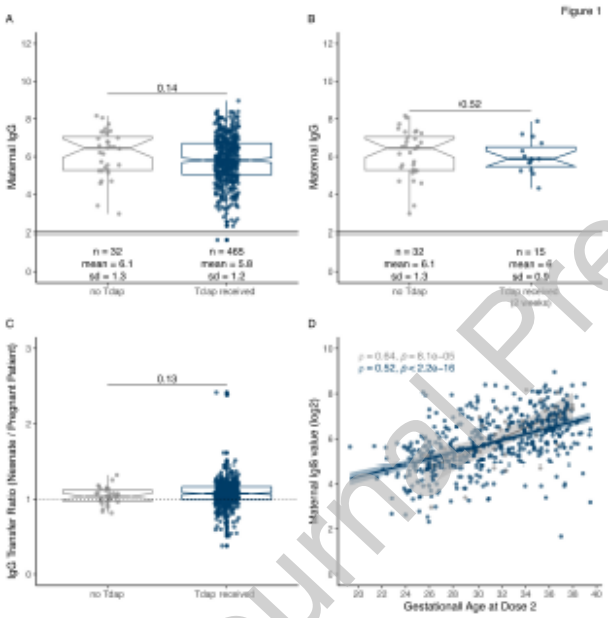
Conclusion

Differences in the number of weeks elapsed between Tdap and SARS-CoV-2 vaccinations do not lead to significant differences in maternal SARS-CoV-2 antibody levels at delivery, suggesting

that no specific schedule between the two vaccines is indicated. Our study did not contain patients with co-administration of the two vaccines and are limited in cohort sizes. Effects on the immune response to Tdap, and follow-up of efficacy of vaccinations need to be studied.

Figure 1: Antibody response to SARS-CoV-2 mRNA vaccination at delivery, stratified by receipt or no receipt of Tdap vaccination Anti-spike (anti-S) immunoglobulin (Ig)G levels, stratified by patients who received (Tdap received, blue) and did not receive Tdap (no Tdap, grey) vaccination. For the Tdap group, all patients received a Tdap vaccine between 5 days and 11 weeks from dose 2 of a SARS-CoV-2 vaccine. For no Tdap group, given the routine administration of Tdap to pregnant patients, only patients with clear confirmation of no receipt of Tdap during the pregnancy but with receipt of 2 doses of a SARS-CoV-2 vaccination were included as no-Tdap controls. A) Analysis of the maternal anti-S IgG in the whole cohort, stratified by patients who received Tdap vaccine (Tdap received, blue), and patients who did not receive Tdap (no Tdap, grey). The relationship between maternal anti-S IgG antibody levels and Tdap vaccination status was studied using Wilcoxon rank sum test on the full cohort of patients. B) Sub-analysis of maternal anti-S IgG, stratified by patients who received Tdap within 2 weeks of dose 2 of a SARS-CoV-2 vaccine (Tdap received 2 weeks, blue), and patients who did not receive Tdap (no Tdap, grey). The relationship between maternal anti-S IgG antibody levels and Tdap vaccination status was studied using Wilcoxon rank sum test. C) Placental transfer ratio (umbilical cord anti-S IgG/maternal anti-S IgG levels) between patients who received Tdap vaccination while pregnant (Tdap received, blue) and patients who did not receive Tdap vaccination while pregnant (no Tdap, grey). The relationship between placental transfer ratio

and Tdap vaccination was studied using Wilcoxon rank sum test. D) Relationship between maternal anti-S IgG levels and gestational age at dose 2 of SARS-CoV-2 vaccination for patients who received Tdap (Tdap received, blue) and patients who did not receive Tdap vaccination (no Tdap, grey). Spearman correlation analysis and linear regression were performed on log_2-scaled maternal IgG values. n=participants included, m=mean, sd=standard deviation. Statistical analysis was performed using R 4.1.0, RStudio 1.4.1106.



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Declaration of Competing Interest
The authors report no conflict of interest.

References

1. Maternal Immunization. ACOG Comm Opin [Internet]. 2018 Jun 1 [cited 2022 Nov 9]; Available from: https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2018/06/maternal-immunization

2. J. W. Uhr, G. Möller, Regulatory effect of antibody on the immune response. *Adv. Immunol.* **8**, 81–127 (1968). 10.1016/S0065-2776(08)60465-4
3. Kubiak JM, Murphy EA, Yee J, Cagino KA, Friedlander RL, Glynn SM, et al. Severe acute respiratory syndrome coronavirus 2 serology levels in pregnant women and their neonates. Am J Obstet Gynecol. 2021 Jul;225(1):73.e1-73.e7.
4. Yang YJ, Murphy EA, Singh S, Sukhu AC, Wolfe I, Adurty S, et al. Association of Gestational Age at Coronavirus Disease 2019 (COVID-19) Vaccination, History of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection, and a Vaccine Booster Dose With Maternal and Umbilical Cord Antibody Levels at Delivery. Obstet Gynecol. 2022 Mar 1;139(3):373–80.
5. Prabhu M, Murphy EA, Sukhu AC, Yee J, Singh S, Eng D, et al. Antibody Response to Coronavirus Disease 2019 (COVID-19) Messenger RNA Vaccination in Pregnant Women and Transplacental Passage Into Cord Blood. Obstet Gynecol. 2021 Aug 1;138(2):278–80.