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Newborns' passive humoral SARS-CoV-2 immunity following heterologous vaccination of the mother during pregnancy

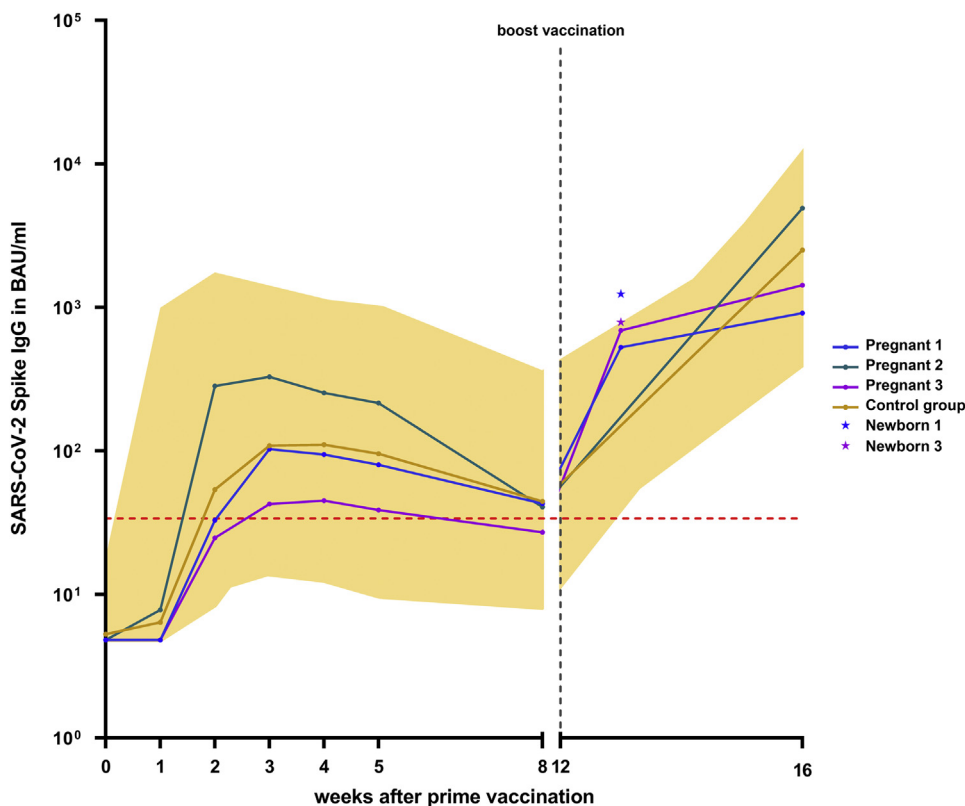


OBJECTIVE: Vaccination in the SARS-CoV-2 pandemic is important, especially to protect pregnant women and the unborn. In 2021, the messenger RNA (mRNA)-based vaccines BNT162b2 (BioNTech/Pfizer) and mRNA-1273 (Moderna), and the vector-based vaccine AZD1222 (AstraZeneca) were approved for use in Germany.¹ Vaccination for pregnant women was considered after weighing the individual benefits and risks of the vaccines without preference for a vaccine type.¹ After national guidelines discouraged the use of AZD1222 in those under 60 years of age,¹ mRNA-based boost vaccination was recommended. In this study we intend to evaluate antibody kinetics following heterologous vaccination in pregnant

women in comparison to their newborns as well as to a healthy nonpregnant control group.

STUDY DESIGN: We recruited 3 pregnant participants (gestational age at primary vaccination between 21 and 28 weeks) and 25 nonpregnant control participants at the Jena University Hospital. They were observed after prime vaccination with AZD1222 and boost vaccination 12 weeks thereafter with either BNT162b2 or mRNA-1273. Ethical approval was obtained for the same (Jena University Hospital ethics commission ref.: 2021-2078). The anti-Spike immunoglobulin G (IgG) antibody levels were determined in the serial serum samples (before and 1, 2, 3, 4, 5, 8, and 16 weeks after prime

FIGURE
S-IgG antibody kinetics after heterologous vaccination



Stars represent values measured in cord blood at time of birth. The orange curve represents the geometric means of concentrations in the control group, the orange area shows the range between minimum and maximum values measured in the control group.

vaccination) and, if available, in the maternal and cord serum at the time of birth using the LIAISON SARS-CoV-2 TrimericS IgG assay on the Liaison XL chemiluminescence analyzer (DiaSorin, Saluggia, Italy), according to the manufacturer's instructions. The neutralization capacity was tested in a neutralization assay using Vero-76 cells and a SARS-CoV-2 strain isolated from a respiratory specimen (SARS-CoV-2/hu/Germany/Jena-vi005588/2020), utilizing WST-1 (CELLPRO-RO, Roche, Basel, Switzerland) to quantify cell viability after infection. The neutralization titer was defined as the inverted maximal dilution at which $\geq 50\%$ of the cytopathic effect caused by the virus was neutralized (ID_{50}). For the pregnant participants, the recomLine SARS-CoV-2 IgG immunoblot (Mikrogen, Neuried, Germany) was performed 16 weeks after the initial vaccination to rule out interfering infection by measuring the nucleocapsid IgG antibodies.

RESULTS: The SARS-CoV-2 Spike IgG antibodies were detected for all the study participants (Figure), with ID_{50} (inhibitory serum dilution showing a 50% neutralization of the viral effects on cell viability) neutralization titers ≥ 160 in maternal and cord serum samples. The immunoblot showed distinct signals in both the receptor-binding domain and the Spike subunit 1 IgG for all the pregnant participants, but showed no signal for nucleocapsid antibodies. Severe adverse events requiring hospitalization were not reported during the observational period, and all the 3 pregnant participants delivered at term.

CONCLUSION: Vaccine-induced SARS-CoV-2 antibodies were already described after the mRNA-based COVID-19 vaccination of pregnant women equivalent to nonpregnant women,² with a correlation of maternal and neonatal antibody levels.^{3,4} The noninferiority of heterologous vaccination when compared with homologous regimens was recently reported in nonpregnant women.⁵ We detected vaccine-induced SARS-CoV-2 Spike IgG antibodies after vector-based prime vaccination in pregnancy, with an average increase of more than one \log_{10} level after an mRNA-based boost. SARS-CoV-2 infection during pregnancy was ruled out because of negative nucleocapsid IgG results. The observed immune response in pregnant women showed no significant difference compared with nonpregnant controls 16 weeks after the initial vaccination (Mann-Whitney U test: $P=.514$).

We found similar levels of anti-Spike IgG antibodies with a high neutralization capacity in the cord serum, indicating a strong passive humoral immunity in the newborns. ■

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Stefan Gloeckner, MD
 Franziska Hornung, MSc
 Institute of Medical Microbiology
 Jena University Hospital
 Am Klinikum 1, D-07747
 Jena, Germany
stefan.gloeckner@med.uni-jena.de

Yvonne Heimann, MSc
 Ekkehard Schleussner, MD
 Department of Obstetrics
 Jena University Hospital
 Jena, Germany

Stefanie Deinhardt-Emmer, MD
 Bettina Loeffler, MD
 Institute of Medical Microbiology
 Jena University Hospital
 Jena, Germany

Janine Zoellkau, MD
 Department of Obstetrics
 Jena University Hospital
 Jena, Germany

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