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Clinical Microbiology and Infection 27 (2021) 1708–1709

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Letter to the Editor

Both SARS-CoV-2 infection and vaccination in pregnancy elicited neutralizing antibodies in pregnant women and newborns

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ARTICLE INFO

Article history:
Received 29 May 2021
Received in revised form
31 July 2021
Accepted 2 August 2021
Available online 8 August 2021

Editor: L. Leibovici

To the Editor

To date, few data on SARS-CoV-2 immune response after infection or vaccination have been reported in pregnant women. So far, maternal immunization during pregnancy inducing transplacental antibody transfer to the newborn is currently supported to reduce morbidity and mortality from infectious diseases after birth.

After having signed written informed consent, two healthcare workers received complete BNT162b2 mRNA vaccination during pregnancy. The first vaccinated woman (VW#1) received the first dose at 31 weeks' gestation and 4 days, the second woman (VW#2) at 27 weeks' gestation and 6 days.

Serum samples from the mother/newborn pairs collected at delivery were tested by ELISA (Euroimmun, Luebeck, Germany) for anti-SARS-CoV-2 Spike IgG and IgA antibodies. Semi-quantitative results are expressed as optical density (OD) ratio with respect to an internal calibrator: a ratio $\geq$1.1 was considered positive.

SARS-CoV-2 Spike-specific IgA antibodies were documented in the two vaccinated women (OD ratio 7.5 and 2.4); as expected, IgA were absent in the two newborns (N#1 and N#2).

Spike-specific IgGs were detectable in N#1 and N#2 (8.0 and 5.4) at higher levels than in VM#1 and VM#2 (6.8 and 4.0), with a newborn-to-maternal serum ratio of 1.2 and 1.4, respectively. As control, the newborn-to-maternal serum ratio for anti-cytomegalovirus (CMV) IgG measured by ELISA (Euroimmun) was 1.0 and 1.3. The neutralizing (NT) antibody titre [1] was higher in VW#2 than VW#1 (1:320 vs 1:20). Similarly, the NT antibody titre was higher in N#2 than in N#1 (1:160 and 1:10).

For comparison, seven women (median age 31 years old; range 23–35) who experienced SARS-CoV-2 infection during pregnancy were analysed: one developed a mildly symptomatic infection during the first trimester, one developed pneumonia during the second trimester and five women had an asymptomatic infection during the third trimester. The seven women were positive for Spike-specific IgA and IgG antibodies at delivery (with the exception of the women infected during the first trimester who was positive only for Spike-specific IgA), and only three of the seven were also positive for Nucleocapsid IgG by ELISA (Euroimmun). The median newborn-to-maternal serum ratio was 1.4 (range 0.5–2.6) for Spike-specific IgG and 1.0 (0.9–1.4) for CMV-specific IgG, while the median NT titre ratio was 0.5 (range 0.03–1). Data are reported in Table 1 and Table S1.

Current data suggest that pregnant women may be at increased risk for admission to an intensive care unit with respect to non-pregnant women, thus vaccination might represent a valuable preventive strategy.

The efficiency of transplacental transfer of anti-SARS-CoV-2 antibody has been claimed to be lower than for other

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https://doi.org/10.1016/j.cmi.2021.08.004

Table 1
Characteristics of two vaccinated pregnant women and seven SARS-CoV-2 seropositive at delivery convalescent pregnant women

	Convalescent pregnant women (median, range)	VW#1	VW#2
Age	31 (23–35)	37	36
Days between infection onset/2nd dose vaccination and delivery	76 (18–175)	33	42
Maternal immunity			
SARS-CoV-2 Spike IgG	1.9 (0.4–4.7)	4.0	6.8
SARS-CoV-2 NCP IgG	0.7 (0.2–2.9)	0.1	0.1
SARS-CoV-2 Spike IgA	1.8 (1.0–4.3)	2.4	7.5
SARS-CoV-2 NT Abs	1:160 (1:40–1:320)	1:20	1:320
CMV IgG	1.3 (0.7–1.5)	2.3	2.0
Newborn immunity			
SARS-CoV-2 Spike IgG	1.4 (1.2–3.3)	5.4	8.0
SARS-CoV-2 NCP IgG	0.9 (0.3–2.8)	0.1	0.1
SARS-CoV-2 Spike IgA	0.1 (0.1–0.1)	0.1	0.1
SARS-CoV-2 NT Abs	1:40 (<1:10–1:320)	1:10	1:160
CMV IgG	1.3 (1.0–1.5)	2.3	2.6

VW#1, vaccinated woman 1; VM#2, vaccinated woman 2; NCP, nucleocapsid protein; NT Abs, neutralizing antibodies; CMV, cytomegalovirus.

pathogens [2]. On the contrary, we observed that antibody transfer occurred efficiently from mothers showing anti-SARS-CoV-2 IgG at delivery (elicited either by infection or vaccination). Our results are in line with another study showing an efficient transplacental transfer of anti-Spike IgG antibodies [3]. However, the median NT titre was twofold reduced in newborns with respect to mothers. This may be due to the contributions to neutralization in maternal serum of Spike-specific IgAs, which are not transmitted to the fetus. It should be taken into account that, when evaluating placental transfer after natural infection, key determinants are time elapsed from infection, severity of the infection and maternal antibody titres. These factors may be at the basis of the conflicting results reported.

A recent report highlighted that the immune response elicited by SARS-CoV-2 vaccine in pregnant women was higher than that induced by natural infection [4]. Moreover, while it was suggested that third-trimester SARS-CoV-2 infection induced a poor transplacental IgG transfer [5], in our study IgG elicited by either infection or vaccination appeared to be efficiently transferred to the fetus. While a sustained neutralizing response was observed in VM#2 and N#2, NT Abs were lower in VM#1 and N#1. These variable results are in the range of those observed in a cohort of immunocompetent vaccinated subjects (unpublished results).

On the other hand, a recent study conducted in Israel [6] reported a lower transfer ratio of anti-Spike IgG (median transfer ratio 0.44) than that observed in our cases. The median time lapse between second dose administration and delivery was 11 days in the Israel cohort, whereas our subjects received the second dose 33 and 42 days before delivery. Therefore, we can hypothesize that the vaccination schedule should be completed at least 1 month before the presumed date of delivery for a better antibody transfer.

As a major limitation, only two vaccinated pregnant women were analysed. However, results are in line with those obtained in a cohort of healthy immunocompetent subjects. This is the first report that compares transplacental SARS-CoV-2 antibody transfer in vaccinated and infected pregnant women. These findings should be extended to a larger cohort and durability of vertically transmitted antibody after maternal vaccination should be investigated. Nevertheless, our preliminary study supports the potentiality of maternal immunization in providing immune protection against SARS-CoV-2 in newborns.

Transparency declaration

The authors have no conflict of interest to declare. Funding: This work was supported by Fondazione Cariplo (grant CoVIM, no. 2020-1374).

Author contributions

F.B., D.L. conceived the study; I.C. analysed the data and drafted the initial manuscript; D.L. revised the manuscript and wrote final draft; E.P., P.Z. performed serological analyses; K.N.N., A.P., V.B., GJ, PS, FP, AS enrolled the subjects and collected clinical data.

Ethics statement

Blood samples were collected according to the Helsinki declaration and after ethical committee approval of Hospital of Padua, AULSS 6 Euganea (P-55422) and Pavia (P-20200046007).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2021.08.004.

References

[1] Percivalle E, Cambiè G, Cassaniti I, Nepita EV, Maserati R, Ferrari A, et al. Prevalence of SARS-CoV-2 specific neutralising antibodies in blood donors from the lodi red zone in lombardy, Italy, as at 06 April 2020. Euro Surveill 2020;25:2001031.
[2] Edlow AG, Li JZ, Collier AY, Atyeo C, James KE, Boatin AA, et al. Assessment of maternal and neonatal SARS-CoV-2 viral load, transplacental antibody transfer, and placental pathology in pregnancies during the COVID-19 pandemic. JAMA Netw Open 2020;3:e2030455.
[3] Flannery DD, Gouma S, Dhudasia MB, Mukhopadhyay S, Pfeifer MR, Woodford EC, et al. Assessment of maternal and neonatal cord blood SARS-CoV-2 antibodies and placental transfer ratios. JAMA Pediatr 2021;175:594–600.
[4] Gray KJ, Bordt EA, Atyeo C, Deriso E, Akinwunmi B, Young N, et al. COVID-19 vaccine response in pregnant and lactating women: a cohort study. Am J Obstet Gynecol 2021. S0002-9378 (21) 00187-3.
[5] Atyeo C, Pullen KM, Bordt EA, Fischinger S, Burke J, Michell A, et al. Compromised SARS-CoV-2-specific placental antibody transfer. Cell 2021;184:628–42.e10.
[6] Rottenstreich A, Zarbiv G, Oiknine-Djian E, Zigron R, Wolf DG, Porat S. Efficient maternofetal transplacental transfer of anti- SARS-CoV-2 spike antibodies after antenatal SARS-CoV-2 BNT162b2 mRNA vaccination. Clin Infect Dis 2021. ciab266.