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Immune Response of Neonates Born to Mothers Infected With SARS-CoV-2

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Abstract

Importance: Although several studies have provided information on short-term clinical outcomes in children with perinatal exposure to SARS-CoV-2, data on the immune response in the first months of life among newborns exposed to the virus in utero are lacking.

Objective: To characterize systemic and mucosal antibody production during the first 2 months of life among infants who were born to mothers infected with SARS-CoV-2.

Design, setting, and participants: This prospective cohort study enrolled 28 pregnant women who tested positive for SARS-CoV-2 infection and who gave birth at Policlinico Umberto I in Rome, Italy, from November 2020 to May 2021, and their newborns. Maternal and neonatal systemic immune responses were investigated by detecting spike-specific antibodies in serum, and the mucosal immune response was assessed by measuring specific antibodies in maternal breastmilk and infant saliva 48 hours after delivery and 2 months later.

Exposures: Maternal infection with SARS-CoV-2 in late pregnancy.

Main outcomes and measures: The systemic immune response was evaluated by the detection of SARS-CoV-2 IgG and IgA antibodies and receptor binding domain-specific IgM antibodies in maternal and neonatal serum. The mucosal immune response was assessed by measuring spike-specific antibodies in breastmilk and in infant saliva, and the presence of antigen-antibody spike IgA immune complexes was investigated in breastmilk samples. All antibodies were detected using an enzyme-linked immunosorbent assay.

Results: In total, 28 mother-infant dyads (mean [SD] maternal age, 31.8 [6.4] years; mean [SD] gestational age, 38.1 [2.3] weeks; 18 [60%] male infants) were enrolled at delivery, and 21 dyads completed the study at 2 months' follow-up. Because maternal infection was recent in all cases, transplacental transfer of virus spike-specific IgG antibodies occurred in only 1 infant. One case of potential vertical transmission and 1 case of horizontal infection were observed. Virus spike protein-specific salivary IgA antibodies were significantly increased (P = .01) in infants fed breastmilk (0.99 arbitrary units [AU]; IQR, 0.39-1.68 AU) vs infants fed an exclusive formula diet (0.16 AU; IQR, 0.02-0.83 AU). Maternal milk contained IgA spike immune complexes at 48 hours (0.53 AU; IQR, 0.25-0.39 AU)

and at 2 months (0.09 AU; IQR, 0.03-0.17 AU) and may have functioned as specific stimuli for the infant mucosal immune response.

Conclusions and relevance: In this cohort study, SARS-CoV-2 spike-specific IgA antibodies were detected in infant saliva, which may partly explain why newborns are resistant to SARS-CoV-2 infection. Mothers infected in the peripartum period appear to not only passively protect the newborn via breastmilk secretory IgA but also actively stimulate and train the neonatal immune system via breastmilk immune complexes.

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Figures

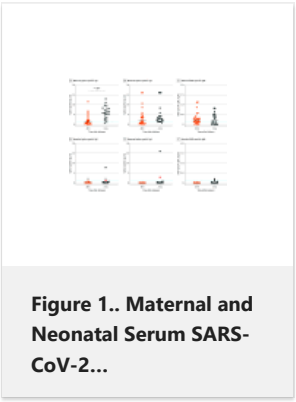

Figure 1.. Maternal and Neonatal Serum SARS-CoV-2...

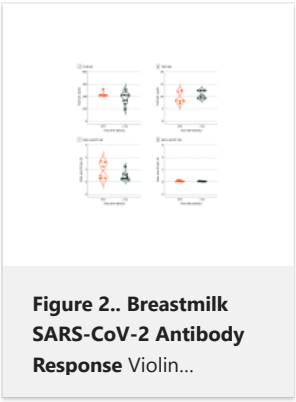

Figure 2.. Breastmilk SARS-CoV-2 Antibody Response Violin...

Figure 3.. Antibody Detection in Saliva of...

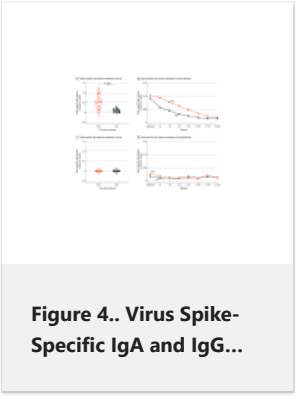

Figure 4.. Virus Spike-Specific IgA and IgG...

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