

Letters

RESEARCH LETTER

Antibodies in Infants Born to Mothers With COVID-19 Pneumonia

Tests for IgG and IgM antibodies for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) became available in February 2020. On March 4, 2020, the seventh edition of the *New Coronavirus Pneumonia Prevention and Control Protocol* for the novel coronavirus disease 2019 (COVID-19) was released by the National Health Commission of the People's Republic of China and added serological diagnostic criteria.¹ A previous study of 9 pregnant women and their infants found no maternal-infant transmission of SARS-CoV-2 based on reverse transcriptase-polymerase chain reaction (RT-PCR).² We applied these new criteria to 6 pregnant women with confirmed COVID-19 and their infants because serologic criteria would allow more detailed investigation of infection in newborns.

Methods | Clinical records and laboratory results were retrospectively reviewed for 6 pregnant women with COVID-19 admitted to Zhongnan Hospital of Wuhan University from February 16 to March 6, 2020, confirmed based on symptoms, chest computed tomography, and positive RT-PCR results.

Blood samples were collected from the mothers at delivery and neonatal blood and throat swab samples were collected at birth. Quantitative RT-PCR for SARS-CoV-2 nucleic acid (RT-PCR Kit, BioGerm) was conducted on neonatal serum and throat swabs. Inflammatory cytokines (CBA Human Th1/Th2 Cytokine Kit II, BD Biosciences) were tested on neonatal serum. Maternal and neonatal sera samples were used to test for IgG and IgM antibodies. All tests were per-

formed by 2 researchers (Y.T. and Q.D.), with SARS-CoV-2 IgG and IgM samples from infants double checked (CLIA assays Kit, YHLO). Sample collection, processing, and laboratory testing followed guidance from the World Health Organization.³ The sensitivity and specificity reported by the manufacturer for IgM are 88.2% and 99.0% respectively, and for IgG are 97.8% and 97.9%.⁴

This study was approved by the Zhongnan Hospital of Wuhan University institutional review board, which waived informed consent because data in this retrospective study were retrieved from medical records.

Results | All 6 mothers had mild clinical manifestations. All had cesarean deliveries in their third trimester in negative pressure isolation rooms. All mothers wore masks, and all medical staff wore protective suits and double masks. The infants were isolated from their mothers immediately after delivery.

All 6 infants had 1-minute Apgar scores of 8 to 9 and 5-minute Apgar scores of 9 to 10. Neonatal throat swabs and blood samples all had negative RT-PCR test results. All 6 infants had antibodies detected in their serum. Two infants had IgG and IgM concentrations higher than the normal level (<10 AU/mL). One infant had an IgG level of 125.5 and IgM level of 39.6 AU/mL; the second infant, had an IgG level of 113.91 AU/mL and IgM level of 16.25 AU/mL (Table 1). Their mothers also had elevated levels of IgG and IgM (Table 2). Three infants had elevated IgG levels (75.49, 73.19, 51.38 AU/mL) but normal IgM levels; all 3 mothers had elevated IgG and 2 also had elevated IgM levels. Inflammatory cytokine IL-6 was significantly increased in all infants. None of the infants presented any symptoms as of March 8, 2020.

Discussion | Among 6 mothers with confirmed COVID-19, SARS-CoV-19 was not detected in the serum or throat swab

Table 1. Antibody and IL-6 Levels in Infant Sera Samples

Clinical value	Reference range	Infant ^a					
		1	2	3	4	5	6
IgM, AU/mL	<10	39.6	16.25	3.79	1.9	0.96	0.16
IgG, AU/mL	<10	125.5	113.91	75.49	73.19	51.38	7.25
IL-6, pg/mL	0.1-2.9	15.07	33.65	19.16	18.15	32.75	19.62

^a Infants and mothers correspond by number between tables.

Table 2. Antibody Levels in Mother Sera Samples

Clinical value	Reference range	Mother ^a					
		1	2	3	4	5	6
IgM, AU/mL	<10	83.97	236.6	5.58	33.26	15.61	1.39
IgG, AU/mL	<10	136.72	117.37	120.63	103.46	70.05	8.12

^a Mothers and infants correspond by number between tables.

by RT-PCR in any of their newborns. However, virus-specific antibodies were detected in neonatal blood sera samples. The IgG concentrations were elevated in 5 infants. IgG is passively transferred across the placenta from mother to fetus beginning at the end of the second trimester and reaches high levels at the time of birth.⁵ However, IgM, which was detected in 2 infants, is not usually transferred from mother to fetus because of its larger macromolecular structure. In a study⁶ of mothers with SARS, the placentas of 2 women who were convalescing from SARS-CoV infection in the third trimester of pregnancy had abnormal weights and pathology. Whether the placentas of women in this study were damaged and abnormal is unknown. Alternatively, IgM could have been produced by the infant if the virus crossed the placenta.

This study is limited by the small sample size, lack of cord blood, amniotic fluid, and breast milk and by incomplete information on the outcome of the infants. These findings are important for understanding the serological characteristics of infants whose mothers are infected with SARS-CoV-2 and further study is necessary.

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1. China NHC. *New Coronavirus Pneumonia Prevention and Control Protocol*. 7th ed. National Health Commission of the People's Republic of China; 2020. Accessed March 4, 2020. <http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eaae415350a8ce964.pdf>
2. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*. 2020;395(10226):809-815. doi:10.1016/S0140-6736(20)30360-3
3. World Health Organization. Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases: interim guidance 2020. Posted January 17, 2020. Accessed February 4, 2020. <https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117>
4. Contribution to Wuhan with SARS-CoV-2 IgG/IgM Assays. News release. YHLO, March 4, 2020. Accessed March 4, 2020. http://www.szyhlo.com/en/news_detail.php?menuid=75&id=125&from=singlemesssage&isappinstalled=0.
5. Kohler PF, Farr RS. Elevation of cord over maternal IgG immunoglobulin: evidence for an active placental IgG transport. *Nature*. 1966;210(5040):1070-1071. doi:10.1038/2101070a0
6. Ng WF, Wong SF, Lam A, et al. The placentas of patients with severe acute respiratory syndrome: a pathophysiological evaluation. *Pathology*. 2006;38(3):210-218. doi:10.1080/00313020600696280