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Dynamic changes of acquired maternal SARS-CoV-2 IgG in infants

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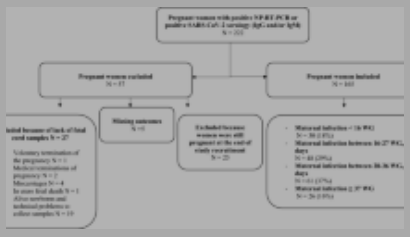
Abstract

At present, there are still ambiguous reports about the perinatal infection of infants born to mothers infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The dynamic characteristics of infantile serum antibodies born to mother with SARS-CoV-2 has not been well described. In this study, we analyzed the seroconversion of 27



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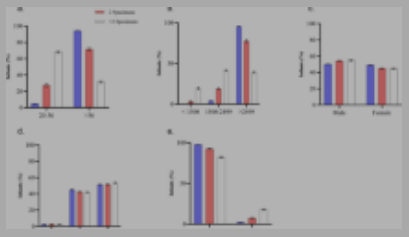

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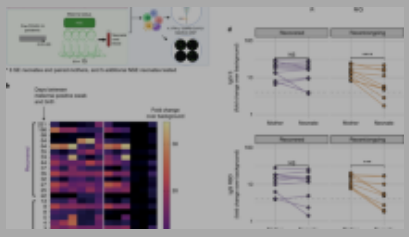

The legacy of maternal SARS-CoV-2 infection on the immunology of the neonate

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Introduction

Pregnant women seem to be more vulnerable to coronavirus infected disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection due to the characteristic immune responses during pregnancy[1, 2]. It has been found that more than 13% admitted pregnant women were symptomatically with SARS-CoV-2 infection[3]. Vertical transmission of SARS-CoV-2 has not yet been detected, whereas perinatal transmission has been suspected in a few cases[4,5,6,7,8,9]. Due to the limitations of viral nucleic acid detection, SARS-CoV-2 serological antibody's detection

of pregnant women with SARS-CoV-2 infection and their infants delivered in Zhongnan Hospital of Wuhan University in Wuhan, China.

Results

Objects and characteristics

Between January 27, 2020 and May 10, 2020, 26 pregnant women were confirmed to be infected with SARS-CoV-2 by laboratory evidences, and their 27 babies were tested for IgM and IgG antibodies against SARS-CoV-2 by chemiluminescence method. The positive rate of viral pneumonia-like in computed tomography (CT), SARS-CoV-2 seroconversion and viral nucleic acid test were 88.4% (23/26), 80.8% (21/26) and 34.6% (9/26) respectively in parturient women, while all infants were negative in SARS-CoV-2 nucleic acid test at birth. The age range of the mothers was 22–41 years, and the range of gestational age at admission was 31^{6+} to 41^{1+} weeks. There were five pregnant women with SARS-CoV-2 infection in the second trimester and 21 cases infected in the third pregnancy. 13 pregnant women had COVID-19-like symptoms such as fever and/or cough before delivery. Of the 27 infants, 21 were full-term, the other 6 were preterm including 1 pair of twins. The infants were normal at birth with Apgar scores all over 7. All infants were separated from their mothers immediately and were not breastfed before SARS-CoV-2 antibodies testing. The median time from onset of SARS-CoV-2 infection to delivery of parturient women was 10.5 days (1–107 days), and the primary seroconversion of IgG and IgM were 80.8% (21/26) and 53.9% (14/26) respectively (Table 1).

SARS-CoV-2 antibody detection was carried out in two stages: mothers who delivered before March 2020 received antibody testing in the follow-up stage after delivery, and pregnant women who gave birth after March 2020 were detected antibody before delivery. 11 pregnant women,who had positive of SARS-CoV-2 nucleic acid test or lung CT examination showed lung viral pneumonia-like changes during pregnancy, underwent serology testing 1–8 days before delivery. The median time from infection to delivery was 70 days (6–107 days), and 69 days (16–99 days) from infection to antibody detection day. All those mothers were IgG positive (11/11, 100%), 63.6% cases were IgM positive (7/11). Their 11 infants were tested for antibody 1–2 days after birth,and the median time from mother's infection to infant's first time of antibody detection was 71 days (7–108 days).The IgG was positive in 9 (9/11, 81.8%) infants born to this group mothers. 15 mothers confirmed with SARS-CoV-2 infection before delivery with symptoms, or without symptoms but with lung viral pneumonia-like changes, were tested for SARS-CoV-2 antibodies after delivery. The median time from infection to delivery was 4.5 days (1–15 days), and 64.5 days (36–81 days) from infection to antibody detection day. Among this group of mothers, 40% (6/15) were IgM positive, and 66.7% (10/15) were IgG positive. Their 16 infants of this group were tested 54–80 days after birth, and the median time from mother's infection to infant's first time of antibody detection was 69 days (57–83 days).Of these 16 infants, only 2 cases (12.5%, 2/16) were IgG positive.

To further understand the serodynamic changes of IgG and IgM in mothers and infants, we compared the correlation between maternal antibody level and infant serum conversion. As shown in Fig. 1a,b, there was no correlation between duration of maternal infection time and the titer of serum IgM and IgG (Fig. 1a,b). And the levels of IgG were positive correlated to that of IgM ($p = 0.0035$) (Fig. 1c). We also compared the correlation of the maternal serum antibodies titer with that of their infants, and found that the serum IgG titer of infants was positive correlated to that their mothers ($p = 0.01$) (Fig. 1d). A similar rule was found in the positive correlation between the serum antibody level of infants and the time of infection of mothers before delivery (Fig. 1e).

Figure 1

and specificity of maternal antibodies transferring into infants. Pearson test was used to analyze the correlation between the two groups, $P < 0.05$ was considered to be statistically significant.

According to the time from onset of SARS-CoV-2 infection to delivery of mothers, we divided this group of data into 2 groups which were within 14-day and more than 14-day. The IgG seroconversion rates of mothers were 66.7% (10/15) and 100% (11/11), while the infants' IgG positive rates were 18.8% (3/16) and 81.8% (9/11), respectively (p value = 0.002). Then we analyzed the relationship between the maternal and infantile IgG antibody titers and found that the two showed a positive correlation (Fig. 1d). The maternal IgG antibody titer was used to predict the positive of infantile IgG after birth (> 1 s/co), with a cutoff value of 8.22 s/co, which had a sensitivity of 84.3% and a specificity of 93.3% (Fig. 1f).

Effects of mothers with and without symptoms on IgG conversion in infants (Table 2)

Table 2 Clinical characteristics of SARS-CoV-2 infected mothers with or without symptoms.

The seroconversion rate of mothers with symptoms before delivery was significantly higher than that of mothers without symptoms, and the IgM seroconversion rate of

between detection and onset of two tests were 26.5 days (17–46 days) and 72 days (62–91 days). The average serum titer of IgG was 11.1 s/co and 8.3 s/co, and the average titer of IgM was 8.5 s/co and 13.6 s/co respectively. The antibodies were also detected twice in their 4 infants on the first day and the day of 31–63 after birth (Fig. 2b). The IgM levels of all infants were below threshold, and the average IgG levels were 9.2 s/co and 1.0 s/co respectively. Infantile IgG levels decreased sharply in the first two months of life, accounting for only 10.7% of the titer at birth (Table 3).

Figure 2

Table 3 Detailed follow-up data of 4 mothers and 4 infants.

Discussion

The impacts of maternal SARS-CoV-2 infection on the fetus may include vertical transmission, abnormal intrauterine growth, abortion and stillbirth[9, 18,19,20]. At present, there are few studies focusing on serodynamic of infants born to mothers with SARS-CoV-2 infection during postpartum period. Due to the role of placental barrier, rare reports include neonatal test results for SARS-CoV-2 with positive cases so far[1]. Our data showed that no positive results of IgM were found in infants born to mothers with SARS-CoV-2, regardless of the mother's clinical symptoms, antibody titer and infection during the second or third trimester. And all infants were negative in SARS-CoV-2 nucleic acid test by RT-PCR detection of throat swabs at birth. Although the absence of IgM and a negative SARS-CoV-2 PCR at the time of birth cannot fully exclude an intra-uterine COVID-19 infection of the infants. We speculated that the SARS-CoV-2 IgG in infants can be used to observe whether they has acquired the passive immunity in this study.

In this study, we report antibody responses to SARS-CoV-2 in 26 pregnant women with COVID-19 and the seroconversion of their 27 babies. The probability of infantile acquisition of maternal antibody was related to the infection time before delivery and the serum antibody concentration of their mothers. The cutoff value was 8.22 s/co in mother,

There are many factors that affect infants to obtain maternal passive immunity. Despite the abundance of antibodies produced by prenatal infection of mothers, infants did not obtain the IgG titer in proportion to their mothers due to the short time period between maternal infection and delivery. This is consistent with our expectations, in which the longer the mother infected the virus before delivery, the higher the seroconversion rate of the maternal IgG, and the greater the probability of infants obtaining maternal antibody.

Mothers who had been infected for more than two weeks give their babies more adequate antibody titers. However, the longer the intrauterine exposure, the more likely to affect the development of fetus, which involve other high-risk factors[21]. The maternal IgG transfer efficiency was also depended on the mother's immune response to SARS-CoV-2. The IgG titer of infants born to high titer IgG mothers also increased. Although the neutralizing capacity of this IgG is not yet clear, the level of SARS-CoV-2 neutralizing antibodies was found to correlate with a wide range of specific antibodies[21, 22]. Most studies suggested that neutralization ability correlated positively with total virus-specific IgG[22,23,24]. Thus, we speculate that the duration of effective concentration of maternal SARS-CoV-2 IgG in infants may be related to their risk of infection after birth. Vertically transferred immunity can dominantly influence the response of offspring to vaccination. High-titer maternal antibodies have often been associated with diminished primary

and disappeared in 2 months after birth. Our study has some limitations. This study is a retrospective study with a small sample size. Since the serological test had not be widely used at the early stage of the epidemic, no comparison was made between the antibody titer of the mother before delivery and the antibody titer of the baby at birth. The IgG neutralizing capacity were not studied, whether the specific antibody in the baby can play a protective effect needs further observation, and more data are needed for following research.

Methods

Objective

In this paper, the serum antibodies of 26 pregnant women who were diagnosed with SARS-CoV-2 infection and 27 infants (1 pair of twins) in Zhongnan Hospital of Wuhan University from January 27, 2020 to May 10, 2020 were analyzed. The infants were admitted to neonatology department for serological antibody test after birth. The mother began breastfeeding if they were asymptomatic after 2 weeks of isolation and negative result of viral nucleic acid detection. During the follow-up with 3 months after the birth of the infant, the results of serum antibody test of SARS-CoV-2 in 4 mothers and 4 infants were obtained.

The timing of serology testing for mothers and infants

tested 54–80 days after birth,and the median time from mother's infection to infant's initial antibody detection was 69 days (57–83 days).

Detection method of serum IgM and IgG antibodies

The serum IgM and IgG levels were quantified by Axceed 400t automatic chemiluminescent immunoanalyzer (Tianjin boassi Biotechnology Co., Ltd. China) and matching reagents.The test was carried out according to the operating instructions of the kit (chemiluminescence method). The test result ≥ 1.0 s/co was defined as positive.

Detection of SARS-CoV-2 nucleic acid

The total RNA was extracted from the pharyngeal swabs and the SARS-COV-2 nucleic acid was detected by qRT-PCR automatically. Operation was under the instruction of China's novel coronavirus (ORF1ab/N) nucleic acid detection kit (Shanghai BioGerm Medical Technology Co., Ltd. China), based on the guidelines of the Center for Disease Control and Prevention in China. The same test system was used throughout the study.

Definition of SARS-CoV-2 infection in mothers

Either positive results of nucleic acid or specific antibodies to SARS-CoV-2 detection.

signed and obtained from all subjects (pregnant women and guardians). The protocol and procedures employed were followed the principles outlined in the Helsinki Declaration.

Ethics statement

The protocol and procedures employed were reviewed and approved by the appropriate institutional review committee and followed the principles outlined in the Helsinki Declaration.

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Contributions

Ethics declarations

Competing interests

The authors declare no competing interests.

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