Int J Physiol Pathophysiol Pharmacol 2022;14(4):267-271
www.ijppp.org /ISSN:1944-8171/IJPPP0140638

Original Article

Immunoglobulin transmission to infants born to mothers with COVID-19

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Received November 18, 2021; Accepted June 28, 2022; Epub August 15, 2022; Published August 30, 2022

Abstract: Background: COVID-19 infection is a severe condition in pregnant women. Previous studies have suggested that anti-COVID-19 antibodies may be able to be transmitted from mother to fetus, which in itself is a protective factor in infants against the disease. However, few studies have been done in this area. In the present study, we aimed to investigate the presence of anti-COVID-19 antibodies in infants born to symptomatic and asymptomatic mothers with positive COVID-19 test. Methods: This is a cross-sectional study performed in 2021 in Abadan on neonates, born to symptomatic and asymptomatic mothers with positive COVID-19 test. All pregnant women over the age of 38 weeks with positive PCR tests for COVID-19 were included. We collected five cc of blood from the umbilical cord of neonates immediately after birth. The samples were sent to the laboratory in laboratory tubes to measure the anti-COVID-19 IgM and IgG levels. Results: We evaluated data of 20 neonates born to mothers with symptomatic COVID-19 and 10 neonates born to asymptomatic mothers with positive COVID-19 tests. In symptomatic groups, sixteen neonates (80%) had positive IgG antibodies and the mothers of all these neonates had positive antibodies. The mean IgG levels in infants was 73.26 ± 12.54 RU/ml and the mean IgM levels were 14.29 ± 3.71 RU/ml. Among neonates born to mothers with no symptoms, 7 neonates (70%) had positive IgG antibody. All mothers had positive antibodies. The mean IgG levels in infants were 74.50 ± 11.37 RU/ml and the mean IgM levels was 12.49 ± 2.88 RU/ml. There were no significant differences between two groups of neonates regarding positivity of IgG and antibody levels (P>0.05 for all). Conclusion: 80% of infants born to mothers with COVID-19 pneumonia had positive IgG levels that were in line with the previous reports.

Keywords: COVID-19, IgG, transmission

Introduction

COVID-19 (Coronavirus or SARS-CoV-2) is responsible for the latest pandemic from Wuhan City, China [1, 2]. Coronaviruses could cause different symptoms in patients, but the most critical complication of COVID-19 is respiratory failure and acute respiratory distress syndrome (ARDS) [3]. Recent studies show that COVID-19 has higher mortality and morbidity rates than other viruses in their family [4].

Symptoms of COVID-19 pneumonia at the onset of the disease include fever, cough and fatigue. At the same time, there are other symptoms such as sputum production, headache, diarrhea, indigestion and lymphopenia that appear approximately five days after incubation [5-7]. The time frame from the onset of COVID-19 symptoms leading to possible death varies from 6 to 41 days, with an average of 14 days [8].

Pregnancy increases the risk of side effects on mother and baby in many respiratory viral infections [9]. Physiological and immunological changes that occur as a natural component of pregnancy can increase the risk of complica-

tions from respiratory diseases [10]. Changes in the cardiovascular and respiratory systems, including increased heart rate, cardiac output, oxygen consumption and decreased lung capacity, and the development of immunological adaptations that allow the mother to tolerate the fetus with different antigens [11, 12]. Data from several studies have shown that influenza increases the morbidity and mortality of pregnant women compared to non-pregnant women [13]. At present we have few information about the complications of COVID-19 pregnancy [14]. Limited information has been provided during studies conducted in Wuhan, China, regarding the pregnancy complications caused by a new virus in the COVID-19 epidemic [15].

One of the most critical concerns of the medical team concerning this disease is its maternal transmission to babies. Despite various studies, it has not yet been determined whether the virus can be transmitted from mother to baby. However, the COVID-19 virus has not been found in breast milk or amniotic fluid [16]. Previous studies have suggested that anti-COVID-19 antibodies may be able to be transmitted from mother to fetus, which in itself is a protective factor in infants against the disease. However, few studies have been done in this area [17]. Previous studies have reported that 65-100% of patients have IgG or IgM seroconversion after COVID-19 pneumonia and almost 75% of babies born to mothers with COVID-19 pneumonia could have positive antibodies. The transplacental immunoglobulin transmission could a critical issue for the further protection of children. It has also been reported that efficient transplacental transfer of SARS-CoV-2 IgG antibodies supports the potential for maternally derived antibodies to provide neonatal protection from SARS-CoV-2 infection.

In the present study, regarding the prevalence and importance of COVID-19 pneumonia and considering the importance of viral transmission from the mothers to neonates, we aimed to investigate the presence of anti-COVID-19 antibodies in infants born to symptomatic or asymptomatic mothers with COVID-19 infection.

Methods and material

This is a cross-sectional study that was performed in 2021 in all educational hospitals affiliated to Abadan University of Medical Sciences. The current study was conducted on neonates, born to mothers with COVID-19 pneumonia. The study protocol was approved by the Research committee of Abadan University of Medical Sciences and the Ethics committee has confirmed it (Ethics code: IR.ABADANUMS.REC.1399.122).

The inclusion criteria were neonates born with gestational age >38 weeks, positive PCR test of COVID-19 for mothers, positive clinical signs and symptoms related to COVID-19 pneumonia for mothers, having COVID-19 pneumonia in mothers based on chest CT scan and signing the written informed consent by parents to participate in this study. The exclusion criteria were mothers with any other infectious diseases and lack of consent.

We included only the neonates, whose mothers had COVID-19 pneumonia and positive PCR test in the third trimester. The sampling method in this study was census. All neonates with the mentioned criteria were recruited. It should be noted that we included 10 mothers with asymptomatic COVID-19 infection based on positive PCR tests. Similar evaluations were conducted on their neonates.

The COVID-19 PCR testing was performed by Real-time PCR-based SARS-CoV-2 detection technique. In this method, we detected SARS-CoV-2 targets the RNA polymerase dependent RNA, ORF1ab fragments, the E gene, the N gene and the S gene by a nasopharyngeal swab.

Initially, all pregnant women over the age of 38 weeks with symptoms of COVID-19 were included in the study. The PCR test for COVID-19 was obtained from all mothers and those with positive results and evidence of pneumonia entered.

We collected 5 mls of blood from the umbilical cord of neonates immediately after birth in the delivery room by experienced nurses and the samples were sent to the laboratory in laboratory tubes to measure the anti-COVID-19 IgM and IgG levels. We used indirect IFA and ELISA (double-antigen sandwich described as SARS-CoV nucleocaspid antigen in Gene-industry) for measurements in this study. Method of measurements were similar to the study of Shi and colleagues in 2005 [17].

Table 1. Clinical presentations of mothers with COVID-19 pneumonia

Clinical presentation	Frequency (%)
Cough	20 (100%)
Muscle pain	20 (100%)
Fatigue	20 (100%)
Fever	17 (85%)
Dyspnea	16 (80%)
Gastrointestinal	16 (80%)
dermatologic	4 (20%)
Neurologic	2 (10%)

The obtained data were entered into the Statistical Package for Social Sciences (SPSS) (version 24, SPSS Inc., Chicago, IL). Quantitative data were reported as mean ± standard deviation and qualitative data as frequency distribution (percentage). We used independent t-test to compare data between groups.

Results

The current study evaluated data of 20 neonates born to mothers with definite COVID-19 pneumonia and 10 neonates born to mothers with asymptomatic COVID-19 infection. All symptomatic mothers had mild to moderate clinical symptoms. During the delivery, all mothers wore masks, and all medical staff wore protective suits and double masks. The infants were isolated from their mothers immediately after delivery.

The mean gestational age of neonates was 39.45 ± 3.10 weeks and the mean age of mothers was 27.15 ± 5.21 years. Evaluation of Apgar score indicated 8 to 9 Apgar score after 1 minute and 9 to 10 Apgar score after 5 minutes.

The clinical symptoms of the symptomatic mothers are provided in **Table 1**. Based on these data, fever, cough, muscle pain and fatigue were the most common clinical symptoms in mothers (100% of cases).

Based on our results, from mothers with symptomatic COVID-19 infection, 16 neonates (80%) had positive IgG antibodies and the mothers of all these neonates had positive antibodies. The mean IgG levels in infants were 73.26 ± 12.54 RU/ml and the mean IgM levels was 14.29 ± 3.71 RU/ml. 4 other neonates (20%) had negative results for antibodies against COVID-19. Of them, three mothers had only positive IgM antibodies and only one mother had low levels of IgG.

Among neonates born to mothers with no symptoms, 7 neonates (70%) had positive IgG antibody. All mothers had positive antibodies. The mean IgG levels in infants were 74.50 ± 11.37 RU/ml and the mean IgM levels was 12.49 ± 2.88 RU/ml. These data are shown in **Table 2**. Based on these data, there were no significant differences between two groups of neonates regarding positivity of IgG and antibody levels (P>0.05 for all).

It should be noted that based on the PCR test, all neonates had negative results.

Discussion

In our study, four infants did not have antibodies against COVID-19 by RT-PCR despite the diagnosis of their mothers with COVID-19 pneumonia. However, the anti-viral antibodies were detected in sera of the other 80%. Furthermore, it was observed that 70% of neonates born to asymptomatic mother with positive COVID-19 tests had positive IgG. Based on the evidence, the IgG could be transferred passively across the placenta. This process initiates at the end of the second trimester and reaches high levels at the time of birth. These data show that IgG transmission through the placenta occurred in 80% of the neonates.

This study was conducted in educational hospitals affiliated to Abadan University of Medical Sciences, where primarily, the symptomatic infected pregnant women are referred. The asymptomatic infected pregnant women are mostly handled in other institutions in our region. Therefore, our study population was symptomatic infected pregnant women.

Similarly, some previous studies have investigated the presence of antibodies against COVID-19 in infants born to mothers with COVID-19 pneumonia. In 2020, Zeng and colleagues showed that from 6 evaluated infants, the IgG levels were increased in 5 neonates (83.3%) [18]. Vendola and others conducted another survey in 2020. By evaluating two mothers, they reported that IgG antibody against COVID-19 was detected in the serum of both infants [19]. These data are in line with

Table 2. Comparison of antibodies based on symptomatic or asymptomatic mothers

Variable	Symptomatic mothers (N = 20)	Asymptomatic mothers (N = 10)	*P*-value*
Positive IgG in neonates (N (%))	16 (80%)	7 (70%)	0.076
Positive IgG in mothers (N (%))	20 (100%)	10 (100%)	>0.99
IgG levels in neonates (RU/ml) (mean ± SD)	73.26 ± 12.54	14.29 ± 3.71	0.336
IgM levels in neonates (RU/ml) (mean ± SD)	74.50 ± 11.37	12.49 ± 2.88	0.812

*Independent t-test.

the findings of our study. As explained earlier, IgG could cross the placenta and we showed that 80% of neonates with symptomatic mothers and 70% of neonates with asymptomatic mothers had positive IgG. We also could not find significant differences between these two groups regarding positivity of antibodies or their concentrations. These data could have high clinical and laboratory significance and we recommend that further research should be conducted on this issue.

Some other case reports have indicated elevated IgG levels in infants born to mothers with COVID-19 infection [20, 21]. But the vital point of our study was that we evaluated data of 20 neonates, a relatively larger study population than previous studies.

In 2021, Bwire performed a systematic review on vertical transmission and natural passive immunity among newborns exposed to COVID-19. By evaluating 33 articles and 205 infants born to COVID-19 positive mothers, they showed IgG/IgM against SARS-CoV-2. IgG/IgM was detected in 90% of infants and the median antibody levels seen were 75.49 RU/ml for IgG [22]. Interestingly, they showed that IgM could be detected in some infants with a 3.79 RU/ml medial levels. Due to the structure of IgM antibodies, they could not pass through the placenta. But it has been assumed that COVID-19 pneumonia might be associated with some degrees of abnormalities in the placenta. As Ng and colleagues reported, the placenta of 2 patients with the severe acute respiratory syndrome had abnormal weights and pathology [23].

The limitations of this study were restricted study population and not evaluating the mother's immunoglobulin after delivery. Another shortcomings of our survey were limited financial resources to conduct further serologic tests. Furthermore, we performed this study when vaccinations against COVID-19 had not been conducted. Therefore, future surveys could evaluate the possible roles of vaccinations on immunoglobulin transmission and production.

The current evidence revealed a low possibility of vertical transmission of COVID-19 and antibodies against SARS-CoV-2 were detected among vertically exposed but negative infants. These data could have high clinical importance.

Conclusion

We reported that 80% of infants born to mothers with COVID-19 pneumonia had positive IgG levels that were in line with the previous reports. However, only a few studies have been conducted in this regard, and most of them had a restricted study population.

Disclosure of conflict of interest

None.

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