

**IgM AND IgG ANTIBODIES AGAINST SARS-COV-2 IN NEONATES BORN TO MOTHERS WITH COVID-19**

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Immunity against the novel coronavirus infection in neonates born to mothers with PCR-confirmed COVID-19 is an understudied field of research. The aim of this study was to analyze the levels of IgM and IgG antibodies against SARS-CoV-2. The study was carried out in 20 mothers aged 19 to 39 years and 21 neonates (including a pair of twins). Babies born to mothers with elevated IgM and IgG against SARS-CoV-2 also had elevated IgG. There is a hypothesis that anti-SARS-CoV-2 IgM are not passed on to the child across the placenta. In all cases studied in this work, neonates were PCR-negative for the virus, which suggests the absence of vertical COVID-19 transmission. Further research is needed.

**Keywords:** novel coronavirus, COVID-19, SARS-CoV-2, transmission routes, neonate, mother, neonatal immunity, immunoglobulin, IgM, IgG, placenta

**Author contribution:** Semeshkin AA — data acquisition, blood collection for antibody tests in neonates, nasopharyngeal swab collection for PCR tests in neonates, analysis of the obtained data, manuscript preparation; Vechorko VI, Averkov OV — study planning, analysis of the obtained data; Silaev BV — study planning, blood collection for antibody tests in mothers, nasopharyngeal swab collection for PCR tests in mothers, data analysis, literature analysis, manuscript preparation; Levchuk NN — data acquisition, laboratory tests for IgM and IgG, analysis of the obtained data; Polikarpova SV — data acquisition, PCR tests in mothers and neonates, literature analysis, analysis of the obtained data.

**Compliance with ethical standards:** the study was approved by the Ethics Committee of Filatov City Clinical Hospital No. 15 (Protocol No. 5 dated May 12, 2020). Informed consent was obtained from all study participants or their legal representatives.

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**АНТИТЕЛА IgM И IgG К ВИРУСУ SARS-COV-2 У НОВОРОЖДЕННЫХ ОТ МАТЕРЕЙ С COVID-19**

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Исследование иммунитета у новорожденных, родившихся от матерей с доказанной новой коронавирусной инфекцией COVID-19, — малоизученный в настоящее время вопрос. Целью работы было проанализировать уровень иммуноглобулинов IgM и IgG к вирусу SARS-CoV-2. Исследование проводили у 20 матерей в возрасте 19–39 лет и 21 новорожденного (родилась одна двойня). В случае обнаружения повышенного уровня иммуноглобулинов IgM, IgG к вирусу SARS-CoV-2 у матери у новорожденного выявляли повышенный уровень IgG. Имеется предположение, что иммуноглобулины IgM к вирусу SARS-CoV-2 не проникают через плаценту от матери к ребенку. Во всех наблюдениях исследование с помощью ПЦР у новорожденных показало отрицательный результат, таким образом, вертикального пути передачи COVID-19, по всей видимости, нет. Необходимы дальнейшие исследования.

**Ключевые слова:** новая коронавирусная инфекция, COVID-19, SARS-CoV-2, пути передачи инфекции, новорожденные, матери, иммунитет новорожденных, иммуноглобулины, IgM, IgG, плацента

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**Соблюдение этических стандартов:** исследование одобрено этическим комитетом Городской клинической больницы № 15 имени О. М. Филатова (протокол № 5 от 12 мая 2020 г.) все участники исследования и их законные представители подписали добровольное информированное согласие на участие в исследовании.

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The ongoing COVID-19 pandemic has raised keen interest in studying the immunity to the novel coronavirus infection in neonates born to mothers with laboratory confirmed COVID-19. So far, there is only a paucity of international literature on this matter, based on few observations that require further in-depth analysis. Currently, vertical (mother-to-child) transmission of the virus is deemed unlikely [1]. A few cases of possible vertical transmission reported in China [2, 3] and Peru [4] are controversial. According to the interim guidance by WHO, testing for COVID-19 should be performed using reverse-transcriptase polymerase chain reaction (RT-PCR), which is a highly accurate and reliable diagnostic tool [5]. RT-PCR can detect the smallest amounts of viral RNA in a human biological specimen. Testing for anti-SARS-CoV-2 IgM and IgG antibodies is widely used in patients with COVID-19 and

might be an alluring technique for studying the immunity of infants born to SARS-CoV-2-infected mothers. The aim of this paper was to study the immunity of neonates born to mothers with PCR-confirmed COVID-19. The presence of IgG antibodies against SARS-CoV-2 in newborns suggests the innate immune response to the virus and might serve as a prognostic marker.

**METHODS**

The study was carried out in a group of pregnant females ( $n = 20$ ) aged 19 to 39 years admitted to the maternity unit of Filatov City Clinical Hospital No. 15 between May 1, 2020 and May 20, 2020. On admission, all females underwent PCR-based tests for COVID-19. Additionally, all neonates ( $n = 21$ ,

including a pair of twins) were also tested for COVID-19 on the first or second day after birth. The following inclusion criteria were applied: COVID-19 diagnosed on admission, with mild or moderate clinical symptoms. The severity of the disease was assessed following the temporary COVID-19 guidelines of the Russian Ministry of Healthcare [6]. Females with acute respiratory infection other than COVID-19 and a negative SARS-CoV-2 test were excluded from the study.

Laboratory (molecular) tests for the novel coronavirus infection were carried out following the temporary COVID-19 guidelines of the Russian Ministry of Healthcare [6].

Biological samples were collected for subsequent PCR as recommended in COVID-19 guidelines [7]. The etiologic diagnosis of COVID-19 is based on establishing the fact of infection with SARS-CoV-2 from the presence of SARS-CoV-2 RNA in the collected specimen by means of nucleic acid amplification. In our laboratory, we use AmpliTest SARS-CoV-2 kits designed at the Center of Strategic Planning and Management of Medical and Biological Health Risks (FMBA; Russia).

IgM and IgG antibodies against SARS-CoV-2 were measured in the serum of mothers and neonates on the first/second day after birth. Collection, shipment and storage of the samples were performed following the manufacturer's instructions.

The samples were analyzed on a CL 6000i Chemiluminescence Immunoassay Analyzer (Shenzhen Mindray Bio-Medical Electronics Co.; China).

Levels of IgG and IgM antibodies against SARS-CoV-2 (SARS-CoV-2-IgG, SARS-CoV-2-IgM) were measured using an immunochemiluminescent technique (the claimed sensitivity and specificity of the assay were 97.8 and 97.9%, respectively). The reference ranges for IgM and IgG titers were 0.00–0.999 OSE and 0.00–9.90 un/ml, respectively.

Sixteen deliveries were vaginal. Cesarean section by the conventional technique was performed in 4 cases. Considering

the epidemiological situation, all patients were wearing face coverings and the medical personnel were wearing protective gowns and FFP2-3 face masks.

## RESULTS

Newborns were isolated from their mothers immediately after birth. All babies scored 8–9 points on the Apgar scale at 1 minute after birth and 9–10 points at 5 minutes after birth. All neonatal nasal and nasopharyngeal swabs collected on day 1 or 2 after birth were PCR-negative for SARS-CoV-2. The collected specimens were also tested for the presence of anti-SARS-CoV-2 IgM and IgG antibodies.

Antibodies against SARS-CoV-2 were detected in all neonatal samples. Both IgM and IgG were elevated in one case. IgM and IgG were within the reference range in 4 neonates; similar results were observed in their mothers. Only IgG was elevated in 14 newborns; their mothers had high titers of both IgM and IgG outside the reference range (Table 1).

No RNA fragments of SARS-CoV-19 were detected in any of the neonates born to mothers with confirmed COVID-19. However, all neonates had virus-specific IgG antibodies in their serum.

IgG was elevated in 16 neonates but only in those cases when maternal IgG levels were also elevated ( $n = 16$ ).

## DISCUSSION

The obtained data allows us to hypothesize that IgG antibodies are passively carried to the fetus across the placenta by the maternal blood flow at the end of the third trimester and reach their peak level by the time of delivery. Some authors report that due to high molecular weight, IgM antibodies, which were detected in only one neonate in our study, are not passed on from the mother to the child [1–4]. It might be possible, though, that IgM is produced by the baby itself if the virus

**Table 1.** Levels of IgM and IgG antibodies against SARS-CoV-2 in mothers and their children

Case	IgM		IgG	
	Mother	Infant	Mother	Infant
1	2.51	0.15	0.40	0.49
2	8.84	0.30	34.76	11.24
3	9.29	0.43	136.02	109.84
4	0.96	0.26	0.53	0.97
5	1.19	0.24	17.54	15.01
6	0.48	0.24	0.32	0.70
7	2.01	0.24	24.81	9.69
8	1.19	0.18	92.40	42.12
9	6.70	0.26	116.04	24.41
10	6.80	0.14	66.32	89.12
11	0.68	0.25	1.54	1.20
12	0.31	0.21	0.32	0.58
13	14.43	0.15	38.86	23.9
14	2.85	1 infant 0.14 2 infants 0.16	47.77	1 infant 8.44 2 infants 6.83
15	1.26	0.62	39.30	12.67
16	2.52	0.95	6.52	2.11
17	0.41	0.12	103.02	38.64
18	1.94	0.41	19.86	12.54
19	2.48	0.94	6.34	1.15
20	10.08	8.54	24.12	16.87

has already crossed the placenta. Our findings are consistent with the findings of our Chinese colleagues who worked with a smaller sample size [8–10]. We did not perform any tests on the placenta; therefore, the proposition above is merely a hypothesis. Our study has a few limitations. Our sample size was small and we did not test the amniotic fluid and breast milk for the presence of the virus and the antibodies. Nevertheless, our findings might be helpful in better understanding the serologic features of neonates born to SARS-CoV-2-infected mothers.

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## CONCLUSION

1. Elevated IgG levels are detected on the first or second day after birth in the blood of neonates born to mothers with PCR-confirmed COVID-19. 2. Elevated virus-specific IgG might indicate the presence of innate immunity to the novel coronavirus. 3. Unelevated virus-specific IgM in neonates born to mothers with PCR-confirmed COVID-19 could be explained by the fact that due to high molecular weight, maternal IgM cannot be carried across the placenta.

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