S.D. Efremova, E.D. Okhlopkova, A.A. Grigorieva,
L.D. Olesova, A.N. Romanova

INDICATORS OF ANTIBODIES IgM AND IgG TO SARS-COV-2 IN RESIDENTS OF YAKUTSK AFTER RECOVERY FROM COVID-19

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A study of IgM and IgG antibodies to SARS-COV-2 was carried out in 161 residents of Yakutsk at the age from 20 to 72 years old who had a new coronavirus infection COVID-19 from 3, 6, 9 and 12 months ago. The aim of the work was to assess the content of serum immunoglobulins IgM and IgG to SARS-COV-2 in persons who have had COVID-19, depending on the duration and severity of the disease. The intensity of the immune response was assessed using the coefficient of positivity (CP) as the ratio of the optical density of the sample to the critical value of the optical density. According to the results of the study, the seroprevalence in all 4 groups of patients with Covid-19 was 100%. Antibodies IgG and IgM to SARS-CoV-2 in those who had been ill with COVID-19 persisted up to 12 months and depended on the postcovid period, age and severity of lung lesions on CT.

Keywords: IgG, IgM, SARS-CoV-2, antibodies, COVID-19.

Introduction. Since December 19, 2019, after the first outbreak of a new coronavirus infection in Wuhan (China), the disease has spread rapidly and within a few months has spread to the whole world. In April 2020, the first cases of the disease were diagnosed in Russia, and in March - in the Republic of Sakha Yakutia.

Currently, to diagnose COVID-19 infection, a laboratory RT-PCR (PCR) test is performed to detect SARS-CoV-2 RNA in samples taken from the nose and throat, but the PCR method does not always determine the presence of infection, since there is a possibility of obtaining false negative results [10.7]. One of the additional methods of timely diagnosis at an early stage of the disease of a new coronavirus infection is the enzyme-linked immunosorbent assay (ELISA) for antibodies (AT) to SARS-CoV-2 (1,5). Joint testing for the detection of class M and G antibodies is of great importance for the epidemiological prognosis and understanding of the treatment of SARS-CoV-2 infection [13].

Yakutsk Scientific Center for Complex Medical Problems: **EFREMOVA Svetlana Dmitrievna** – junior researcher laboratory of immunology, esd64@mail.ru; **OKHLOPKOVA Elena Dmitrievna** – Candidate of Biological Sciences, leading researcher, head of the laboratory of Immunology elena_ohlopkova@mail.ru; **GRIGORIEVA Anastasia Anatolyevna** – researcher, laboratory of biochemistry, Nastiagrigoryeva@gmail.com; **OLESOVA Lyubov Dygynovna** – Candidate of Biological Sciences, leading researcher, head of the Laboratory of Biochemistry oles@mail.ru; **ROMANOVA Anna Nikolaevna** – Doctor of Medical Sciences, Director ranik@mail.ru

The mechanisms of the development of the body's immune response to the SARS-CoV-2 coronavirus are being studied. Experts are interested in the question of how long antibodies can persist in the body in persons who have had COVID-19. Some studies provide data on the presence of (AT) M and G not only in persons with a positive, but also a negative PCR result after 1-3 weeks from the moment of infection with the virus, as well as pregnant mothers and newborns, seriously ill, and deceased patients [1,6,12,14]. From the moment the coronavirus enters the body, immunoglobulins G (IgG) are synthesized last 5-6 weeks about the coronavirus, i.e. are the archive of the memory of the transferred infections, in most cases for life, or for several years. It remains unclear whether persistent immunity is being formed, which requires in-depth study. But in any case, the detection of IgG indicates the fact that the coronavirus has entered the body and the body's immune response. Currently, various sources provide data on the presence of AT in patients with COVID-19 from 3 months to a year ago [7,8]. Of great interest is the timing of maintaining a high level of antibodies after suffering COVID-19, which requires further study of the resistance, weakening and duration of protection of antibodies to SARS-CoV-2.

The aim of the study was to assess the content of serum immunoglobulins IgM and IgG to SARS-COV-2 in people who had been ill with COVID-19, residents of Yakutsk, depending on the duration and severity of the disease.

Materials and methods: On the basis of the Yakutsk Scientific Center for Complex Medical Problems clinic, 161 people who had undergone COVID-19 with laboratory-confirmed 2019-n CoV infection by PCR were examined, with varying degrees of lung damage. Age ranged from 20 to 72 years, of which 56 (34.8%) young people (20-44 years old), 53 (32.9%) middle-aged (45-59 years old); (60-74 years old) elderly - 51 (31.7%) and (75-90 years) old age - 1 (0.6%) age, respectively (Table 2). Women accounted for 101 (62.7%) and men - 60 (37.1%). The criterion for exclusion from the group was persons with signs of ARVI and active infection with COVID-19 at the time of the study. Data on the degree of lung lesions by the type of "ground glass" were assessed according to the results of computed tomography (CT), taken from the discharge epicrisis: CT0 (zero) - no manifestations; CT1 (lung) - the prevalence of the lesion is less than 25% of the lung volume; CT2 (moderate) –25-50%; CT3 (heavy) 50 -75%; CT4 (critical) - more than 75%. All subjects were divided into 4 groups, depending on the duration of recovery from the moment of the illness: up to 3, 6, 9 to 12 months ago. The study was approved by the decision of the Local Ethics Committee at the Federal State Budgetary Scientific Institution "YSC CMP" no 52 dated March 24, 2021 and was carried out with the informed consent of the subjects in accordance with the ethical standards of the Declaration of Helsinki (2000).

The study material was venous blood serum. Blood sampling was performed from the cubital vein in the morning hours from 8-10 hours on an empty stomach. A qualitative determination of antibodies (AT) M and G against SARS-CoV-2 was carried out by the enzyme immunoassay using the test systems of the "Vec-

tor-Best" company (Novosibirsk), on the "Uniplan" photometer (the "Picon" company, RF), according to the instructions manufacturer's firm. The intensity of the immune response was assessed using the coefficient of positivity (CP) as the ratio of the optical density of the sample to the critical value of the optical density, which reflects the relative amount of the corresponding antibodies in the sample. This indicator allows you to track the dynamics of the level of antibodies in human blood by examining samples taken at different times, and thus to clarify the patient's immune status. According to the value of the coefficient of the qualitative test, the sample was considered negative or borderline (CP less than 1.1), positive (CP from 1.2 and higher) result. Seroprevalence (presence of AT G) and the presence of serological markers of acute infection (IgM) were assessed. The level of rheumatoid factor (RF) and C-reactive protein (CRP) was also determined on a biochemical analyzer "Sapphire" (Japan).

The results were processed using the SPSS Statistics 26 statistical software package. The descriptive analysis data are presented in the tables as Me (median), Q1 and Q3 (quartiles 25% and 75%). The significance of differences was assessed using Student's t-test and ANOVA for independent samples with normal distribution and Mann-Whitney test for abnormal distribution. The critical value of the level of statistical significance of differences (p) was taken equal to 5%. Correlation analysis of the data was performed using the Pearson method.

Results and discussion. A positive test for immunoglobulins suggests that the person has potentially been exposed to SARS-CoV-2. According to the results of the study, seroprevalence in all 4 groups of patients with Covid-19 was 100%, had no gender differences, which is consistent with literature data [9]. However, IgG antibodies were not at a high level in all and differed significantly.

According to the value of KP IgG, all the patients were divided into three subgroups. Low CP from 1 to 3,49 was detected in 8,7%, the average level of antibodies from 3,5 to 9,99 was recorded in 19,3%, high - from 10 or more was found in 72,0% of patients (Table 1) There was a direct correlation relationship (r = 0,309; p<0,000), (r = 0,312; p<0,000), respectively, between the level of CP IgG and the groups who underwent Covid-19 with varying degrees of severity (CT) and age groups. The mean CP IgG value increased depending on the degree of lung damage and was statistically significant between the groups CT0 with CT2, 3, CT4 (p = 0,005; p = 0,001; p = 0,007) and CT1 with CT2, CT3 (p =0,038p = 0,0210) (Table 1). According to our data, the frequency of occurrence of a high IgG content increases from CT1 to CT4; in those examined with CT3 and CT4, individuals with a low IgG content were not detected (Table 1). In age groups, statistically significant differences in IgG CP were found between young and middle-aged people with the elderly (p =0,001 and p =0,017) (Table 2). In the elderly group, the most significant incidence of IgG with a high KP value is noted, which is possibly associated with the high severity of the disease in this age group. According to the literature, the severity of the course of COVID-19, according to the CT protocol, had a direct relationship with age; in young age groups, a mild form of lung lesion with CT1 was more common, in middle-aged and elderly groups with lung damage with CT2 and CT3 [4].

Depending on the duration of the Covid-19 disease, an inverse correlation was obtained (r = -0,238; p<0,002). The frequency of occurrence of persons with a high content of CP IgG remained the highest in 3 groups in those who had recovered from 3 months ago in 12 (80%), from 6 in 58 (77,3%) to 9 months in 36 (75 In those who had been ill up to a year ago, the frequency of AT decreases by 10 (43,5%), which does not contradict the literature data, antibodies can persist for up to 1 year (11). postform period (Table 3). IgG, as a rule, are the main factor of the humoral link of the immune defense, which counteracts the development of the infectious process in the body. The presence of specific immunoglobulins of class G, which appeared in a person as a result of a previous illness or vaccination, in most cases indicates the formation of sterile immunity to the corresponding bacterial or viral infection [5].

When the infectious disease passes without complications, the anti-IgM antibodies that appear from the first week of acute infection should gradually de-

Table 1

Indicators of IgG seropositivity depending on CT

Level CT	CP Me (Q1 – Q3)	Level CP IgGn/%			Total «+» Absolute number/%
		low	medium	high	
CT(0)	10.30 (4.04;11.53)	5/18.5	8/29.6	14/51.9	27/16.8
CT(1)	11.44 (6.00;11.60)	6/10.0	16/26.7	38/63.3	60/37.3
CT(2)	11.52 (11.13;11.69) [1]p=0.005; [2]p=0.038;	3/7.1	4/9.5	35/83.3	42/26.1
CT(3)	11.59 (11.38;11.77) [1]p=0.001; [2]p=0.007	-	3/11.5	23/88.5	26/16.1
CT(4)	11.59 (11.42;11.59) [1]p=0.021	-	-	6/100	6/3.7
Total		14/87	31/19	116/72	161/100

Note: n - is the number of patients who have been ill; "+" - the number of persons with the presence (AT); 1-statistically significant differences from CT0; 2-significance of differences from CT1.

Table 2

Indicators of IgG seropositivity in different age groups

Age group	CP Me (Q1 – Q3)	Level CT IgGn/%			Total «+» Absolute number/%
		low	medium	high	
Young	11.42 (4.90-11.60)	9/16.1	14/25.0	33/58	56/34.8
Middle aged	11.42 (7.84;11.56)	5/9.4	11/20.8	37/69.8	53/32.9
Old-aged	11.59 (11.47;11.72) [1]p=0.000; [2]p=0.017;	-	6/11.8	45/88.2	51/31.7

Note: n - is the number of patients who have been ill; "+" - the number of persons with the presence (AT); 1-statistically significant differences from CT0; 2-significance of differences from CT1.

Table 3

Indicators of IgG seropositivity depending on the postcovid period

Postcovid period, month	CP Me (Q1 – Q3)	Level CT IgGn/%			Total «+» Absolute number/%
		low	medium	high	
up to 3	11.28(11.52;11.62) [1]p=0.005	1/6.7	2/13.3	12/80.0	15/9.3
up to 6	10.88 (11.50;11.66) [1]p=0.001	4/5.3	13/17.3	58/77.3	75/46.6
up to 9	10.20 (11.47;11.59)[1]p=0.004;	5/10.4	7/14.6	36/75.0	48/29.8
up to 12	4.34 (9.4;11.60)	4/17.4	9/39.1	10/43.5	23/14.3

Note: "+" - the number of persons with the presence (AT); 1-statistically significant differences with a postcovid period of up to 12 months.

crease and disappear after a month. The specific gravity of the serological marker of acute IgM infection in patients with Covid-19 was 62,1%, a negative IgM result was detected in 61 (37,9%) people, a low CP from 1,2 to 2 in 41 (25,5%), the average CP was 2,1 to 4,9 in 36 (22,4%) and a high level of CP was higher than 5 in 23 (14,3%) examined (Pic.1). It is possible that these results may be associated with a weakened immune response or a strong attack by the SARS-CoV-2 virus in critically ill patients and with a nonspecific M antibody response, leading to a false positive result. Processes associated with inflammation in the body can lead to a nonspecific reaction with the test system: acute and chronic inflammatory processes, autoimmune diseases, problems with the thyroid gland, pregnancy, and so on. Our data are consistent with the literature data that with coronavirus IgM can persist for a long time (up to 1,5-3 months from the onset of symptoms, when the virus is gone) [8]. Also, the IgM level had a direct correlation with the severity of the disease (CT) (r = 0,192; p<0,014), rheumatoid factor (RF) (r = 0,191; p<0,016) and an inverse relationship with the duration of the disease (r = -0,240; p <0,002), possibly due to the defeat of Covid-19 joints. There were no differences in the CRP content in the groups. A negative result of CP IgM was more often observed in the group of patients with CT0 (48,1%) and CT1 (40,0%), CT2 (35,7%), CT3 (30,8) CT4 (16,7) gradually decreased (Pic. With an increase in the postcovid period, the frequency of occurrence of persons with a negative IgM result increase, and with an average and high level of IgM CP, it decreases.

The highest frequency of occurrence of a high level of IgM is observed in those who have been ill up to 3 months (33,3%), then a decrease is observed from the duration of the recovery period (Pic.3).

Conclusions:

1. A high level of seroprevalence per-

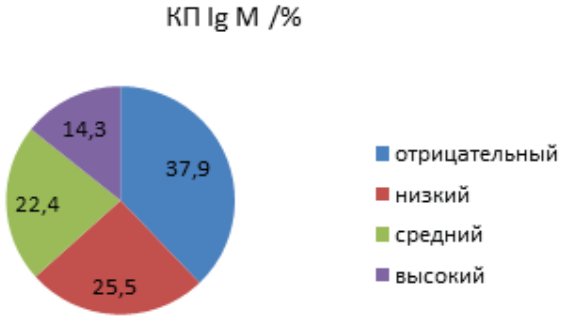

Fig. 1. CP level Ig M in patients with COVID-19, %

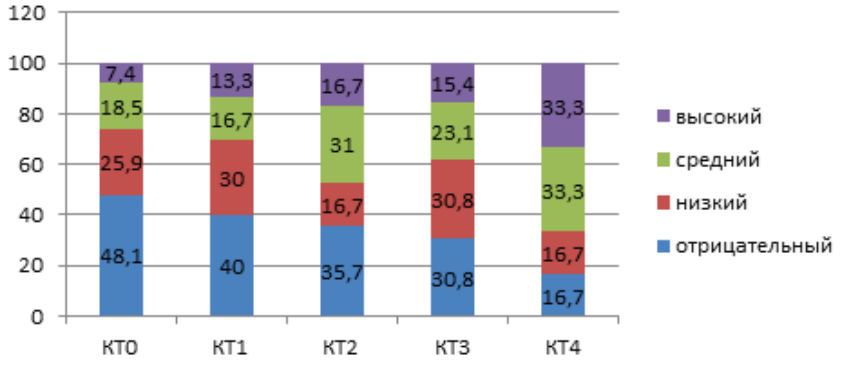

Fig. 2. Frequency of occurrence of persons with different levels of CP IgM depending on the severity of the disease according to CT, %

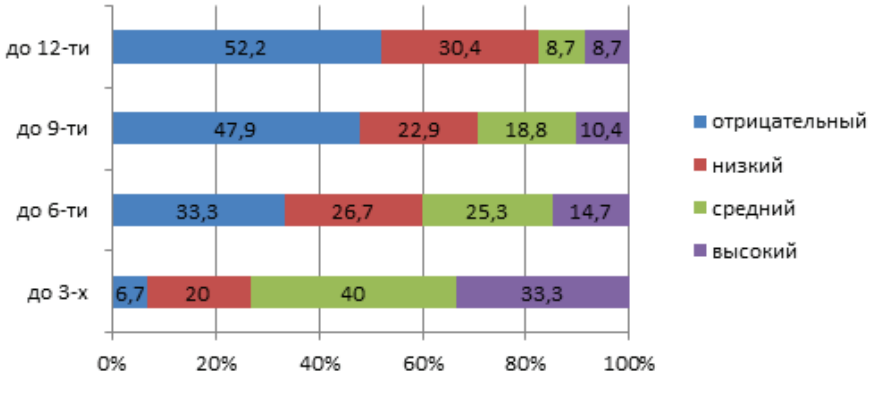

Fig. 3. Frequency of occurrence of persons with different levels of CP Igg depending on the waxy period, %

sists in persons who have undergone COVID-19 with a more severe form of lung damage, since the maximum seropositivity was observed in 100% of patients with CT4, 88,5% with CT3, and 83,3% with CT2.

2. The content of antibodies of immunoglobulin G to SARS-CoV-2 in patients with COVID-19 depends on age: a high level of seroprevalence was found in the group of elderly people (60-74 years) in 88,2% and average (45-59 years) in 69,8 %.

3. IgG antibodies to SARS-CoV-2 in those who have had COVID-19 persist for up to 12 months, and the frequency of high levels of antibodies decreases over time: The maximum level of serovalence in those who had recovered up to 3 months ago was detected in 80%, up to 6 months - in 77,3%, up to 9 - in 75,0%, up to 12 - in 43,3%.

4. The presence of IgM antibodies to SARS-CoV-2 in patients with COVID-19 depends on the postcovid period, the severity of lung damage on CT, and the possibility of obtaining false positive results associated with an increase in rheumatoid factor.

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