UDC 616.921.5-022.6+612.398.132-097

IgG, IgM and neutralizing antibodies to SARS-COV-2 in medical workers during the year (2020-2021) before the start of mass vaccination

V.M. Kornatskyi[1], N.O. Ryzhkova[1], T.I. Gavrilenko[1], A.M. Dorokhina[1], Yu.V. Kornatskyi[1], O.A. Pidgaina[1], S.M. Babii[2], O.M. Pasichnichenko[2]

[1]State Institution National Scientific Center «M.D. Strazhesko Institute of Cardiology National Academy of Medical Sciences of Ukraine», Kyiv;
[2]Taras Shevchenko National University of Kyiv, Ukraine; e-mail: tala.ruzh@gmail.com

The purpose of the work is to assess the levels of IgG, IgM and neutralizing antibodies to SARS-CoV-2 in medical workers during the year (2020-2021) before the start of mass vaccination, depending on the presence of clinical symptoms and positive PCR test. It is established that people without antibodies to SARS-CoV-2 do not have neutralizing antibodies. The antibody levels, as well as percentage of neutralization, were higher in individuals who had just recovered from Covid-19 and have positive PCR at the beginning of the disease compared to those who had no clinical manifestation. There was a positive correlation between the level of IgG and percentage of neutralization. In persons without pronounced clinical symptoms of coronavirus infection, moderately positive neutralizing antibodies prevail, whereas in the vast majority of recovered individuals they are highly positive.
Key words: antibodies; coronavirus.

INTRODUCTION

SARS-CoV-2 is a β-coronavirus that has four structural proteins: the nucleocapsid, membrane, envelope, and surface-anchored spike glycoprotein (S).The latter includes two subunits: S1 and S2. S1 consists of an amino-terminal domain and a receptor-binding domain (RBD) that interacts with the human angiotensin-converting enzyme (hACE2) as the target receptor of the host cell. Binding of RBD to ACE2 triggers SARS-CoV-2 virion endocytosis and exposes it to endosomal proteases. The subunit S2 is necessary to acquire the correct conformation and induces the fusion of the virus with the membrane of the target cell [1-5]. For this reason, protein S is an interesting target for the rational production of vaccines or therapeutic antibodies to prevent infection [3, 6]. N and S proteins are the main immunogenic proteins of SARS-CoV-2. Antibodies that block the interaction of the RBD domain S1 subunit of the "spike " protein with ACE2 and prevent the virus from penetrating the cell and its subsequent replication are called neutralizing antibodies. It is well known that a neutralizing humoral immune response is the main mechanism for preventing viral infections [7]. Neutralization of the virus is an important mechanism of action of antibodies, but the specific titer and specificity of the repertoire of antibodies needed for protection remain uncertain [3, 4].

Detection of anti-SARS-CoV-2 IgM and IgG antibodies is considered diagnostic. Although serological tests do not confirm the presence of an active virus, they have some impressive advantages compared to antigen tests. They include a much longer detection window, convenience and safety of the operator for blood collection rather than respiratory tract samples, the stability of human antibodies compared to viral RNA during sampling, preparation, transportation and storage, more even distribution of antibodies in

blood than virus in respiratory samples. Antibodies can also be successfully detected in saliva in addition to blood. In addition, these tests do not require special laboratories. Serological tests may play an additional but irreplaceable role in the diagnosing suspected cases with a negative test for viral RNA or past COVID-19 infection; epidemiological assessment, immune response monitoring to assess the course, degree and stability of immunity; identification of potential donors of reconvalescent plasma; development and evaluation of therapeutic antibodies; development and evaluation of vaccine; contact tracing to determine further chains of events [8, 9]. However, as previous studies indicate, the IgG and IgM antibodies levels are highly variable, and no correlation between antibody titers and clinical characteristics of patients has been found [3, 10]. Whether the levels of antibody measured with serological tests can be used as an assessment of serum neutralizing activity is a topical issue [11] and requires further research.

The purpose of the work is to assess the level of IgG, IgM and neutralizing antibodies to SARS-CoV-2 in medical workers during the year (2020-2021) before the start of mass vaccination, depending on the presence of clinical symptoms and a positive PCR test.

METHODS

The examination of the employees of the State Institution NSC «M.D. Strazhesko Institute of Cardiology National Academy of Medical Sciences of Ukraine» was carried out according to the order of the Ministry of Health 1227 from 20.05.2020 "Changes to the Standards of medical care "Coronavirus disease (Covid-19)". The research took place in the Department of Immunology from June 2020 to May 2021 compliance with the standards of bioethics. During this period, there were 3 waves of Covid-19 incidence. In this regard, we divided our research into 3 stages: 1st - from June to September (inclusive) 2020 (527 people were examined), 2nd - from October to 2020 to January (inclusive) 2021, (414 people were examined), 3rd - from February 2021 to May (inclusive) 2021 (259 people were examined). In turn, all subjects were divided into two subgroups: subgroup A (2A, 3A) - persons who had no clinical manifestations, but had antibodies to SARS-CoV-2; subgroup B (2B, 3B) - persons who have just been diagnosed with Covid-19, had antibodies and positive PCR at the beginning of the disease.

The presence of IgG and IgM antibodies with the calculation of the positivity index (PI) was performed on kits for enzyme-linked immunosorbent assay «EQUI SARS-CoV-2 IgG» and «EQUI SARS-CoV-2 IgM» (Ukraine). The product is used to detect IgG and IgM antibodies to nucleocapsid and «spike» (S1) antigens of the SARS-CoV-2 virus. PI, according to the instructions to the kits, <0.9 is considered negative (in our study it was evaluated as a zero - 0), 0.9-1.1 - equivocal, >1.1 - positive. The maximum value is possible on these sets = 12.0. We regarded PI <4.0 as low antibody level, 4.0-7.0 as medium, >7.0 as high. Total neutralizing antibodies (NA) were determined on the ELISA kit "EQUI SARS-CoV-2 Neutralization antibody". Their determination is based on blocking the binding of the RBD domain of the S1 subunit of the "spike" glycoprotein absorbed in the wells of a plate with human ACE2 cell receptor (hACE2) conjugated with horseradish peroxidase. The percentage of neutralizing antibodies (PN), according to the instructions, can be negative (<30%) or positive (>30%). In our study, we divided positive results into moderately positive (30-80%) and highly positive (>80%). The control group for the presence of NA was made by persons who did not have disease and did not have antibodies to SARS-CoV-2 (21 people).

The obtained results were processed by methods of variation statistics and Microsoft Excel program. They are represented in tables as the mean ± arithmetic mean error (M ± m). Differences between sample groups were probably by $P < 0.05$.

DISCUSSION

At the first stage, almost all employees of the medical institution were examined. Antibodies were detected in 40 people (7.6%). These people had no clinical manifestations of coronavirus disease and had a negative PCR test. In 22.5%, only IgM was detected, which in the next examination in a month was not detected. In 2 people (5%) both IgM and IgG were detected. Others (76.9%) had only IgG. The PI in this case was low and averaged 2.6 ± 0.3. We would like to note that 30.8% of them later fell ill with Covid-19 with a pronounced clinical picture and a positive PCR test. Clinical manifestations of the disease and a positive PCR test for the specified period of examination had only 4 people (0.76%). The percentage of neutralizing antibodies at this stage was not determined in the absence of the necessary test systems. But as further studies indicated in this work showed, individuals with low antibody levels do not have NA in most cases.

In parallel with the presence of IgM, IgG antibodies and NA to SARS-CoV-2 292 people were examined in the 2nd and 3rd waves of (Table 1). In the control group (persons without IgM or IgG antibodies) the PN was within 0-29.7%. That is, the result for the presence of NA was negative. A general review of the situation showed (Table 1) that, on the one hand, the level of antibodies to SARS-CoV-2, as well as PN probably increased with an increase in the incidence of the disease during the year. On the other hand, IgG, as well as PN, were higher in those who have just relapsed to Covid-19 and have positive PCR at the beginning of the disease compared to those who had no clinical manifestations. Detailed analysis of the results showed the heterogeneity of the 2nd and 3rd groups at the level of IgG, NA and in the presence or absence of IgM.

At the 2nd stage 414 people were examined, without taking into account those who detected antibodies at the 1st stage. Antibodies to SARS-CoV-2 were detected in 22.9% of people without severe clinical manifestations of the disease (group 2A) and in 29.2% of people who had a coronavirus infection and had a positive PCR test (group 2B). Parallel studies on the presence of IgM, IgG antibodies and NA were conducted in 158 people. In group 2A, almost a third of those examined (Table 2) had a low PN - 14.7 ± 1.6%, which indicates a negative reaction. Their PI IgG was also low and was 3.5 ± 0.5, 2 people had equivocal IgM. In most people from this group a moderately positive result for PN was found - 55.7 ± 2.0%. Among them, 15.7% had PI IgM = 0.9-4.7 interval, and PI IgG averaged 5.1 ± 0.3. Others received a highly positive result on PN - 90.9 ± 1.0%. Among them, 42.1% had PI IgM = 0.9-4.6 interval, and PI IgG averaged 6.9 ± 0,5. Overall 18.8% of people in this group had

Table 1. Indicators of IgM and IgG levels and the percentage of neutralization to SARS-CoV-2 in different groups of subjects

Groups	IgM (positivity index)	IgG (positivity index)	Neutralizing antibodies (percentage of neutralization, %)
Control group (n = 21)	0	0	11.9 ± 2.0
Persons without clinical manifestations (2nd wave), n = 96	0.4 ± 0.1	5.0 ± 0.2	51.6 ± 2.9
Persons who became ill (2nd wave), n = 62	0.4 ± 0.1	6.2 ± 0.3[1]	77.3 ± 2.9[1]
Persons without clinical manifestations (3rd wave), n = 80	0.6 ± 0.1	6.2 ± 0.3[2]	67.2 ± 2.7[2]
Persons who became ill (3rd wave), n = 15	1.1 ± 0.2	7.2 ± 0,4[12]	82.7 ± 4.2[12]

[1]P < 0.05 between subgroups A i B. [2]P < 0.05 between groups 2 and 3

IgM antibodies. Their PI IgM averaged 2.0 ± 0.3, PI IgG 6.1 ± 0.5 and PN 70.7 ± 6.2%. There was a high correlation dependence r = +0.7 between PI IgG and PN. In the persons who did not have IgM, IgG was significantly lower (4.8 ± 0.3; P < 0.05), as well as PN (47.2 ± 3.1%; P < 0.05). The correlation dependence was also lower - r = +0.5. In group 2B, only two people (Table 2) had low PN (5.4 and 27.2%). Their PI IgG were also low, 2.7 and 1.2, respectively. IgM was not detected in them. Moderately positive PN (58.3 ± 3.2%) was observed in one third of people in this group. Among them, only two (8.3%) had positive IgM, and PI IgG the average 5.0 ± 0.5. The main majority were individuals with a highly positive result in PN (93.3 ± 0.3%) and PI IgG (7.1 ± 0.2). IgM is found among them in 33.3% of respondents. Overall, in this group 22.6% of respondents had both IgG and IgM antibodies. Their PI IgM was an average 1.9 ± 0.3, PI IgG - 7.5 ± 0.3, PN - 90.2 ± 1.9%. The correlation is found between IgM and PN - r = +0.4, where it was absent between PI IgG and PN. In persons who did not have IgM in the examination, IgG was significantly lower (5.7 ± 0.3; P < 0.05), as well as PN (73.5 ± 3.6%; P < 0.05). However, there is a high correlation between IgG and PN - r = + 0.7.

The antibody-dependent response is described against SARS-CoV-2, as well as their kinetics [8, 12]. Seroconversion in patients with COVID-19 is achieved after symptoms appear by producing IgM, IgA and IgG antibodies. The accumulation of IgM is observed within 7 days after the onset of symptoms, which is treated as a marker of acute infection. The average time of appearance of IgG was recorded at 14 day after the onset of symptoms and is considered diagnostic. IgA and IgM antibodies can be stored in the body for about 2 months, while IgG can be stored for more than 3 months. However, IgG and IgM levels have been found to be highly variable, and no correlation has been found between antibody titers and clinical characteristics of patients [3, 10]. At the 2nd stage we found that PI IgG, as well as PN, were higher in individuals who had just undergone from Covid-19 and have positive PCR at the beginning of disease compared to those who had no clinical manifestations. IgM antibodies was positive in 41.4% of those examined during this period which indicates an active infectious process. Compared to those who did not have these antibodies, they had significantly higher IgG antibodies and PN.

At the 3rd stage, 259 people were examined, without taking into account those who detected antibodies at the 1st and 2nd stage. In 44.7% of them, the antibodies to SARS-CoV-2 without severe clinical manifestations of the

Table 2. The proportion of individuals with a certain level of neutralizing antibodies in different groups of subjects

Groups	Proportion of persons with the percentage of neutralization <30%	Proportion of persons with the percentage of neutralization 30-80%	Proportion of persons with the percentage of neutralization 81-100%
Persons without clinical manifestations (2nd wave), %	27.1	53.1	19.8
Persons who became ill (2nd wave), %	3.2[1]	38.7	58.1[1]
Persons without clinical manifestations (3rd wave), %	8.8	53.8	37.5[2]
Persons who became ill (3rd wave), %	12.1	15.2[12]	72.7[1]

[1]P < 0.05 between subgroups A i B. [2]P < 0.05 between groups 2 and 3

disease (group 3A), and 30.5% had Covid-19 and a positive PCR test (group 3B). Parallel studies on the presence of IgM, IgG antibodies and NA were conducted in 95 people. In group 3A negative PN (19.6 ± 3.3%), was observed in a small number of the examined individuals (Table 2). Their PI IgG was also low (2.8 ± 0.6) and IgM was not detected. Most people in this group have found a moderately positive result on PN (59.1 ± 2.4%). Among them, 18.6% have PI IgM = 1.0-6.8 interval, and PI IgG averaged 5.9 ± 0.4. Others received a highly positive result on PN (89.9 ± 1.0%) as well as PI IgG (7.5 ± 0.3). Among them, 30% had PI IgM (0.9-5.0) interval. 21.3% of people had IgM in group 3A. Their PI IgM averaged 2.6 ± 0.4, PI IgG - 7.3 ± 0.7, and PN - 78.6 ± 4.6%. There was a positive correlation between IgG and PN - r = + 0.4. In individuals who did not have IgM in the survey, IgG was slightly lower than in the previous subgroup (6.0 ± 0.3), although no probably difference was found, as well as PN (64.1 ± 3.1%; P < 0.05). In this case the correlation dependence was high - r = + 0.6. In group 3B negative PN (26.5 ± 2.7%) was observed, as in the previous group, in a small number of examined. Their PI IgG was low - 3.3 ± 0.7. IgM was not detected. A small number of people also had a moderately positive PN result (66.6 ± 2.3%). Among them, two people had equivocal IgM, although the PI IgG was high enough - 8.1 ± 1.1. The main majority were those who had a highly positive result on PN (95.5 ± 1.1%) and PI IgG (7.9 ± 0.3). Among them, 62.5% of respondents had IgM, of which averaged 2.2 ± 0.2. In this group, the most of those examined (51.5%) had both IgG and IgM antibodies. Their PI IgM was on average 2.1 ± 0.2, the PI IgG - 8.2 ± 0.4, and the PN - 93.2 ± 2.4%. The correlation dependence was found between IgM and PN (r = +0.5), whereas it was absent between PI IgG and PN. The same pattern was observed in similar patients in the second wave of the disease. In persons who did not have IgM in the examination, PI IgG was significantly lower (6.4 ± 0.7; P < 0.05), as well as the percentage of PN (71.6 ± 7.5%; P < 0.05). But there is a positive correlation between PI IgG and PN (r = +0.6), and between the IgM and PN it was absent.

Some authors have observed a correlation between an increased serum concentration of anti-S IgA and IgG proteins and a decrease in the number of viruses, as well as the time between the onset of symptoms and hospitalization to the intensive care unit. A significant link between serum anti-S IgG titers and survival patients in critical condition has been demonstrated [3, 13]. In addition, there is a correlation when the development of acute respiratory distress syndrome coincides with the seroconversion of antiviral IgG in 80% of patients [14]. Patients who developed NA to the S protein at the beginning of the infection had a higher level of disease; patients who died from infection took an average of only 14.7 days to reach their peak NA activity, as opposed to 20 days for patients who recovered [15]. Similar to our study, the literature data suggests that patients with severe disease have higher antibody titers than patients with mild disease [16, 17], although there is also a claim that the delay in the development of an antibody response is associated with the disease [18]. Judging by the neutralizing serum activity of the examined employees, the greatest confidence in full protection is among patients with a pronounced clinical picture, who have a highly positive PN. We also noted that they have a higher proportion of IgM detection and are growing significantly during development of the disease during the year, which indicates a greater number of patients with an active process.

In addition to neutralization, antibodies can lead to antiviral protection through other mechanisms, such as antibody-dependent cellular cytotoxicity, antibody-dependent phagocytosis mediated by mononuclear cells and granulocytes. They bind to antibody-coated viruses through Fc receptors and complement activation by the classical route with the participation of IgM and IgG [19, 20]. Such complexes can also activate the complement system and lead to further undesirable inflammation [19, 20]. It

is known that many viral infections can cause not only specific antiviral protective immune responses, but also impair tolerance and induce autoimmune responses and diseases through various mechanisms, primarily molecular mimicry of antigens. Antibodies to Sars-CoV-2 virus, namely S-protein, cross-react with human antigens [21], leading to the development of autoimmune pathology. An increased expression and secretion of a number of autoantigens, which correlates with the severity of the disease, is observed during COVID-19 [22].

Binding of the antibody-virus immune complexes to the activating Fc receptors on alveolar macrophages and neutrophils may induce expression of pro-inflammatory factors that enhances the immunostimulatory response [23]. If macrophages, predominantly pro-inflammatory cytokines and proteolytic enzymes are expressed, then neutrophils are active oxygen radicals and the formation of NET. Creating too much or no disposal of NET is pathogenic and can lead to occlusion of small vessels. Many authors show that the formation of NET in the bloodstream mechanically disrupts blood circulation in tissues and organs and makes a significant contribution to tissue damage in acute diseases such as acute myocardial infarction, acute lung injury, etc. [24, 25]. Detection of antibodies may be relevant for the late stages of infection after elimination of virus, as it allows to determine the presence of protective immunity in persons who have been fallen ill or vaccinated, as well as to monitor the degree of spread of the virus and the presence of population immunity at the general level.

CONCLUSIONS

• Individuals who do not have antibodies to SARS-CoV-2 have no NA. Similarly, NA are absent in individuals with PI IgG <4.0, indicating that this level of antibodies is not protective.

• IgG as well as PN were higher in individuals who had just been diagnosed with Covid-19, have positive PCR at the beginning of the disease compared to those who had no clinical manifestations. There is a positive correlation between PI IgG and PN. IgM was positive in 27.5% of those examined in the first wave of the disease, in 41.4% in the second and in 72.8% in the third. Compared to individuals who did not have these antibodies, they had significantly higher PI IgG and PN.

• Depending on the presence of clinical signs of coronavirus infection, a different proportion of NA is detected. In persons without severe clinical sings of coronavirus infection moderately positive NA predominate. In the vast majority of patients, highly positive levels of NA are observed.

• The level of antibodies to SARS-CoV-2, as well as PN is probably increased with increased incidence during the year. With an increased incidence during the year, the share of NA changes. In persons without pronounced clinical signs of coronavirus infection, the proportion of highly positive NA (19.8 vs 37.5%) increased almost 2 times due to a decrease, in predominantly negative indicators (27.1 vs 8.8%). In relapsed patients, the proportion of highly positive NA also increased significantly (58.1 vs 72.7%), but due to the decrease in the proportion of moderately positive results (38.7 vs 15.2%).

The authors of this study confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations and/or individuals who may have been related to the study, and interrelations of co-authors of the article.

В.М. Корнацький[1], Н.О. Рижкова[1], Т.І. Гавриленко[1], А.М. Дорохіна[1], Ю.В. Корнацький[1], О.А. Підгайна[1], С.М. Бабій[2], О.М. Пасічніченко[2]

IgG, IgM ТА НЕЙТРАЛІЗУЮЧІ АНТИТІЛА ДО ВІРУСУ SARS-COV2 У МЕДПРАЦІВНИКІВ ДО ПОЧАТКУ МАСОВОЇ ВАКЦИНАЦІЇ

[1]ДУ Національний науковий центр «Інститут кардіології ім. академіка М.Д. Стражеска» Національної академії медичних наук України, Київ;
[2]Київський національний університет ім. Тараса Шевченка; e-mail: tala.ruzh@gmail.com

Метою роботи була оцінка вмісту імуноглобулінів (IgG, IgM) та нейтралізуючих антитіл до вірусу SARS-CoV2

у медичних працівників протягом року (2020-2021) до початку масової вакцинації залежно від наявності клінічних симптомів та позитивного ПЛР-тесту. Встановлено, що особи без антитіл до вірусу SARS-CoV2 не мають і нейтралізуючих антитіл. Вміст антитіл, так само як і відсоток нейтралізації, вірогідно підвищувався з наростанням захворюваності впродовж року та був вищим у осіб, які щойно перехворіли на Covid-19, мали позитивний ПЛР-тест на початку захворювання в порівнянні з тими, які не мали клінічних проявів. Спостерігалася позитивна кореляційна залежність між вмістом IgG та відсотком нейтралізації. В осіб без виражених клінічних ознак коронавірусної інфекції переважають помірно позитивні нейтралізуючі антитіла, тоді як у переважної більшості осіб, які перехворіли - високопозитивні.
Ключові слова: антитіла; коронавірус.

REFERENCES

1. Hofmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020; 181(2):271280. e8.
2. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature. 2020;581(7807):215-20.
3. Valdez-Cruz NA, García-Hernández E, Espitia C, Cobos-Marín L, Altamirano C, Bando-Campos CG, et al. Integrative overview of antibodies against SARS-CoV-2 and their possible applications in COVID-19 prophylaxis and treatment. Microb Cell Fact. 2021; 20:88.
4. Tay MZ, Poh CM, Rénia L, Paul A, MacAry PA, Ng LFP. The trinity of COVID-19: immunity, inflammation and intervention. Nature reviews. Immunology. 2020; 20(6):363-74.
5. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020 Mar;579(7798):270-3.
6. Chen X, Li R, Pan Z, Qian C, Yang Y, You R, et al. Human monoclonal antibodies block the binding of SARS-CoV-2 spike protein to angiotensin converting enzyme 2 receptor. Cell Mol Immunol. 2020;17(6):647-9.
7. Zinkernagel RM, LaMarre A, Ciurea A, Hunziker L, Ochsenbein AF, McCoy KD, et al. Neutralizing antiviral antibody responses. Adv Immunol. 2001;79:1-53.
8. Liu G, Rusling JF. COVID-19 Antibody Tests and Their Limitations ACS Sensors Cite This: https://dx.doi.org/10.1021/acssensors.0c02621.
9. Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Spijker R, Taylor-Phillips S, et al. Antibody tests for identification of current and past infection with SARS-CoV-2 (Review). Cochrane COVID-19 Diagnostic Test Accuracy Group. 2020.
10. Long QX, Liu BZ, Deng HJ, Wu CG, Deng K, Chen YK, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med. 2020;26(6):845-8.
11. Valdivia A, Torres I, Latorre V, Francés-Gómez C, Albert E, Gozalbo-Rovira R, et al. Inference of SARS-CoV-2 spike-binding neutralizing antibody titers in sera from hospitalized COVID-19 patients by using commercial enzyme and chemiluminescent immunoassays. Eur J Clin Microbiol Infect Dis. https://doi.org/10.1007/s10096-020-04128-8.
12. Isho B, Abe KT, Zuo M, Jamal AJ, Rathod B, Wang JH, et al. Persistence of serum and saliva antibody responses to SARS-CoV-2 spike antigens in COVID-19 patients. Sci. Immunol. 2020;5,eabe5511.
13. Fourati S, Hue S, Pawlotsky JM, Mekontso-Dessap A, de Prost N. SARSCoV-2 viral loads and serum IgA/IgG immune responses in critically ill COVID-19 patients. Intens Care Med. 2020;46(9):1781-3.
14. Peiris JS, Chu CM, Cheng VCC, Chan KS, Hung IFN, Poon LLM, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet. 2003;361:1767-72.
15. Zhang L, Zhang F, Yu W, He T, Yu J, Yi CE, et al. Antibody responses against SARS coronavirus are correlated with disease outcome of infected individuals. J Med Virol. 2006;78:1-8.
16. Arabi YM, Hajeer AH, Luke Th, Raviprakash K, Balkhy H, Johani S, et al. Feasibility of using convalescent plasma immunotherapy for MERS-CoV infection. Saudi Arabia Emerg Infect Dis. 2016;22:1554.
17. Drosten C, Meyer B, Müller MA, Corman VM, Al-Masri M, Hossain R, et al. Transmission of MERS-coronavirus in household contacts. N Engl J Med. 2014;371:828-35.
18. Park WB, Perera R, Choe PG, Lau E, Choi SJ, Chun JY, et al. Kinetics of serologic responses to MERS coronavirus infection in humans. South Korea Emerg Infect Dis. 2015;21:2186-9.
19. Lu LL, Suscovich TJ, Fortune SM, Alter G. Beyond binding: antibody efector functions in infectious diseases. Nat Rev Immunol. 2018;18:46.
20. Zohar T, Alter G. Dissecting antibody-mediated protection against SARS-CoV-2. Nat Rev Immunol. 2020; 20:392-4.
21. Kanduc D. From Anti-SARS-CoV-2 Immune responses to COVID-19 via molecular mimicry. Antibodies. 2020;9(3):33.
22. Lisyany NI. Covid-19 infection and autoimmune reactions. Fisiol Zh. 2022;68(1):87-92. [Ukrainian].
23. Nimmerjahn F, Ravetch JV. Fcgamma receptors as regulators of immune responses. Nat Rev Immunol. 2008;8:34-47.
24. Gavrilenko TI, Ryzhkova NO, Parkhomenko OM, Dovgan OV, Dovgan NV, Pasichnichenko OM, Babiy SM. Modern views on the role of neutrophils in the immune response. Fisiol Zh. 2021;67(3):75-86. [Ukrainian].
25. Reusch N, De Domenico E, Bonaguro L, Schulte-Schrepping J, Baßler K, Schultze JL and Aschenbrenner AC Neutrophils in COVID-19. Front Immunol. 2021; 12:652470.

Received 03.02.2022