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THE PROFILE OF SPECIFIC ANTIBODIES TO SARS-COV-2 IN RESIDENTS OF THE CENTRAL AND EASTERN REGIONS OF UKRAINE

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Determination of the level of antibodies in individuals living in certain regions provides insight into the epidemiology of the infection and is crucial for the development of strategies to reduce the spread of COVID-19. The study analyzed the results of IgM and IgG tests for the SARS-CoV-2 virus in 7142 residents of eastern and central regions of Ukraine from July 2020 to January 2021. Patients' visits to COVID-19 for IgM and IgG mainly occurred in the autumn-winter period of 2020–2021, confirming the seasonality of the disease. The most popular test among residents of Poltava and Donetsk regions was the test for IgM immunoglobulins, and the vast majority of results were negative. As of January 2021, the number of people who had IgG antibodies to the pathogen COVID-19, among those surveyed approached 50 % in both Poltava and Donetsk regions.

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

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ПРОФІЛЬ СПЕЦИФІЧНИХ АНТИТІЛ ДО SARS-COV-2 У ЖИТЕЛІВ ЦЕНТРАЛЬНОГО ТА СХІДНОГО РЕГІОНІВ УКРАЇНИ

Визначення рівня антитіл у осіб, які проживають у певних регіонах, дає уявлення про епідеміологію інфекції та має вирішальне значення для розробки стратегій зниження поширення COVID-19. У дослідженні проаналізовано результати досліджень IgM та IgG до вірусу SARS-CoV-2 у 7142 жителів східного та центрального регіонів України з липня 2020 року по січень 2021 року. Звернення пацієнтів щодо визначення IgM та IgG до збудника COVID-19 переважно відбувалися в осінньо-зимовий період 2020–2021 років, що підтверджує сезонність захворювання. Найпопулярнішим тестом серед мешканців Полтавської та Донецької областей був тест на імуноглобуліни IgM, і переважна більшість результатів була негативною. Станом на січень 2021 року кількість людей, які мали антитіла IgG до збудника COVID-19, серед досліджених, наблизилася до 50 % як у Полтавській, так і в Донецькій областях.

Ключові слова: COVID-19, SARS-CoV-2, антитіла, IgM, IgG.

The study is a fragment of the research project “Study of the role of opportunistic and pathogenic infectious agents with different sensitivity to antimicrobial and antiviral drugs in human pathology”, No 0118U004456.

At the end of 2019, an emerging coronavirus infection caused by the SARS-CoV-2 virus emerged and began to spread around the world in China. Already in early 2020, COVID-19 was recognized as a global priority problem of the global health care system. On 19 January in 2022, 335 521 830 cases of COVID-19 coronavirus disease have been confirmed worldwide; 5 574 726 people have died [7].

In Ukraine, coronavirus infection COVID-19 was firstly diagnosed on March 3, 2020, in Chernivtsi. As of January 19, 2022, in Ukraine COVID-19 was diagnosed in 3 780 903 people (9.2 % of the population). However, the spread of new coronavirus infection, morbidity and mortality, the level of specific immune protection in different regions of Ukraine differed throughout the pandemic period. In particular, the analysis of epidemiological indicators in the Poltava region, which represents the central (mostly agrarian) region of Ukraine, showed that on January 19, 2022, 145 073 people fell ill on its territory (10.69 % of the region's population). The Donetsk region, which is an example of the eastern region (mostly industrialized), was identified in 171 582 cases (4.22 % of the region population) [3].

Given the rapid spread of this infection, the danger to human health and significant socio-economic consequences, diagnosis, the pathogenesis of the disease, the nature and duration of the body's immune response to the pathogen, the development of specific prevention methods have gained international

importance. With increasing awareness of the new coronavirus infection, the approaches to the detection of the disease have partially changed. Under such conditions, the advantage of IgM and IgG detection methods in patients with suspected COVID-19 is their greater availability, simplicity while maintaining high sensitivity [9]. Therefore, the determination of specific immunoglobulins to SARS-CoV-2 antigens has become widespread among the diagnostic directions of the new coronavirus disease. High efficiency of serological methods of investigation in the diagnosis of coronavirus infection has also been shown in Ukraine [1, 2].

In response to infection with SARS-CoV-2, the body produces anticoronavirus antibodies, the intensity of formation of which correlates with the activity of the infectious process [6, 12]. The study of the regional peculiarities of the immune response to the pathogen, distributed in different countries of the world, is of considerable scientific interest. Determination of the level of specific humoral immunity in individuals living in certain regions provides insight into the epidemiology of the infection, the immune protection of the population of these territories and is crucial for the development of strategies to reduce the spread of COVID-19 [12]. It still remains uncertain whether the level of humoral immunity to SARS-CoV-2 depends on the region of Ukraine and the age of those examined.

The purpose of the study was to determine the profile of IgM and IgG class immunoglobulins to the SARS-CoV-2 virus in residents of the central and eastern regions of Ukraine.

Materials and methods. The study analyzed the results of IgM and IgG class immunoglobulin tests for the SARS-CoV-2 virus in 7142 residents of the eastern and central regions of Ukraine from July 2020 to January 2021. Among them are 2841 results obtained by testing residents of Poltava and surrounding villages, 1307 results obtained by testing residents of Pokrovsk, 1160 by residents of Dobropillia, 445 by residents of Bahmut, 419 by residents of Selidovo, 396 by residents of Kramatorsk, 394 by residents of Avdiivka and 180 by residents of Sloviansk (Donetsk region).

Patients were tested by enzyme immunoassay using EQUISARS-CoV-2 IgM and IgG kits for the quantitative determination of IgM and IgG antibodies to SARS-CoV-2 virus (EKVITEST-LAB LLC, Ukraine). The results were evaluated by determining the sample positivity index (PI), with a value greater than 1.1, the result was considered positive [14].

The study was carried out after the patient signed an informed consent in accordance with the Declaration of Helsinki of the World Medical Association "Ethical Principles of Medical Research Involving Human Subjects". Research results were provided by a certified private laboratory in Zaporizhzhya, preserving the confidentiality of the personal data of patients.

To determine the epidemiological indicators, the results of patient studies were divided by class of immunoglobulins determined by patients and by place of residence for residents of the region with a large share in gross agricultural output (Poltava and surrounding villages) and regions with high industrial development area).

The obtained data were subjected to statistical processing using the standard program SPSS 16.0 software (IBM, Armonk, NY, USA) and expressed as the arithmetic mean (M) and the arithmetic mean error ($\pm m$). The presence of differences between the indicators of the studied groups of patients was assessed by Student's t-test. The results were considered reliable at p values $p < 0.05$.

Results of the study and their discussion. Analyzing the results of patients who applied to the laboratory for detection of antibodies to the SARS-CoV-2 virus in July 2020–January 2021, it was found that on average women were tested more frequently than men. The gender ratio in Poltava and Donetsk oblasts was 0.75:1 and 0.84:1, respectively (table 1). The mean age of those examined ranged from 24 to 71 years, with an average of 60 ± 11.0 years for residents of Poltava and nearby villages and 47.7 ± 10.0 years for residents of towns in Donetsk Oblast.

Table 1

Demographic indices of patients

Index Town	Number of respondents	Average age, $M \pm m$	Males/females, n
Poltava	2841	60 ± 11.0	1220/1621
Kramatorsk	396	41 ± 5.0	165/231
Dobropillia	1160	45 ± 7.0	512/648
Pokrovsk	1307	47 ± 10.0	655/652
Bahmut	445	53 ± 10.0	180/265
Selidovo	419	50 ± 8.0	193/226
Sloviansk	180	50 ± 6.0	75/105
Avdiivka	394	48 ± 11.0	183/211

During this period, residents of the Poltava region applied for determination of total antibodies (IgM, IgG) to the causative agent of coronavirus disease only 6 times, and all the results were negative (fig.1).

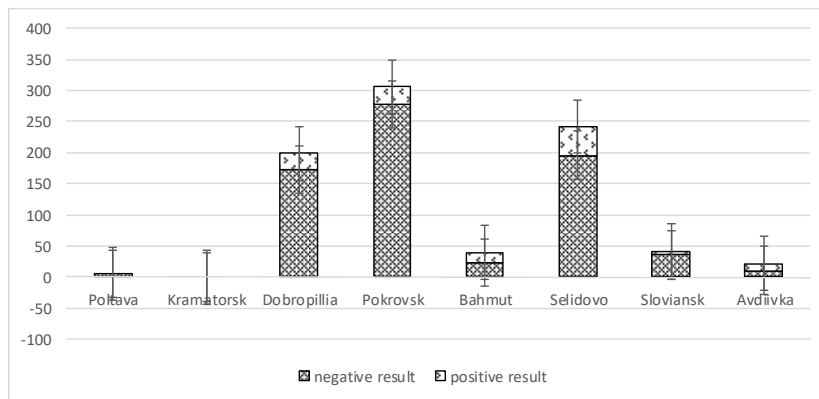


Fig.1. Number of studies on the detection of total antibodies of IgM, IgG to SARS-CoV-2 virus

IgG to SARS-CoV-2 virus. The percentage of positive tests ranged from 14.4 % (abs. 122) of the total. It should be noted that among the 122 positive results for the detection of total antibodies of IgM, IgG to SARS-CoV-2 virus, their maximum titer reached 138.8 IP.

It turned out to be quite natural that patients from both regions most often went to the laboratory to detect IgM for the SARS-CoV-2 virus as an early indicator of morbidity. In general, 72.8 % (abs. 5196) of tests for antibodies in the studied cities during the summer of 2020 – winter of 2021 accounted for the detection of immunoglobulins of the IgM class (fig. 2).

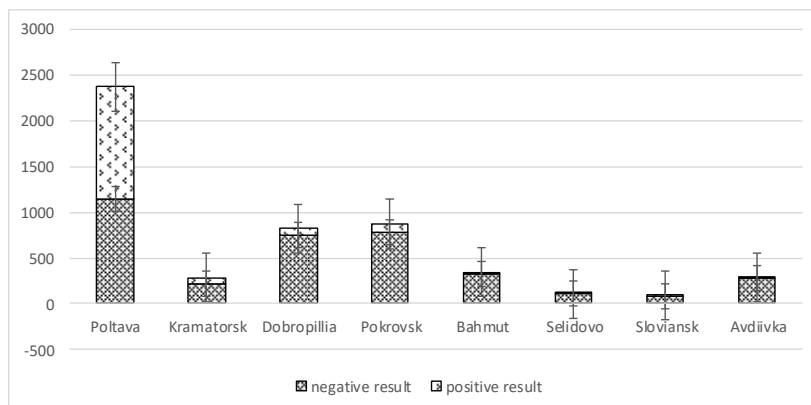


Fig.2. Number of studies on the detection of IgM antibodies to SARS-CoV-2 virus

requests for detection of IgM to the causative agent of coronavirus disease in the Donetsk region were recorded in the autumn-winter period. We revealed only 25 cases of tests for detection of IgM class antibodies in summer 2020 among inhabitants of 7 cities in Donbas.

Along with this, patients of the Poltava region applied for detection of these immunoglobulins in the summer and autumn-winter period to the same extent. Thus, during the summer months of 2020, residents of Poltava and neighbouring villages contacted the laboratory for detection of SARS-CoV-2 IgM

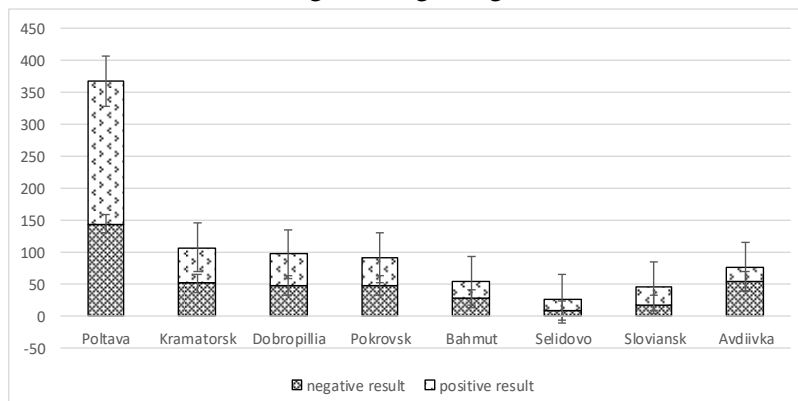


Fig.3. Number of studies on the detection of IgG antibodies to SARS-CoV-2 virus

This test was more common among patients in the Donetsk region, especially in the autumn-winter period. Thus, among 850 appeals to determine the total antibodies, only 32 (3.8 %) cases occurred in the summer months.

Moreover, it was found that the number of negative results in all cities of the Donetsk region significantly exceeded the number of results of people with detected IgM,

However, analyzing the data on detection of this type of antibodies among residents of the Poltava region and cities of Donetsk region, a significantly higher frequency of positive results among patients from Poltava city and nearby villages (46.8 %) was established. This indicator among the residents of the Donetsk region was 5 times lower and amounted to 9.3 % of 2821 studies. It should be noted that the vast majority of patients'

requests for detection of IgM to the causative agent of coronavirus disease in the Donetsk region were recorded in the autumn-winter period. We revealed only 25 cases of tests for detection of IgM class antibodies in summer 2020 among inhabitants of 7 cities in Donbas. Along with this, patients of the Poltava region applied for detection of these immunoglobulins in the summer and autumn-winter period to the same extent. Thus, during the summer months of 2020, residents of Poltava and neighbouring villages contacted the laboratory for detection of SARS-CoV-2 IgM 977 times, representing 41.1 % of the total number of visits. Moreover, the vast majority of the results obtained in the summer were negative between both residents of Poltava and Donetsk.

IgG immunoglobulins to SARS-CoV-2 virus were determined in serum by patients in towns/cities in both Poltava and Donetsk region 5 times less frequently compared to determination of IgM antibodies (fig. 3).

Analyzing the results of this study, seasonality similar to the determination of total antibodies and IgM antibodies are observed: in Poltava and surrounding villages did not identify a single request for IgG testing for coronavirus in summer, and among 499 studies in Donetsk only 10 patients (2.0 %) applied in July-August 2020.

However, the frequency of positive results in the case of SARS-CoV-2 IgG determination was quite high and maintained a similar trend regardless of the location of the settlement. Thus, 223 results (47.6 %) out of 468 tests for this class of immunoglobulins in Poltava and neighbouring villages were positive. In turn, 246 patients (49.3 %) out of 499 who tested positive for IgG to SARS-CoV-2 in the Donetsk region tested positive for this class of antibodies. In other words, as of January 2021, the number of individuals who had IgG antibodies to the pathogen COVID-19 among those examined was close to 50 % in both Poltava and Donetsk oblasts/regions.

Despite the wide range of laboratory diagnostic methods for SARS-CoV-2 that have recently appeared in the world, the determination of antibody levels by ELISA has the greatest importance. Of course, genetic methods are highly sensitive and accurate, but at the beginning of the pandemic, there were some limitations in accessing them. Today, the cost of one PCR study remains high for residents of different regions of Ukraine. This creates the preconditions for wider use of ELISA as a method of choice in the diagnosis of coronavirus disease.

Given the frequency of positive results of a specific humoral response to COVID-19 in patients in both Poltava and Donetsk regions during the autumn-winter period and only isolated cases in the summer, epidemiological data on the seasonality of coronavirus infection were confirmed. After all, the epidemiology of airborne infections, which include coronavirus disease, depends on environmental factors. Such infections are seasonal in nature with a higher incidence in the autumn-winter period due to the inverse relationship between rising air temperatures and the spread of the virus [5]. In addition, it should be noted that after the strong wave of COVID-19 in March 2020, during the summer months there was a decline in morbidity in the world and the weakening of anti-epidemic measures. Strictly speaking, this also explained the decrease in patient requests for antibodies to the pathogen [11, 13]. The data we obtained correlate with data on the level of testing for COVID-19 in Europe with a significant reduction in the number of patient visits per thousand people by 3.5 times from May to the end of October 2020 [15].

It is known that IgM and IgG antibodies are diagnostic for all airborne infections, the presence of which is used to assess the presence and stages of the disease. Usually, early signs of the disease are the detection of high titers of IgM immunoglobulins, followed by an increase in IgG levels. However, scientists have found that in diseases caused by the SARS-CoV-2 virus, the early stage of infection is characterized by an increase in immunoglobulins of the IgG class, not IgM, or their simultaneous appearance. Therefore, the results obtained during the study showed a significantly lower number of detections of IgM antibodies compared to the detection of IgG in patients of the Poltava and Donetsk region [8, 12].

At the beginning of the SARS-CoV-2 virus pandemic, children were thought to be free of COVID-19 because they did not have to target angiotensin-converting receptors for the virus itself. However, our observation confirmed the data of meta-analysis and research of domestic infectious disease specialists and immunologists, according to the statistics of which infection and morbidity of children occurs according to the same epidemiological patterns as in adults [4, 10]. The only difference is the specifics of the clinical course, depending on the age of the child. The low level of requests for examination of children in the country's diagnostic laboratories is due to the high percentage of subclinical events and the lack of awareness of doctors in the first and second waves of the pandemic.

Conclusions

In Poltava and surrounding villages, as well as in the cities/towns of the Donetsk region, women are more likely than men to be tested for antibodies to the SARS-CoV-2 virus.

Patients' visits to COVID-19 for IgM and IgG mainly occurred in the autumn-winter period of 2020–2021, confirming the seasonality of the disease.

The most popular test among residents of Poltava and Donetsk regions is the test for IgM immunoglobulins, and the vast majority of results were negative.

As of January 2021, the number of people who had IgG antibodies to the pathogen COVID-19, among those surveyed approached 50 % in both Poltava and Donetsk regions.

Prospects for further research. The formation of population immunity is the key to successful and rapid overcoming of the pandemic. Therefore, further continuous monitoring of the situation regarding the detection of antibodies to the pathogen COVID-19 among the population of different regions of Ukraine at different intervals is promising.

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