Features of the population immunity to SARS-CoV-2 development in staff members of medical organizations during the spread of COVID-19

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Abstract

Background. The ongoing COVID-19 pandemic generates the urgent need of monitoring the herd immunity among healthcare workers as a high-risk group for infection.

Aim. Determining the level and structure of population immunity to SARS-CoV-2 in the medical workers during the second peak of COVID-19 from August to November 2020.

Material and methods. The study involved 15,158 medical workers from 91 medical organizations of the Republic of Tatarstan. The age of the examined stuff members varied from 18 to 74 years, the average age was 45.48±0.1016 years, most of them were women (13 627, 89.87±0.258%). Testing for the presence of total antibodies (immunoglobulin classes G, A and M) to SARS- CoV-2 was performed once by the enhanced chemiluminescence method. Statistical processing was carried out by methods of variation statistics and correlation analysis according to the Pearson method using MS Excel and WinPepi.

Results. Seroprevalence to SARS-CoV-2 in medical workers was 35.23±0.388%. An increase in seropositive individuals level from 27.44±0.265% in August to 57.91±0.499% in November and an increase in the average geometric mean titer of total antibodies (immunoglobulin classes A, M, G) from 84.43 in August to 101.09 in November 2020 were detected. The level of individuals with antibodies increased with age from 18 to 59 years and decreased in group of 60–70 years. The largest proportion of seropositive to SARS-CoV-2 individuals was found among junior (42.01±1.384%) and middle grade (37.5±0.527%) medical staff of hospitals for patients with COVID-19, ambulance and emergency stations. Among the seropositive to the SARS-CoV-2 workers the proportion of asymptomatic forms of infection was 84.97±0.498%. According to the level of seroprevalence, municipal districts of the Republic of Tatarstan were divided into three groups: moderate — 8.9–39.0; average — 42.9–49.6, high level — 53.1–64.4.

Conclusion. An increase in seroprevalence to SARS-CoV-2 was revealed among medical workers of the Republic of Tatarstan from August to November 2020 during the second peak of COVID-19.

Keywords: COVID-19, seroprevalence, medical workers, Republic of Tatarstan.

Background

From the first days of the outbreak of the novel coronavirus infection COVID-19 in China, there have been reports of cases of nosocomial infection with SARS-CoV-2, including among medical wor- kers (MW) [1, 2]. A high incidence among MWs was registered in Italy during the COVID-19 epi- demic in April and May 2020 [3]. Studies of the humoral immunity level to the SARS-CoV-2 virus among MWs, who are much more likely to encoun-

ter the virus than the average population, are few, contradictory, and of particular importance.

According to Chinese colleagues, cases of COVID-19 in MWs have made a significant contribution to the incidence rate. In 422 medical institutions, since the start of the epidemic, as of February 11, 2020, 1,716 laboratory-confirmed cases had been detected among MWs (5 of them fatal), namely in 64.0% Wuhan, 23.3% in Hubei province, and 12.7% in other provinces of China [4]. According to researchers from the People's Republic of China, when 19,555 MWs were examined, specific immunoglobulins (Ig) class G to SARS-CoV-2 were detected in only 4.0% [5].

Data from a study of the immunity level to the SARS-CoV-2 virus in MWs in one of the hospitals in Milan (Italy) in early April 2020 showed that IgG antibodies were detected in 7.4% of those examined, and IgM antibodies were detected in 14.4% of cases [6]. When assessing the prevalence of a new coronavirus infection, many researchers use the term "seroprevalence" (that is, the proportion of people in a population who have developed antibodies to the virus).

The seroprevalence among healthcare workers in the Russian Federation in wave 1 of the epidemic can be determined from the results of a large-scale project of the Russian Federal State Agency for Health and Consumer Rights (Rospotrebnadzor) to study population immunity to the SARS-CoV-2 virus in the population of the Russian Federation: this figure was 27.1% in St. Petersburg [7], 18.1% in the Leningrad Region [8], 11.6% in the Saratov Region [9], 16.1% in the Tyumen Region [10], and 18.9% in the Khabarovsk Territory [11].

The ongoing COVID-19 pandemic necessitates new seroepidemiological information [12]. It is relevant to monitor the dynamics of seroprevalence to assess the level of community immunity to the new coronavirus infection COVID-19 among MWs as a group at high risk of infection, and testing for antibodies to SARS-CoV-2 among various categories of MWs is necessary. Such studies are required in order to identify the frequency of COVID-19 spread in healthcare facilities, as well as asymptomatic forms of the disease, and to establish previous infection [12].

During the resurgence of COVID-19, the Ministry of Health of the Republic of Tatarstan initiated large-scale serological monitoring for SARS-CoV-2 among healthcare workers.

Aim

The study aimed to determine the level and structure of population immunity to SARS-CoV-2 among medical personnel of the Republic of Tatarstan in the period from August to November 2020.

Materials and methods

Monitoring was performed according to the protocol recommended by the World Health Organization and used in the Rospotrebnadzor project to assess population immunity to the SARS-CoV-2 virus in the population of the Russian Federation [13, 14]. The study was approved by the local ethics committee of the Kazan Research Institute of Epidemiology and Microbiology of Rospotrebnadzor (protocol No. 2 of 08/26/2020).

The questionnaire used in the study included sections on passport data, including place of work, and position; clinical data, including the presence of symptoms of acute respiratory disease on the day of examination, the results of polymerase chain reaction (PCR) testing for SARS-CoV-2; data on the diagnosis of COVID-19, including, for patients with a confirmed diagnosis of COVID-19, the date of onset of symptoms of acute respiratory disease and the method of testing for COVID-19 (PCR or enzyme immunoassay); the presence of chronic diseases; and epidemiological history (presumed place of infection with COVID-19, contacts with COVID-19 patients in the family or at work, and departure from the country or to other regions of the Russian Federation in the last 3 months).

The study participants were selected by the method of random number generation. The exclusion criterion was active COVID-19 infection at the time of the survey. The study included MWs without and with a history of a new coronavirus infection according to the patient registry, who had laboratory confirmation (U07.1) or a diagnosis established by computed tomography (U07.2), and who did not have documented evidence of disease history, including those who had recovered from an acute respiratory viral infection (ARVI) in the autumn and spring of 2020.

In all, 15,158 MWs from 91 medical institutions of the Republic of Tatarstan took part in the study. The age of the MWs examined varied from 18 to 74 years, with an average age of 45.5 ± 0.1 years. Overall, 73.2 ± 0.4% MWs were aged 30–59 years. In the cohorts examined, women predominated (13,627 people, 89.9 ± 0.3%).

Blood sampling from each MW of the Republic of Tatarstan was performed once from August 24 to November 30, 2020. Tests were performed for the presence of total antibodies (IgG, IgA, and IgM) to the SARS-CoV-2 coronavirus using the enhanced chemiluminescence method on a VITROS 3600 analyzer using VITROS Anti-SARS-CoV-2 Total Reagent Pack test systems in the laboratories

Table 1. SARS-CoV-2 seroprevalence of medical workers of different age groups in the Republic of Tatarstan in the period from August to November 2020.

Age group, years	Positive for IgA, IgM, and IgG to SARS-CoV-2	Negative for IgA, IgM, and IgG to SARS-CoV-2	Seroprevalence, % (M ± m)
18–19	10	19	34.5 ± 8.83
20–29	670	1258	34.8 ± 1.08
30–39	1048	1951	34.9 ± 0.87
40–49	1381	2610	34.6 ± 0.75
50–59	1553	2560	37.8 ± 0.76
60–69	603	1264	32.3 ± 1.08
70+	75	156	32.5 ± 3.08
Total	5340	9818	35.2 ± 0.39

Note: Ig, immunoglobulin.

of the City Clinical Hospital No. 7 (2664 patients) and the Republican Clinical Infectious Diseases Hospital (12,494 patients).

To determine the proportion of asymptomatic patients among those seropositive for antibodies to SARS-CoV-2, we followed the methodology that was used as part of a large-scale Rospotrebnadzor project to study aspects of the formation of seroprevalence in the population of the Russian Federation [14]. Among seropositive patients, we determined the proportion of people who did not have at least one sign, namely a diagnosis of COVID-19 or a positive PCR result, or symptoms of ARVI.

Statistical processing was performed using the methods of variation statistics with the Excel statistical package and the WinPepi software product (version 11.65). To assess the significance of differences between the compared indicators, the probability level $p \leq 0.05$ was used. Correlation analysis was performed according to the Pearson method.

Results

The SARS-CoV-2 seroprevalence in all age groups from 18 to 49 years was not significantly different, in the range of 34.4%–34.9%, and tended to increase (increase rate 1.813%) as age increased from 18 to 59 years, followed by a decrease (decrease rate 7.741) in the 60–70 years age group. The highest seroprevalence was noted at the age of 50–59 years, significantly ($p < 0.05$) exceeding the seroprevalence in groups aged 20–29 years, 30–39 years, 40–49 years, and 60–69 years (Table 1).

Gender-based differences in seropositivity were established; the proportion of seropositive patients was significantly higher among women (4849 people, 35.6 ± 0.41%) than among men (491 people, 32.0 ± 1.19%) ($p = 0.0047$).

The SARS-CoV-2 seroprevalence among MWs in various medical institutions of the Republic
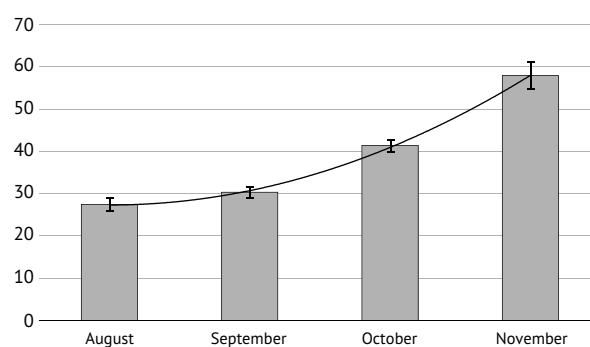

Fig. 1. Dynamics of seroprevalence from August to November 2020 among employees of municipal medical institutions of the Republic of Tatarstan; seroprevalence (%) is along the ordinate, and months are along the abscissa.

of Tatarstan over the period analyzed averaged 35.23 ± 0.39%. There was a statistically significant increase in the proportion of seropositive individuals from 27.4 ± 0.26% in August to 30.3% in September ($p < 0.01$), 41.4% in October ($p < 0.001$), and 57.9 ± 0.49% in November ($p < 0.001$), as well as a significant increase in the geometric mean titer of total antibodies (IgA, M, and G) from 84.43 in August, to 97.57 in September, 94.57 in October, and 101.09 in November 2020 ($p < 0.001$ in all compared groups) (Fig. 1, 2).

Correlation analysis showed an average (moderate) direct correlation between seroprevalence (%) and immunity level (geometric mean antibody titer) (0.523, $p < 0.01$) (Fig. 3).

An increase in the level of seropositivity among MWs and an increase in the geometric mean titer of total antibodies indicate the formation of both individual immunity to the SARS-CoV-2 coronavirus and community immunity in the studied population.

The increase in the proportion of seropositive individuals and the geometric mean antibody titer occurred along with an increase in the incidence of COVID-19 in the Republic of Tatarstan (899 cases

Table 2. The level of seroprevalence among various categories of medical workers in the Republic of Tatarstan from August to November 2020.

Professional group	Positive for IgA, IgM, and IgG to SARS-CoV-2	Negative for IgA, IgM, and IgG to SARS-CoV-2	Proportion of seropositive patients, %
Doctors	949	2165	30.5 ± 0.83
Nursing staff	3166	5276	37.5 ± 0.53
Junior medical staff	534	737	42.0 ± 1.38
Managers	14	29	32.6 ± 7.15
Others	677	1611	29.6 ± 0.95
Total examined	5340	9818	35.2 ± 0.39

Note: Ig, immunoglobulin.
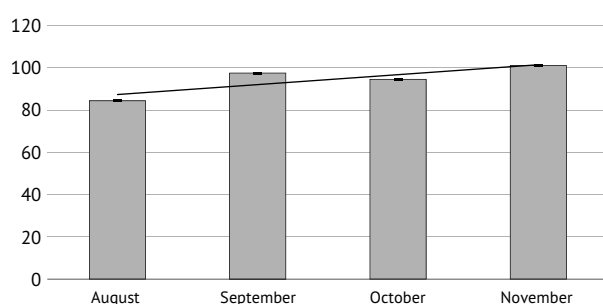
Fig. 2. Dynamics of the geometric mean antibody titer from August to November 2020 among seropositive employees of municipal medical institutions of the Republic of Tatarstan; geometric mean antibody titer is along the ordinate, and months are along the abscissa.
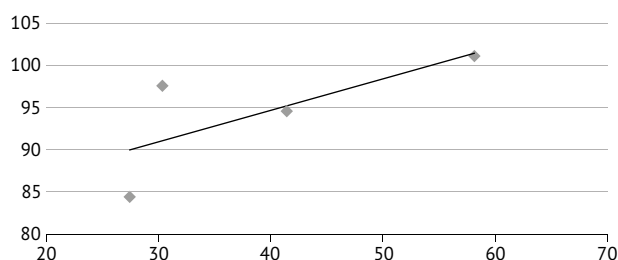
Fig. 3. Correlation between seroprevalence and immunity level to SARS-CoV-2 in employees of municipal medical institutions of the Republic of Tatarstan (Pearson's method); geometric mean antibody titer is along the ordinate, and seroprevalence (%) is along the abscissa.

in August, 721 cases in September, 1222 cases in October, 2008 cases in November, and 2950 cases in December) [15].

The regions of the Republic of Tatarstan were divided into three groups according to the significance of differences in MW seroprevalence (moderate, average, and high levels) (Fig. 4).

The seroprevalence was moderate (8.9–39.0) in the Agryz, Bavly, Leninogorsk, Aksubaevo, Aznakaevo, Chistopol, Buinsk, and Tetyushy districts, as well as in the Kazan, Drozhzhanoye, Baltasy, Menzelinsk, Nizhnekamsk, Almetyevsk, Zelenodolsk, Pestretsy, Kukmor, Atnya, Saby, and Laishevo districts. *The seroprevalence was average* (42.9–

49.6) in Bugulma, Sarmanovo, Nurlat, Kamskoye Ustye, Yutaza, and Cheremshan districts. *The seroprevalence was high* (53.1–64.4) in the Tukaevsky, Naberezhnye Chelny, Muslyumovo, and Arsk districts. The observed differences may be attributed to inequalities in the course epidemic progression across regions of the Republic of Tatarstan.

The highest levels of SARS-CoV-2 seropositivity were registered among junior medical (42.01 ± 1.38) and nursing (37.5 ± 0.53) personnel, and they were significantly higher than those among doctors ($p < 0.001$) and other MW categories ($p < 0.001$) (Table 2).

The largest proportion of patients seropositive for antibodies to SARS-CoV-2 was detected among the medical staff in hospitals dedicated to COVID-19 patients. MWs in ambulance and emergency care stations ranked second, and MWs in non-infectious hospitals and outpatient and polyclinic institutions ranked third. The lowest seroprevalence rates were detected among MWs in infectious hospitals; this may have been due to greater precautions taken by MWs in infectious diseases hospitals (Table 3).

Among MWs seropositive for antibodies to the SARS-CoV-2 virus in the Republic of Tatarstan during the study period, the proportion of asymptomatic forms of infection was 84.97 ± 0.5% and was significantly higher in MWs aged 20–29 and 30–39 years than in those aged 40–49 years ($p < 0.05$), 50–59 years ($p < 0.001$), 60–69 years ($p < 0.001$), and 70 years and older ($p < 0.05$). In the 40–49 years age group, the proportion of asymptomatic forms of COVID-19 was significantly higher than in the groups aged 50–59 and 60–69 years ($p < 0.05$). An almost linear, inverse relationship was revealed between age and the proportion of people with asymptomatic forms of COVID-19 ($p < 0.05$) (Fig. 5).

The group of MWs who indicated the presence of any clinical symptoms of COVID-19 included 868 people (16.3%). The proportion of seronegative persons among MWs with a history of COVID-19

Table 3. Seroprevalence among medical workers in various types of medical institutions of the Republic of Tatarstan from August to November 2020.

Type of medical institution	Positive for IgA, IgM, and IgG to SARS-CoV-2	Negative for IgA, IgM, and IgG to SARS-CoV-2	Proportion of seropositive patients, %
Non-infectious hospitals	4200	8255	33.7 ± 0.42
Infectious hospitals	20	81	19.8 ± 3.97
COVID-19 hospitals	522	490	51.6 ± 1.57
Ambulance stations	329	396	45.4 ± 1.84
Outpatient and polyclinic institution	271	599	31.2 ± 1.57
Total	5342	9821	35.2 ± 0.39

Note: Ig, immunoglobulin.
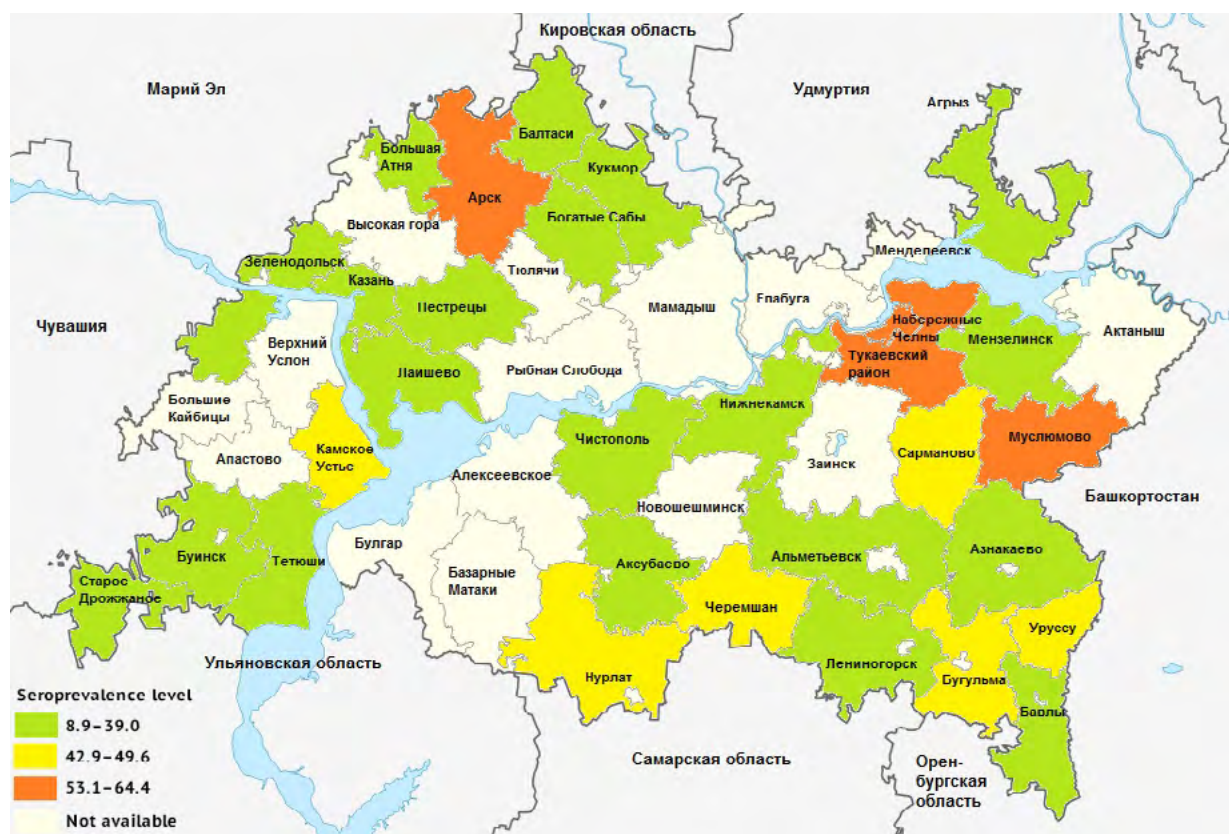
Fig. 4. SARS-CoV-2 seroprevalence in medical workers in municipal districts of the Republic of Tatarstan from August to November 2020.

was significantly lower in the 60–69-year and 50–59-year age groups compared with the groups 18–29 years and 30–39 years old ($p < 0.05$; Table 4).

Among MWs who had recovered from COVID-19, antibodies in blood plasma were detected in 775 out of 868 people (89.3 ± 1.05%). The number of seronegative patients in the cohort of MWs with a history of COVID-19 amounted to 93 out of 868 people (10.7 ± 3.2%).

Discussion

The study results showed that the seroprevalence of antibodies to SARS-CoV-2 among MWs of various medical institutions in the Republic of Tatarstan over the analyzed period from August to November 2020 averaged 35.2 ± 0.4%. There was an increase in the proportion of seropositive individuals from 27.4 ± 0.3% in August to 57.9 ± 0.5% in November and an increase in the geometric mean titer of total antibodies (IgA, M, and G) from 84.43 in August to 101.09 in November 2020, which took place in the context of an increase in the intensity of the epidemic process and an increase in the incidence of new coronavirus infections in the Republic of Tatarstan from 899 cases in August to 2950 in December 2020.

Correlation analysis showed the presence of an average (moderate) direct correlation between seroprevalence and the geometric mean antibody titer.

Table 4. Proportion of seronegative individuals among medical workers with a history of COVID-19 in the Republic of Tatarstan from August to November 2020.

Age group, years	Positive for IgA, IgM, and IgG to SARS-CoV-2	Negative for IgA, IgM, and IgG to SARS-CoV-2	Proportion of seropositive patients, %
18–29	71	12	14.5 ± 1.45
30–39	114	20	14.9 ± 1.19
40–49	189	21	10 ± 2.07
50–59	279	30	9.7 ± 1.68
60–69	106	8	7 ± 2.39
70+	16	2	11.1 ± 7.40
Total	775	93	10.7 ± 1.05

Note: Ig, immunoglobulin.
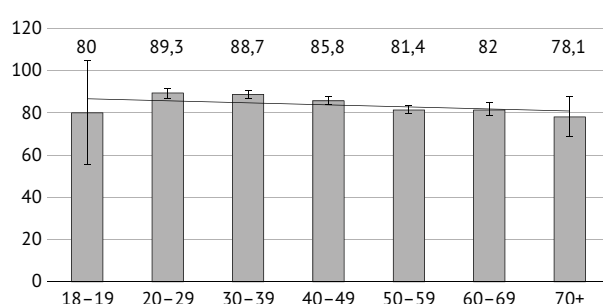
Fig. 5. The proportion of people with asymptomatic forms out of the total number of medical workers seropositive for SARS-CoV-2 in medical institutions in the Republic of Tatarstan from August to November 2020; the proportion of people with asymptomatic forms of all seropositive patients (%) is along the ordinate, and age (years) is along the abscissa.

An increase in individual antibody titers indicates the formation of both an individual humoral adaptive immune response and population immunity in the MW cohort, evidenced by an increase in the proportion of seropositive individuals.

The seroprevalence tended to increase with increasing age from 18 to 59 years, followed by a downward trend toward 70 years and older. The highest seroprevalence was registered in the 50–59-year age bracket (38%). The low seroprevalence in the categories 60–69 and 70 years and older could be due to lower mobility and social activity and, consequently, a lower probability of contact with carriers of the SARS-CoV-2 virus. It is possible that the physiological aspects of the immune response, which are characterized by age-related involution of both the cellular and the humoral components of the immune system, are also significant [14].

In total, within the study, 5157 MWs seropositive for antibodies to the SARS-CoV-2 virus were identified, including 4382 (85%) patients without any symptoms characteristic of COVID-19, a history of ARVI, or the presence of a positive PCR result. Probably, these cohorts recovered from asymptomatic disease, that is, they developed antibodies in the absence of symptom manifestation [16–18].

The results obtained indicate the importance of asymptomatic forms of COVID-19 in the formation of SARS-CoV-2 seropositivity among MWs in the Republic of Tatarstan. The high proportion of patients with asymptomatic disease is evidenced by the results of earlier population studies of seroprevalence in different regions of the Russian Federation as part of a large-scale project of Rospotrebnadzor in wave 1 of the COVID-19 epidemic, when seroprevalence figures varied and ranged from 81.2 ± 3.2% in the Irkutsk region to 82.4 ± 1.6% in Moscow, 98.3 ± 1.6 in Primorsky Territory, and 98.8 ± 0.7% in Krasnodar Territory [14]. In the Republic of Tatarstan, the proportion of patients with asymptomatic disease was 94.5 ± 0.8% [14, 19].

Our study revealed an almost linear inverse relationship between age and the proportion of people with asymptomatic forms of COVID-19. The proportion of people with asymptomatic forms was significantly higher in MWs aged 20–49 years compared with those aged 50–69 years. Asymptomatic carriers are important participants in the epidemic process of the spread of coronavirus infection [7, 8, 19].

An analysis of the geographical distribution of SARS-CoV-2 seroprevalence among MWs of municipal districts of the Republic of Tatarstan enabled us to divide the regions of the republic into three groups in accordance with the significance of differences between seroprevalence levels, 8.9–39.0 defined as a moderate level, 42.9–49.6 as an average level, and 53.1–64.4 as a high level.

The significant differences revealed in the seroprevalence of MW between municipal districts may be due to regional variation in the epidemic process, which requires further monitoring and correlation analysis between seroprevalence and incidence.

An analysis of SARS-CoV-2 seroprevalence among different categories of MWs showed that the largest proportion of seropositive patients was registered in junior medical (42%) and nursing (38%) personnel, compared with doctors and other categories of MWs. The data presented require a more in-depth study of causal factors, namely differences in the representativeness of the sample, compliance with anti-epidemic requirements during medical procedures, the correct use of personal protective equipment, and hand washing, as well as the level of education and social responsibility.

The largest proportion of SARS-CoV-2 seropositive patients was registered among the medical staff in hospitals dedicated to COVID-19 patients (52%); MWs at first-aid stations ranked second (45%), and MWs in non-infectious hospitals (34%) and outpatient clinics (31%) ranked third. Probably, the differences in seroprevalence levels in MWs in hospitals dedicated to the treatment of COVID-19 patients and first-aid stations, compared to non-infectious institutions and outpatient clinics, was due to different levels, frequencies, and intensities of professional contacts with patients and carriers of a new coronavirus infection [7, 8]. The lowest seroprevalence rates were noted among MWs of infectious hospitals (19.8%), possibly due to greater alertness and better preparedness of MWs in these institutions compared to those in other types of medical institutions.

The group of MWs who indicated the presence of any clinical symptoms of previous COVID-19 consisted of 868 people (16%), while antibodies were detected in blood plasma in 89% of cases, which indicates a formed humoral adaptive immune response to infection in most MWs. The proportion of seronegative individuals among MWs with a history of COVID-19 was significantly lower in the 60–69-year (7.0%) and 50–59-year (9.7%) age groups, compared to the 18–29-year (14.5 %) and 30–39-year age brackets (14.9%).

An increase in SARS-CoV-2 seroprevalence was revealed among MWs in the Republic of Tatarstan from August to December 2020 during the COVID-19 virus recurrence. The results of serological monitoring can be used to predict the epidemiological situation and plan measures for specific and non-specific prevention of COVID-19.

Conclusions

1. For the period from August to November 2020, among MW in medical institutions of the Republic of Tatarstan, the percentage of seropositive individuals increased from 27% in August to 58% in November.

2. The level of seroprevalence tended to increase as age increased from 18 to 59 years, followed by a downward trend up to an age of 70 years.

3. The largest proportion of SARS-CoV-2 seropositive patients was registered among junior medical and nursing personnel, compared with doctors and other categories of MW.

4. The largest proportion of SARS-CoV-2 seropositive patients was revealed among the medical staff of hospitals for COVID-19 patients; while the lowest rates of seroprevalence were registered among MW in infectious hospitals.

5. Among MW in the Republic of Tatarstan seropositive for antibodies to the SARS-CoV-2 virus, the proportion of asymptomatic forms of infection was 85%.

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