ДОСТИЖЕНИЕ МАКСИМАЛЬНОГО КОЛЛЕКТИВНОГО ИММУНИТЕТА SARS-CoV-2 СРЕДИ НАСЕЛЕНИЯ ТАДЖИКИСТАНА К МАРТУ 2022 ГОДА

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Резюме. Несмотря на все усилия мирового сообщества, пандемия COVID-19 остается одним из главных эпидемиологических вызовов современности. Даже при широком распространении инфекция может иметь определенные локальные особенности, обусловленные социальными, географическими и климатическими факторами. Задача – изучить коллективный иммунитет к SARS-CoV-2 у населения Республики Таджикистан.

Проведено поперечное рандомизированное исследование коллективного иммунитета по программе, разработанной Роспотребнадзором и Санкт-Петербургским институтом Пастера с учетом рекомендаций ВОЗ. Проведение исследования одобрили комитеты по этике соответствующих организаций: Министерства здравоохранения и социальной защиты населения Республики Таджикистан; и Санкт-Петербургский институт Пастера (Россия). По результатам анкетирования было отобрано 4022 человека, что составляет 0,15% (95% ДИ: 0,14-0,15) от общей популяции, рандомизированной

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по возрасту и региону. В последующем лабораторном анализе приняли участие 3682 человека. Распределение и количественное содержание антител (АТ) к вирусному нуклеокапсиду (N Ag) и рецепторсвязывающему домену (RBD Ag) определяли методом ИФА. При опросе 69,7% (95% ДИ: 68,2-71,2) когорты добровольцев указали на вакцинацию против SARS-CoV-2 в анамнезе. Наиболее часто использовались векторные вакцины (50,6%; 95% ДИ: 48,7-52,5), на втором месте – цельновирионные инактивированные препараты (23,0%: 95% ДИ: 21,4-26,6) и мРНК-вакцины – на третьем месте (21,0%; 95% ДИ: 19,4-22,6).

В когорте (n = 3682) было 27,5% мужчин и 72,5% женщин. Общая серопревалентность составила 98,5% (95% ДИ: 97,7-99,2) у мужчин и 99,4% (95% ДИ: 99,0-99,6) у женщин (различия статистически незначимы). Общая серопревалентность в когорте составила 99,2% (95% ДИ: 98,8-99,4) и колебалась от 97,2% до 100% в некоторых подгруппах. Бессимптомная серопозитивность во всей когорте составила 98,4% (95% ДИ: 97,6-99,1). В результате программы обязательной вакцинации, внедренной в Таджикистане в рамках Проекта экстренной помощи в связи с COVID-19, уровень коллективного иммунитета среди вакцинированных лиц достиг 99,5% (95% ДИ: 99,1-99,7), что аналогично уровню, достигнутому в когорте в целом.

Эпидемическая ситуация, сложившаяся в Таджикистане к середине марта 2022 г., характеризовалась практически абсолютным уровнем коллективного иммунитета, о чем свидетельствует отсутствие выявленных манифестных случаев заболевания COVID-19 с конца февраля (2022).

Ключевые слова: SARS-CoV-2, COVID-19, Республика Таджикистан, население, коллективный иммунитет, бессимптомное течение, вакцинация

ACHIEVEMENT OF MAXIMAL SARS-CoV-2 COLLECTIVE IMMUNITY AMONG THE TAJIK POPULATION BY MARCH 2022

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Abstract. Despite all efforts of the world community, the COVID-19 pandemic remains one of the main epidemiological challenges of our time. Even with its widespread distribution, the infection may have certain local features due to social, geographic, and climatic factors. Objective: to study collective immunity to SARS-CoV-2 in the population of the Republic of Tajikistan.

A cross-sectional, randomized study of herd immunity was carried out according to a program developed by Rospotrebnadzor and the St. Petersburg Pasteur Institute, taking into account WHO recommendations. The ethics committees of the corresponding entities approved the study: Tajik Ministry of Health and Social Protection; and the St. Petersburg Pasteur Institute (Russia). Based on questionnaire results, 4,022 people were selected, representing 0.15% (95% CI: 0.14-0.15) of the total population randomized by age and region. In subsequent laboratory analysis, 3682 people took part. The distribution and quantitative content of antibodies (Abs) to viral nucleocapsid (N Ag) and receptor binding domain (RBD Ag) were determined by ELISA. When questioned, a history of SARS-CoV-2 vaccination was indicated by 69.7% (95% CI: 68.2-71.2) of the volunteer cohort. Vector vaccines were most frequently used (50.6%; 95% CI: 48.7-52.5), with whole-virion inactivated preparations in second place (23.0%: 95% CI: 21.4-26.6) and mRNA vaccines in third place (21.0%; 95% CI:19.4-22.6).

The cohort (n = 3682) featured 27.5% men and 72.5% women. The overall seroprevalence was 98.5% (95% CI: 97.7-99.2) in men and 99.4% (95% CI: 99.0-99.6) in women (differences statistically insignificant). Overall seroprevalence in the cohort was 99.2% (95% CI: 98.8-99.4) and ranged from 97.2 to 100% in certain subgroups. Asymptomatic seropositivity in the whole cohort was 98.4% (95% CI: 97.6-99.1). As a result of a mandatory vaccination program introduced in Tajikistan under a COVID-19 Emergency Project, the level of herd immunity among vaccinated individuals reached 99.5% (95% CI: 99.1-99.7), which is similar to the level reached in the cohort as a whole.

The epidemic situation that developed in Tajikistan by mid-March 2022 was characterized by an almost absolute level of herd immunity, as evidenced by an absence of detected overt COVID-19 cases since the end of February (2022).

Keywords: SARS-CoV-2, COVID-19, Republic of Tajikistan, population, herd immunity, asymptomatic course, vaccination

Introduction

Since the unwelcome arrival of the global COVID-19 pandemic, many scientific papers have been published describing its nuances and progression. Many countries have featured similar dynamics and outcomes, but there have been exceptions. One of them, The Republic of Tajikistan, has featured unique characteristics worth noting. This text focuses on the uniquely high level of collective immunity reached there, including analysis of antibody dynamics in its subpopulations.

As of March 18, 2022, it has caused 467,384,850 infections [18], representing 58,654 per 1 million global population. Among them, 2,697,741 people have died from COVID-19, or 0.58% of all infected individuals. One of the states that managed to reduce COVID-19 incidence in the ex-Soviet region was the Republic of Tajikistan (RT). According to official data, the last case in the RT was registered on February 21, 2022, although COVID-19 cases were detected in all neighboring states during this period of time: 238 in Uzbekistan (8th week of 2022); 24 in Kyrgyzstan; and 1068 in Kazakhstan [12]. Understandably, such disparate outcomes raise interesting questions.

The RT is a Central Asian country located between 36°40 -41°05 North latitude and 67°31 -75°14 East longitude. The Republic borders: Uzbekistan from the west; Kyrgyzstan from the north; China from the east; and Afghanistan from the south. About 93% of the Republic's territory is occupied by the highlands of the Pamir-Alay system and the gravelly deserts of the eastern Pamirs. The RT has no access to the sea, resulting in a sharply continental climate with high air dryness [16]. This may be a factor that increases the risk of environmental SARS-CoV-2 spread [25] since it is believed that certain winter conditions (low air humidity, temperature) likely promote the active circulation of respiratory viruses in the autumn-winter period [15]. However, this factor is likely to be insignificant in the RT since the majority of the population lives in mountain valleys with a high annual number of frost-free days (210-250). There is little precipitation (mostly from November to March), while average temperatures in the valleys are from -2 to +2 °C in the winter and from +19 to +27 °C in the summer [4]. The climatic conditions in the RT in relation to the epidemic process can generally be characterized as neutral.

The RT features high population growth [32, 35]. As of the end of 2021, the population was 9,857,502 people, with more than 73% being rural residents. Only 27% of the population lives in cities. The overall population density was 69.2 km^{-2}. In large settlements, population densities range from 273 to 982 km^{-2}. The largest cities are Dushanbe (pop. 880,800), Khujand (pop. 183,356), Kulob (pop. 95,200), Bokhtar (pop. 75,359), and Istaravshan (pop. 63,500). Other cities have populations below 50,000. When describing the population, it is worth noting that, more than 1 million Tajik citizens have migrated outside the country, mainly to Russia [35].

All these features certainly influence the epidemiological situation in the country. The generally low density of the predominantly agricultural population, as well as significant labor migration (egress), have likely attenuated COVID-19 spread. However, it seems the main factor that positively influenced the pandemic, nevertheless, should be recognized as the implementation by Tajik authorities of the Emergency COVID-19 Project, consistently implemented with the active support of the World Bank [7].

According to international databases [12, 18], 17784 or 1804 COVID-19 cases per million population were registered in the RT during the entire pandemic period. The incidence dynamics included three waves of different intensity, followed by pauses wherein there were no new cases or they could not be detected (Figure 1).

Starting on 04/05/2020, the first outbreak continued until the first ten days of January 2021. The maximum number of patients was identified on week 21, 2021 (209 cases). The second peak occurred from June to September (2021) and was significantly smaller than the first. Its maximum level was noted

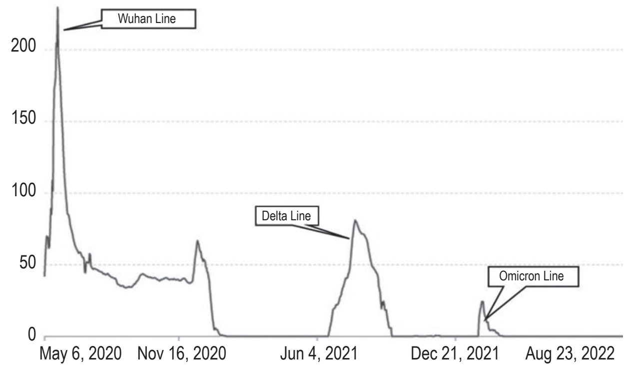

Figure 1. Dynamics of COVID-19 incidence in the Tajik population for the entire observation period (as of 21/08/2022) [12, 18]

Note. Y-axis: number of cases, calculated as an average over 7 days of observation. X-axis: date of registration (beginning 04/05/2020, last 23/08/2022).

on the 26th week of 2021, amounting to 79 registered patients. All dates in this text use the format DD/MM/YY (day, month, and year). The third and final peak (the smallest in terms of case numbers) was detected from 22/01/22-16/02/2022, with a maximum of only 24 cases (29/01/2022). Since February 21, 2022, no new cases of overt COVID-19 have been recorded.

To effectively combat COVID-19, Tajik authorities introduced mandatory COVID-19 vaccination among citizens over 18 years of age (starting on June 27, 2021). Initially, the AstraZeneca vaccine from India and CoronaVac from Cinovac (China) were used [27]. According to the official Tajik Ministry of Health data (https://stat.tj/storage//1.01.2022.pdf), 5,596,907 people (58.9%) were eligible for vaccination. Of the eligible, 86.0% completed vaccination. Vaccines created on all four platforms were used in the RT (Table 1).

Here, we briefly summarize the features of these vaccine design groups. The vector vaccines AZD1222 (based on ChAdOx1, Oxford-AstraZeneca) and Gam-COVID-Vac (Gamaleya Research Institute) feature S protein genes inserted into an adenoviral vector. Both vaccines induce the synthesis of antibodies (Abs) to the complete S protein and induce strong immune protection against many or all SARS-CoV-2 variants [30]. Messenger RNA vaccines, including mRNA-1273 (Moderna) and BNT162b2 (Pfizer-BioNTech), contain messenger RNA of the S protein antigen, which induces strong humoral immune responses against reference and mutant viral variants [11]. The whole-virion vaccines (WVV) CoronaVac, and CoviVac have 100% homology with S protein. It is believed that the immunogenicity of vaccines is about 86% overall, and the formation of a full-fledged immune response against SARS-CoV-2 may require the introduction of booster doses [13]. A peptide vaccine, EpiVacCorona, was produced by the 'Vector' State Scientific Center for Virology and Biotechnology (Russia) [29]. It was used only in isolated cases; data for it were omitted due to non-representative sampling.

The aforementioned programs and preparations, alongside immunity from natural infections, clearly formed favorable conditions leading to cessation of overt COVID-19 incidence in the period from February to August 2022. In addition, one cannot exclude the additional influence of climatic, demographic, and immunological factors. Jointly, they may have supported the achievement of a high level of herd immunity. The purpose of this cross-sectional, randomized study was to analyze the structure and features of the herd immunity to COVID-19 formed in the Tajik population.

TABLE 1. STRUCTURE OF COVID-19 VACCINATION IN THE TAJIK POPULATION (AS OF 18/03/2022)

Vaccine	Individuals vaccinated		
	one dose	two doses	third dose (booster)
mRNA-1273 (Moderna)	1,263,915	1,114,216	299,333
BNT162b2 (Pfizer)	318,396	304,839	73,064
AZD1222 (Oxford/AstraZeneca)	1,125,058	1,008,461	184,448
Gam-COVID-Vac (Sputnik V)	48,654	47,596	0
CoronaVac (Sinovac)	2,387,804	2,335,468	345,657
overall	**5,143,827**	**4,810,580**	**902,502**
share of overall population	52.0%	48.7%	9.1%
share of eligible group*	91.9%	86.0%	16.1%

Note. *, persons who had no contraindications to vaccination.

Materials and methods

Methodology for the formation of the volunteer cohort

The study was organized and conducted as part of scientific cooperation between countries of Eastern Europe, Transcaucasia and Central Asia to assess population immunity to novel coronavirus infection in accordance with: Rospotrebnadzor order (No. 512, dated 09/09/2021) on "Implementation Procedure for Russian Government Decree" (No. 1658-r, dated 18/06/2021); and order of the Tajik Ministry of Health and Social Protection (No. 164, dated 4/03/2022). Organization and research were carried out by the Saint Petersburg Pasteur Institute and the Tajik Research Institute of Preventive Medicine (Tajik Ministry of Health and Social Protection).

A cross-sectional, randomized cohort study of herd immunity was conducted from March 14 to 18, 2022 according to a program developed by the Federal Service for Supervision of Consumer Rights Protection and Human Welfare with the participation of the Saint Petersburg Pasteur Institute, taking into account WHO recommendations [20, 34]. The scheme and organization of the study have been described earlier [19, 20].

Three days before the start of the study, an extensive explanatory campaign was conducted (on TV, mass media, social networks) about the start of free testing for the presence of Abs to SARS-CoV-2, with an internet link for completing the survey. Volunteers wishing to take part in the study applied via an internet link, filled out a questionnaire (Table 1S, see Supplementary data), and submitted it to the cloud service. Received questionnaires were subjected to algorithmic analysis to determine satisfaction of inclusion criteria.

According to questionnaires received, a total of 4,022 people expressed their desire to participate. If the candidate met the criteria, he/she received a letter to their indicated e-mail address with a unique ID number and an invitation to choose (via the internet) a convenient point and time for blood collection. Grounds for non-inclusion in the study were: the refusal of subsequent laboratory testing; or the presence of manifest COVID-19 at the time of questionnaire completion. In the cloud resource, the number of participants was registered, with simultaneous logging of distribution by age and place of residence. When maximum levels were reached, registration of incoming questionnaires was terminated. In this case, the individual received a rejection letter. This approach made it possible to effectively form a volunteer cohort randomized by age and regional characteristics. In the end, 340 people declined to participate. Thus, the final volunteer cohort size was 3,682 people.

Each volunteer, or their legal representative (in the case of child participation), was acquainted with the goals and conditions of the upcoming study and signed an informed consent. The study was organized in accordance with the provisions of the Declaration of Helsinki and approved by the ethics committee of the Tajik Ministry of Health and Social Protection (protocol No. N2, dated 21/02/2022); and the ethics committee of Saint Petersburg Pasteur Institute (protocol No. 64, dated 26/05/2020).

Characteristics of the volunteer cohort

Studies of SARS-CoV-2 seroprevalence in the Tajik population were carried out in ten areas, including three cities (Dushanbe, Khujand, Bokhtar) and seven districts (Vahdad, Hisor, Istaravshan, Isfara, Kulob, Panjakent, Tursunzade). According to climatic, geographic, and demographic principles, areas contributing to the volunteer cohort can be conditionally divided into 4 regions: (1) in the northwest region is the Panjakent district in the Sughd region, located in the Zeravshan river valley. The population of the city and adjacent settlements amounted to 304,200, of which 14% were urban and 86% rural. (2) The Dushanbe agglomeration, located in central Tajikistan in the Hisor valley, combines the capital Dushanbe city and three districts (Vahdat, Hisor, Tursunzage). The total population was 1,928,700, among which 57.6% were urban and 42.4% rural. (3) In the northeast is the Khujand agglomeration (part of the Sughd region). Residents of Khujand city, Isfara district, and Istaravshan district participated in the program. The total population of the agglomeration was 759,800 people, of which 41.8% were urban and 58.2% rural. (4) In the southwest is the Khatlon region, which was represented by two areas in the study, Bokhtar city and Kulob district, with a total population of 341,100 people, of which 66.8% were urban and 33.2% were rural.

Due to sparse population and logistical difficulties in obtaining/transporting peripheral blood samples in the Gorno-Badakhshan Autonomous Region (located in the Pamir-Alay Mountain system), the formation of a volunteer cohort was not carried out there. In total, 3,333,800 people (33.9% of the national population) live in the ten listed Tajik areas which contributed volunteers to the study. From this number, in accordance with the de Moivre-Laplace limit theorem [3], a representative volunteer cohort was formed: 3,682 people, or 0.11% of all residents of these areas. Urban and rural population shares were 51% and 49%, respectively. Participant representation averaged 0.11% of the population of the cities included in the study, ranging from 0.03% (Hisor district) to

0.14% (Dushanbe city) (Table 2S, see Supplementary data).

After exclusion of eight non-valid samples, the number of volunteers included in the analyzed cohort was 3,674. Of them, 359 people (9.8%; 95% CI: 8.9-10.8) had a history of a verified clinical form of COVID-19. The volunteer cohort was represented by seven age groups: 1-17; 18-29; 30-39; 40-49; 50-59; 60-69; and ≥ 70. Taking into account previously identified aspects of the formation of immunity in children [21], the group '1-17 years old' was further divided into 3 subgroups (1-6, 7-13, 14-17 y. o.) (Table 3S, see Supplementary data).

The general cohort included representatives of most Tajik professional groups (Table 4S, see Supplementary data). The largest share of participants was from medical professionals (40.3%; 95% CI: 38.7-41.9). The smallest was from the military (0.3%; 95% CI: 0.1-0.5) and the Arts (0.1%; 95% CI 0.03-0.3). Agricultural workers represented only 0.5% (95% CI: 0.3-0.5). However, these figures do not reflect the real contribution of the rural population. Some of them, having one or more specialties, were included in other professional groups.

Organization of laboratory research

At the appointed time, volunteers visited the collection point, where a medical worker took a 3 mL peripheral venous blood sample using vacutainers containing EDTA. Samples were centrifuged to separate plasma from cellular elements. Plasma were transferred into plastic tubes and stored until analysis (≤ 24 hrs) at 4 °C. Antibodies to the nucleocapsid (Nc) antigen (Ag) and S protein receptor binding domain (RBD) were quantified by ELISA using the appropriate test systems as previously described [19]. Analysis results were expressed as BAU/mL.

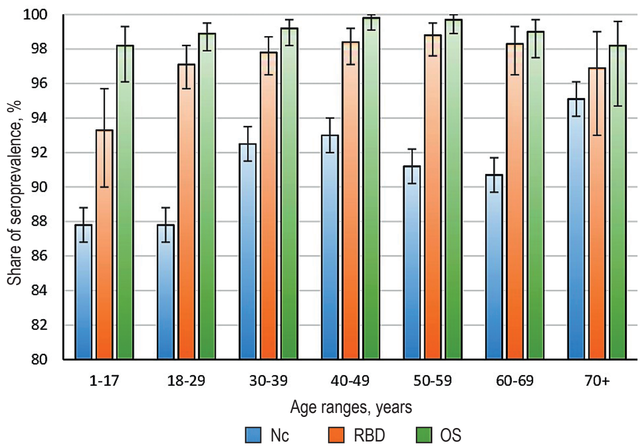

Figure 2. Distribution of seropositivity (Nc, RBD, OS) by age group. Black vertical lines are 95% confidence intervals

Note. Numerical data are given in Table 5S.

Statistical analysis

Population seroprevalence was assessed according to three parameters: the share of individuals with detectable serum Nc Abs; the share of individuals with detectable serum RBD Abs; and the share of individuals containing any of these Abs, or their combination (overall seropositivity, OS). Statistical data analysis was performed using Microsoft Excel 2010. Mean values and confidence intervals of shares were calculated by the method of A. Wald and J. Wolfowitz [33] with the correction of A. Agresti and B.A. Coull [1]. Spearman's rank correlation, multivariate regression, and multivariate analyses were performed using Statistica version 12 (StatSoft). For other statistical calculations not mentioned in this section, we used Statistica version 12. Unless otherwise indicated, $p \leq 0.05$ was used as the threshold of statistical significance. Illustrations were made in Excel 2010 or Statistica version 12.

Results

Gender distribution of SARS-CoV-2 seroprevalence

The cohort of 3,674 included 1,010 men and 2,664 women. The gender ratio was 1:2.6, specifically: 27.5% (95% CI: 26.1-29.0) males and 72.5% (95% CI: 71.0-73.9) females. By serological analysis, men showed the following pattern: SARS-CoV-2 OS 98.5% (95% CI: 97.7-99.2); Nc Abs 90.1% (95% CI: 88.2-91.9); and RBD Abs 96.7% (95% CI: 95.6-97.8). Seroprevalence in women was (insignificantly) higher than in men: OS 99.4% (95% CI: 99.0-99.6); Nc Abs 91.1% (95% CI: 90.0-92.2); and RBD Abs 97.8% (95% CI: 97.2-98.3).

Age distribution of SARS-CoV-2 seroprevalence

Analysis of seroprevalence (Nc, RBD, OS) in different age groups was performed (Figure 2, Table 5S, see Supplementary data). High seropositivity was noted in all age groups, albeit with some peculiarities. Nc Abs seroprevalence was the lowest (compared to RBD, OS) in the age groups 1-17 years and 18-29 years. This difference was significant compared to other age groups ($p < 0.001$), except for the 70^+ group (Figure 2).

A different distribution was found with RBD Abs analysis. Seroprevalence among those aged 1-17 and 18-29 years was again low compared to other groups. However, the difference was less noticeable, reaching significance only among children aged 1-17 y. o. ($p < 0.001$).

Overall seropositivity was the highest category, reaching 99.2% (95% CI: 98.8-99.4). In the age groups 40-49 and 50-59 years, the upper limit of the confidence interval reached 100%.

Thus, the level of collective immunity, at least among the examined volunteers, reached a maximum

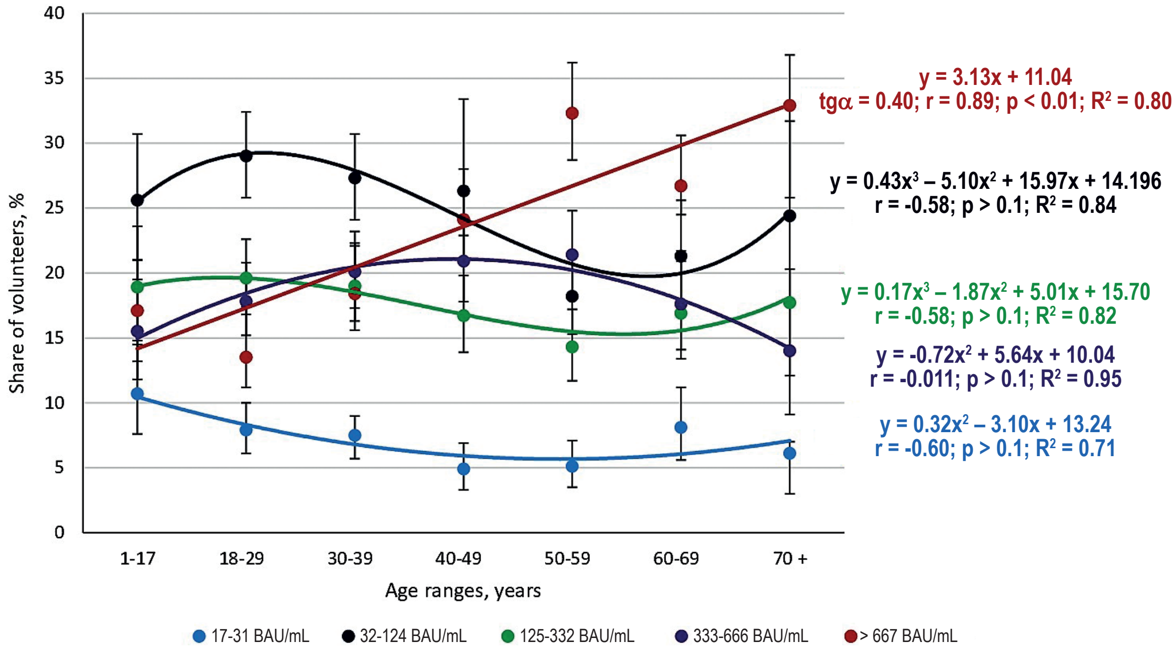

Figure 3. Quantitative distribution of plasma Nc Abs among volunteers of all age groups

Note. Legend: Plasma Abs ranges are expressed as BAU/mL. Colored curves are trend lines for each Abs range. Regression equations, coefficients (rank correlation, determination), significance of differences (p), and angular coefficient (tgα) are shown on the right, highlighted in the color of the corresponding range. Vertical black lines are 95% confidence intervals. For numerical data, see Table 6S.

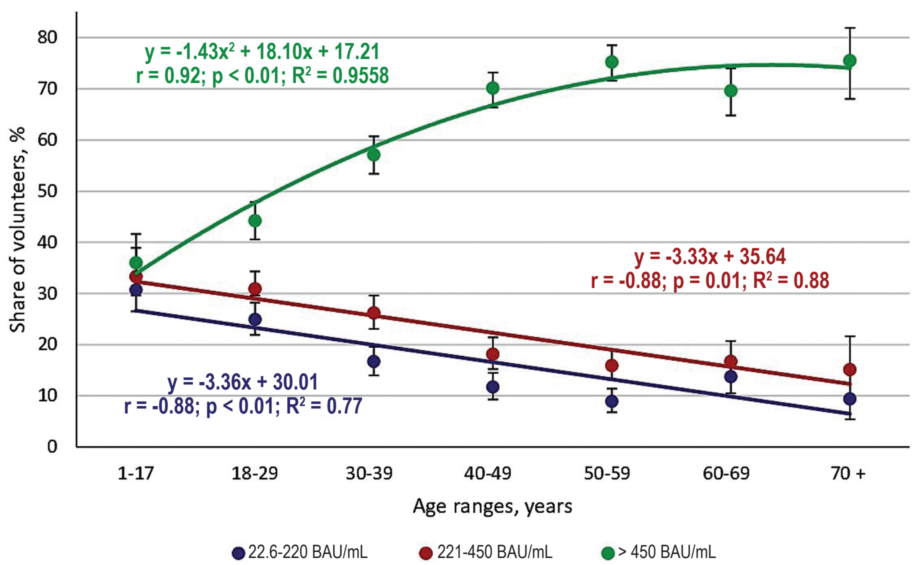

Figure 4. Quantitative distribution of plasma RBD Abs among volunteers of all age groups

Note. Legend: Plasma Abs ranges are expressed as BAU/mL. Colored curves are trend lines for each Abs range. Regression equations and coefficients (rank correlation, determination) are highlighted in the color of the corresponding range. Vertical black lines are 95% confidence intervals; p is the statistical significance of differences. For numerical data, see Table 7S.

value. This fully corresponded with the zero incidence in the Tajik population (end of February 2022 to August 2022) noted above (Figure 1). To analyze the structure of seroprevalence, the shares of volunteers with quantifiable levels of Abs to Nc and RBD was determined (Figures 3, 4).

Volunteers were distributed over five Nc Abs ranges (BAU/mL): 17-31; 32-124; 125-332; 333-666; and ≥ 667 (Figure 3, Table 6S, see Supplementary data). Among volunteers with minimal Nc Abs levels (17-31 BAU/mL), a slight downward trend was observed. The smallest share of volunteers in this group was found among those aged 40-49 years (4.8%; 95% CI: 3.2-6.7); the largest was among children aged 1-17 years (10.7%; 95% CI: 7.6-14.5). The differences were significant ($p < 0.001$), but the rank correlation coefficient of the distribution over all age intervals was insignificant at -0.60 ($p > 0.1$). The regression curve was a 2nd order polynomial with a determination coefficient $R^2 = 0.71$, described by the equation $y = 0.32x^2 - 3.10x$

A different distribution was noted among volunteers with Nc Abs levels in the range 32-124 BAU/mL. The corresponding regression curve was S-shaped with a peak in the 18-29 age group (29.0%; 95% CI: 25.8-32.4) and a valley in the 50-59 age group (18.1%; 95% CI: 15.2-21.2). The rank correlation coefficient was $r = -0.58$ ($p > 0.1$). The regression curve corresponded to a 3rd order polynomial with a determination coefficient $R^2 = 0.84$, described by the equation $y = 0.43x^3 - 5.10x^2 + 15.97x + 14.196$.

A similar distribution, only with less pronounced curvature, was noted among volunteers with Nc Abs levels in the range 125-332 BAU/mL. As in the previous group, the largest proportion of seropositive volunteers was noted in the age group 18-29 years (19.5%; 95% CI: 16.7-22.4), and the minimum was found among those aged 50-59 years (14.3%; 95% CI: 11.7-17.3). The noted differences were insignificant ($p > 0.05$), as was the rank correlation coefficient value ($r = -0.58$; $p > 0.1$). The regression curve was a 3rd order polynomial with a determination coefficient $R^2 = 0.82$, described by the equation $y = -0.17x^3 + 1.86x^2 + 5.01x + 15.7$.

The form of the regression curve in the group with Abs in the range 333-666 BAU/mL changed to a 2nd order polynomial, while the signs of the coefficients in the regression equation (a, b) changed to opposite relative equations for the group 13-31 BAU/mL. The rank correlation coefficient, as in other groups, remained insignificant ($r = -0.11$; $p > 0.1$). The regression curve, with coefficient of determination $R^2 = 0.95$, was described by the equation $y = 1.72x^2 + 5.64x + 10.04$. With maximum Nc Abs levels (> 667 BAU/mL), the regression became linear with a determination coefficient $R^2 = 0.8$, described by the equation $y = 3.13x + 11.04$. At the same time, the rank correlation coefficient was 0.89 and significant ($p < 0.01$). The regression curve shows that: the lowest seroprevalence was typical for the age groups 1-17 and 18-29 years; and the maximum was seen among those aged 70+ years (Figure 3, Table 6S).

When analyzing the quantitative distribution of RBD Abs among volunteers of different ages, the results were grouped into three ranges: 22.6-220; 221-450; and > 450 BAU/mL (Figure 4, Table 7S, see Supplementary data).

The smallest shares of seropositivity were noted among volunteers with RBD Abs levels in the range 22.6-220 BAU/mL. The relationship between volunteer age and RBD Abs levels was satisfactorily described by the linear regression equation $y = 3.36x + 30.01$, with a coefficient of determination of 0.77. It is interesting that, as with Nc Abs, the largest proportion of seropositive individuals was noted in the age groups 1-17 and 18-29 years. The smallest was seen among those aged ≥ 40 years. The proportion of Nc seropositive individuals was largely uncorrelated with age (rank correlation coefficient significance $p > 0.05$). Regarding the distribution of RBD seropositive individuals, the correlation coefficient was -0.88 and significant ($p < 0.01$).

A similar relationship was found in the group of individuals with RBD Abs levels of 220-450 BAU/mL. Only the numerical values of the coefficients a and b changed, and the coefficient of determination increased to 0.88. The main trend remained unchanged: a lower proportion of seropositive individuals in the age ranges 1-17 and 70+ years. This lower proportion was significant with a rank correlation coefficient of $r = -0.93$ ($p < 0.001$).

Achievement of the maximum RBD Abs level (> 450 BAU/mL) was accompanied by a trend change from negative to positive. The linear regression transformed into a 2nd order polynomial ($y = -1.43x^2 + 18.10x + 17.21$), and the coefficient of determination increased to 0.92. The trend change was not accidental. The rank correlation coefficient changed sign, and its value was 0.96 ($p < 0.01$). Interestingly, a similar transformation was seen when analyzing the distribution of Nc Abs seropositivity in the > 667 BAU/mL group (Figure 3).

Quantitative analysis of the age distribution of Nc and RBD Abs showed similar dynamics. Interestingly, the results are unlike a study of seroprevalence in Russian regions in the early stages of the COVID-19 pandemic, wherein the highest Abs levels were noted in children aged 1-17 years [13]. In the RT, a high level of herd immunity was established from the end February, with no registration of overt forms of COVID-19. The lowest level of seropositivity was observed among the child population. Among volunteers over 60 years of age, it was identified: a lower share of individuals with low Abs levels; and a significantly higher share of individuals with the maximum levels of all measured Abs. This is likely due to geographical, professional, or other factors.

Volunteer seroprevalence in different Tajik geographic regions

The study of herd immunity was carried out mainly in the western regions of the RT. In the northwest, it was Panjakent district with a population of 304,200.

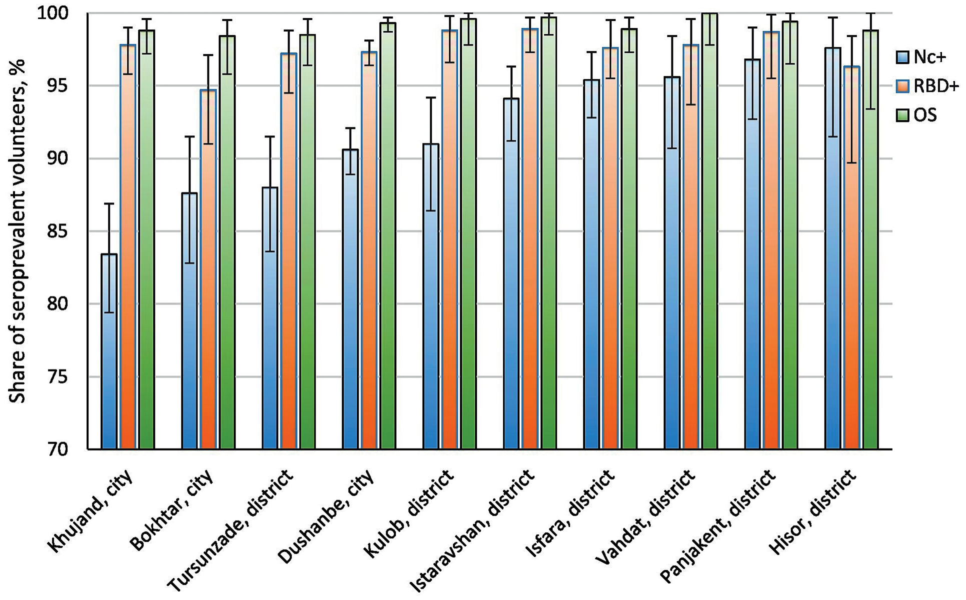

Figure 5. Distribution of seropositivity (Nc, RBD, OS) by place of residence

Note. The legend is shown in the upper right. Black vertical lines are 95% confidence intervals.

The central region was represented by Dushanbe city and three districts (Vahdat, Hisor, Tursunzade) with a total population of 1,611,400. In the north, the study was carried out in the city of Khujand and two districts (Istaravshan, Isfara) with a population of 759,800. In the southwest, volunteers from Bokhtar city and the Kulob district participated in the project. The total population of the regions included in the program was 3,333,800 (1,600,600 urban, 1,733,200 rural). In total, 3,674 individuals took part in the program in these regions, of which 3,644 (99.2%; 95% CI: 98.8-99.4) were found to have Abs to SARS-CoV-2. It is necessary to note certain differences in the structure of Nc and RBD Abs seropositivity (Figure 5, Table 8S, see Supplementary data).

The smallest proportion of volunteers seropositive for Nc was noted in Khujand city. The largest was noted in the Panjakent and Hisor districts. An attempt to group seropositive volunteers on a regional basis was not successful. For example, the Istaravshan and Isfara districts had a significantly higher proportion of Nc seropositive individuals than Khujand city (located in the same geographic region). A similar situation was noted in the Dushanbe agglomeration (Dushanbe city, Tursunzade dist., Vahdat dist., Hisor dist.). Determination of the proportion of RBD seropositive individuals showed an almost uniform level, varying in a narrow confidence interval, of 97.5% (95% CI: 97.0-98.0). The proportion of OS persons was even higher, 99.2% (95% CI: 98.8-99.4).

Correspondence analysis was performed assessing seroprevalence and regions (Figure 6). Such regions as the Hisor, Panjakent, Vahdat, and Isfara featured a high degree of association with seropositivity. Relatively low correspondence was noted with the Khujand region. The total chi-square of the correspondence analysis was 60.7488 ($p < 0.0001$)

The results may indicate regional features of herd immunity. These may have formed under the influence of certain socioeconomic conditions or in connection with the level of development in the region. Most of the cohort lived in areas located in intermountain valleys with favorable climatic conditions. We were not able

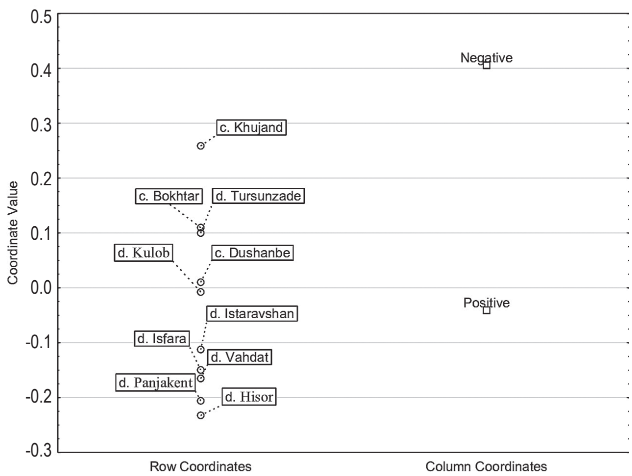

Figure 6. Regional distribution of seroprevalence frequency

Note. c, city; d, district; Positive, positive SARS-CoV-2 Abs test; Negative, negative SARS-CoV-2 Abs test. The figure shows the regions located in the conditional space on the same level with the category corresponding to the positive test result.

to establish any impact of climatic/geographic factors on seroprevalence.

Effect of occupation on cohort seroprevalence

Occupation is another potential factor influencing SARS-CoV-2 seropositivity levels. In processing questionnaires, seventeen professional groups were identified. Six of them featured less than thirty individuals. Hence, some professional groups were combined (Figure 7). Civil servants and military personnel were combined into one group. Workers in industry, agriculture, and transport were combined into another group. Other groupings were: preschool children combined with schoolchildren; and scientists combined with creative workers (the Arts). In result, the total number of professional groups was reduced to twelve. The resulting sample was ranked from

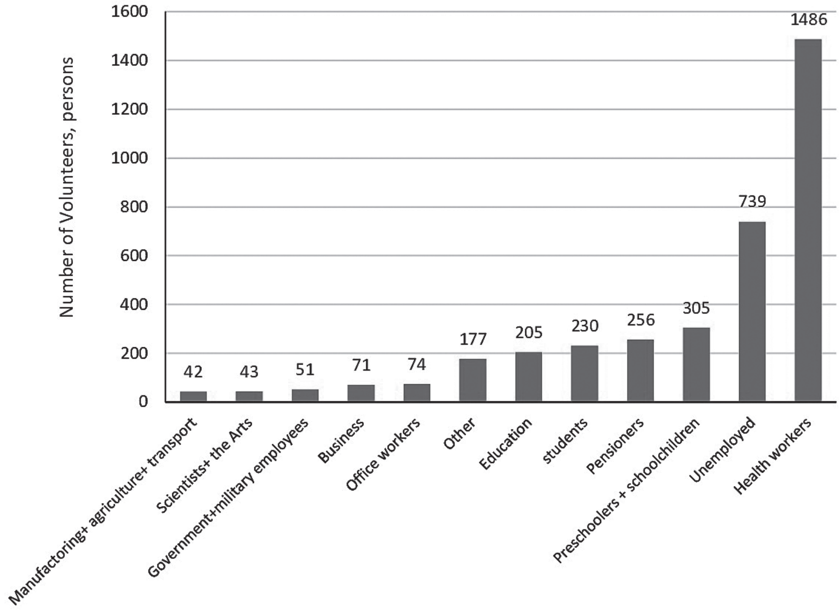

Figure 7. Distribution of volunteers by occupation

Note. Groups with small sample sizes were combined ('government and military employees', 'workers in industry, agriculture and transport', 'children of preschool and school age', 'scientists and the Arts').

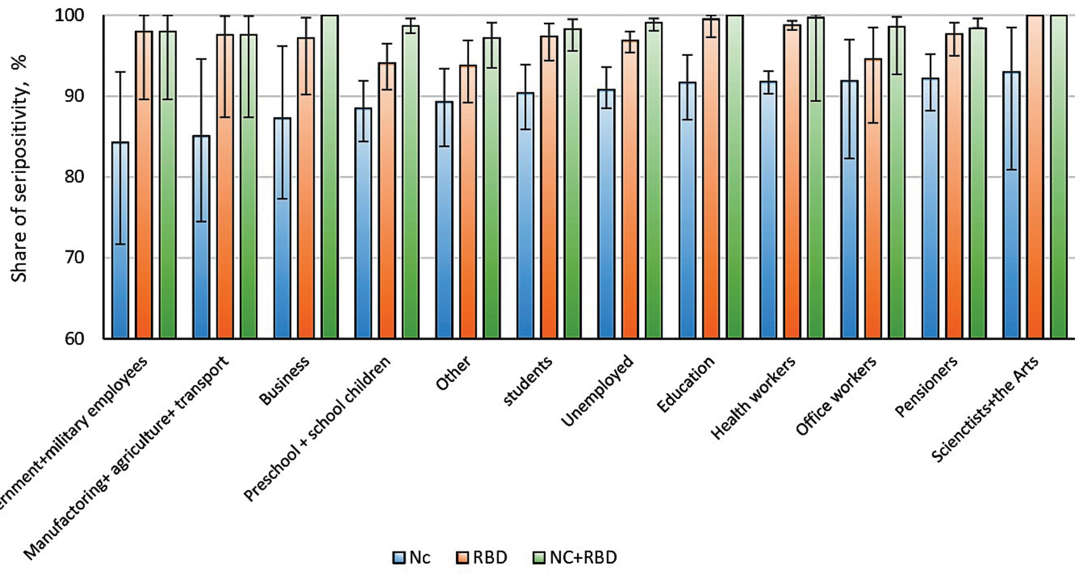

Figure 8. Distribution of seropositive individuals (Nc, RBD, OS) by occupation

Note. As for Figure 7. Black vertical bars are confidence intervals.

minimum to maximum proportion Nc seropositive. This made it possible to more clearly show the real volunteer distribution by occupation, taking into account group (Figure 7).

The presented data indicate a significant variation in the number of volunteers in each sample. The maximum number were employed in healthcare, followed by persons unemployed at the time of the survey. The minimum number of participants belonged to three combined groups: 'industry, agriculture, transport'; 'scientists and the Arts'; and 'civil service and the military employees'.

When analyzing the ranked series for Nc seroprevalence, the order was slightly different than with RBD. The minimum level of seroprevalence was noted in the groups 'government + military employees' and 'manufactoring + agriculture + transport'. The highest level was among 'scientists+the Arts' (Figure 8, Table 9S, see Supplementary data). The largest group, healthcare workers, with a score of 91.8% (95% CI: 90.3-93.1) is located between education workers and office workers. In this context, cohort RBD seroprevalence averaged 97.5% (95% CI: 97.0-98.0), and the share OS almost reached its limit (99.2%; 95% CI: 98.8-99.4). As expected, there were no significant differences in the last two groups.

Correspondence analysis (Figure 9) assessing SARS-CoV-2 seroprevalence and field of professional activity did not reveal any association between the parameter 'presence of antibodies' and field of activity. The total chi-square of the performed correspondence analysis was 15.7416 ($p < 0.4712$).

The results likely reflect an important factor. The continuous mass vaccination approach adopted by Tajik authorities led to almost absolute seroprevalence (exceeding 90% in the population without contraindications to immunization). In result, distinctions between professional groups that may have existed at an earlier stage inevitably blurred. An example would be the noticeable, yet insignificant, dependence of Nc seropositivity on professional activity.

Seroprevalence pattern with asymptomatic infection

As noted, the cohort featured quite high seroprevalence (Nc, RBD, OS), regardless of age, place of residence, or professional affiliation (Figure 2, 5, 8). The most likely cause is the mass vaccination program mentioned. However, this is not the only reason, given the low incidence rate throughout the pandemic (Figure 1). It is possible that portions of the population experienced asymptomatic infection, leading to production of associated Abs (notably anti-Nc). This possibility has been repeatedly shown earlier [22, 23, 24, 31]. An additional factor, characteristic of the RT, is large families with several

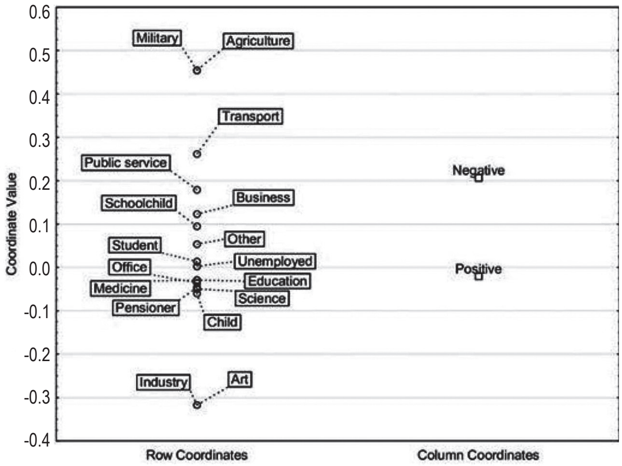

Figure 9. Distribution of seroprevalence by occupation

Note. Positive, positive SARS-CoV-2 Abs test; Negative, negative SARS-CoV-2 Abs test. The figure shows the occupation located in the conditional space on the same level with the category corresponding to the positive test result.

children of different ages. In such conditions, infection often occurs in a latent or asymptomatic form. Due to high viral transmissibility, infection can spread from a sick child to other family members, conferring asymptomatic infection [8, 14]. As part of this study, the proportion of individuals without any history of manifest COVID-19 was assessed in a group of Nc^+ unvaccinated volunteers ($n = 998$). These were classified as those with a likely history of asymptomatic infection (Figure 10).

The largest proportion of volunteers with a likely history of asymptomatic infection was found among children aged 1-17 years (97.1%; 95% CI: 94.5-98.8), those aged 18-29 (97.7%; 95% CI: 94.3-99.4), and those aged 70^+ (100%). In all these groups, the differences from the mean were significant ($p < 0.05$). The smallest share of asymptomatic individuals was found in the group 40-49 years old (88.2%; 95% CI: 79.8-94.0). Unfortunately, the authors cannot offer a logical explanation for the identified differences. It can only be assumed that the high frequency of asymptomatic infection among children is associated with the aforementioned increased resistance of this group to COVID-19 [14]. Among those aged 70^+, it can be explained, to some extent, by closer contact with children [20]. However, these assumptions require further research, and they do not explain the higher proportion of asymptomatic individuals in the 18-29 age group.

The role of vaccination in herd immunity formation

After analyzing the structure of volunteer seropositivity (Nc, RBD) according to social factors (age, region, profession), we assessed the impact of

TABLE 2. SEROPOSITIVITY FOR Nc AND RBD ANTIBODIES IN THE ENTIRE COHORT (n = 3674)

		Nc Abs status, n, % (95% CI)		Total, n, % (95% CI)
		Nc^+	Nc^-	
RBD Ab status	RBD^+	3279 89.2 (88.2-90.2)	305 8.3 (7.5-9.2)	3584 97.5 (97.0-98.0)
	RBD^-	60 1.7 (1.3-2.1)	30 0.8 (0.6-1.2)	90 2.4 (1.9-3.0)
	total	3339 90.9 (90.0-91.8)	335 9.1 (8.2-10.1)	3674 (100)

the various vaccines on seroprevalence. Initially, the level of collective immunity (Nc, RBD) of the entire cohort was determined, regardless of cause (Table 2). The results showed that the proportion of seropositive volunteers in the entire cohort was 99.1% (95% CI: 98.8-99.4).

The largest group was individuals who had both tested Abs (Nc^+RBD^+, 'double positive'), reaching 89.2% (95% CI: 88.2-90.2) in the entire cohort. RBD monopositivity was 8.3% (95% CI: 7.4-9.2), and Nc monopositivity was only 1.7% (95% CI: 1.3-2.1). Such high seroprevalence inevitably raises questions about the phenomenon's causes and structure.

As noted, in accordance with the Emergency COVID-19 Project [7], the Tajik Ministry of Health and Social Development launched a mandatory vaccination program on June 26, 2021. By March 18, 2022, the proportion of individuals who had received two immunizations had reached all 48.7% of the population without medical contraindications. For one reason or another, 52.3% remained unvaccinated. It is logical to expect lower seroprevalence in the unvaccinated portion of the population, which were inevitably in the examined cohort. However, the data refutes this initial hypothesis (Table 3).

In the cohort of 3674 people, 1113 were not vaccinated (30.3%; 95% CI: 28.8-31.8). Among them, the proportion double seropositive (Nc^+RBD^+) was 85.8% (95% CI: 83.6-87.7). The proportion RBD monopositive was significantly lower (8.8%; 95% CI: 7.2-10.6), and the proportion of Nc monopositive was minimal (3.9%: 95% CI: 2.8-5.2). In other words, the seropositivity frequency among unvaccinated volunteers was almost the same as that of the overall cohort (Table 3). These data require further explanation. The most logical assumption may be that asymptomatic infections are widespread in the Tajik population, with some influence from convalescents, although their share was only 10.8% (95% CI: 9.8-11.9).

The most important factor in the collective immunity of the Tajik population is specific vaccination. The range of vaccines was quite wide and included preparations created on all major platforms

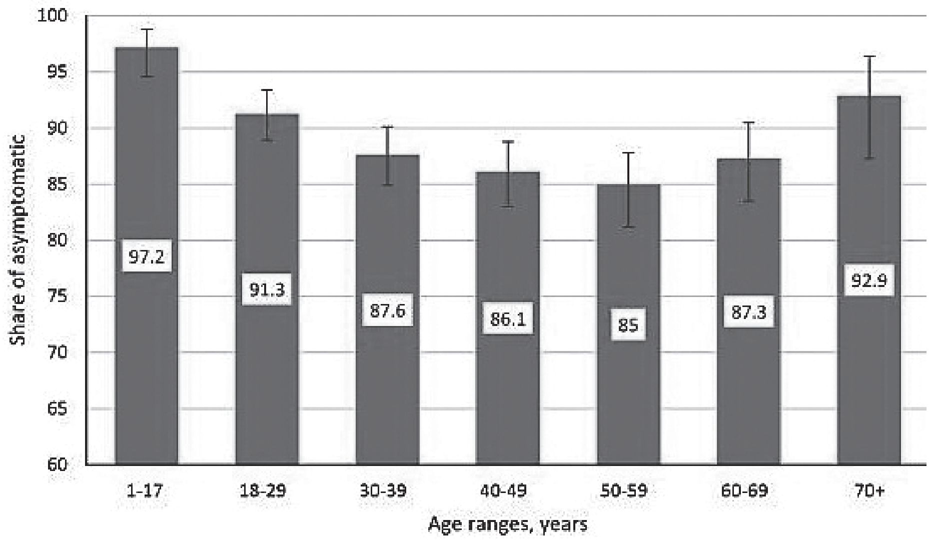

Figure 10. Distribution of volunteers with asymptomatic COVID-19 by age (in the group of unvaccinated volunteers seropositive for Nc Abs)

Note. Black vertical lines are confidence intervals.

(Table 1). Some vaccines, however, were used relatively widely, while others were used only among small groups (Figure 11).

The most frequently used vector vaccine was AZD1222, better known as AZD 1222, with a share of 49.2% (95% CI: 47.2-51.1). Less widely used was the CoronaVac (25.2%; 95% CI: 23.5-26.9). The mRNA-1273 and BNT162b2 vaccines were utilized about 4.5-fold less frequently than AZD1222. These four vaccines accounted for 95.3% of immunized individuals. The remaining five preparations accounted for only 3.9%. In 0.8% of cases, the volunteer could not name the preparation used (Figure 11, indicated as 'unknown'). Two vaccines produced in Russia (Sputnik V, Sputnik Light) were combined under the common name Gam-COVID-Vac. Mass immunization, as expected, led to the formation of a high level of humoral immunity (Table 4).

The data obtained mainly corresponded with the structure of herd immunity of the entire volunteer cohort (Table 2). The largest number of vaccinated volunteers contained both serum Abs ('double positive', Nc^+RBD^+); their share was 90.8% (95% CI: 89.6-91.8). The proportion of RBD monopositive individuals was 11-fold lower (8.1%; 95% CI: 7.0-9.2), and the proportion of Nc monopositive individuals was only 0.7% (95% CI: 0.4-1.1). Differences between seropositivity levels in the entire cohort (Table 3) and among vaccinated individuals (Table 4) were not statistically significant.

As noted above, a total of eight different vaccines created on four platforms were used in the process of mass vaccination (Table 5). Vaccines from different platforms can have different compositions and, obviously, effectiveness. Therefore, we initially analyzed possible differences in volunteer seroprevalence based on the platforms used for vaccine production (Tables 6-8).

Out of 1,296 volunteers who had received vector vaccines, 90.3% (95% CI: 88.5-91.8) were double positive (Nc^+RBD^+) (Table 6). Those monopositive for RBD represented 8.9% (7.4-10.6), and those monopositive for Nc represented only 0.3% (95% CI: 0.08-0.8). The results were not significantly different from the level of herd immunity in the cohort (Table 2).

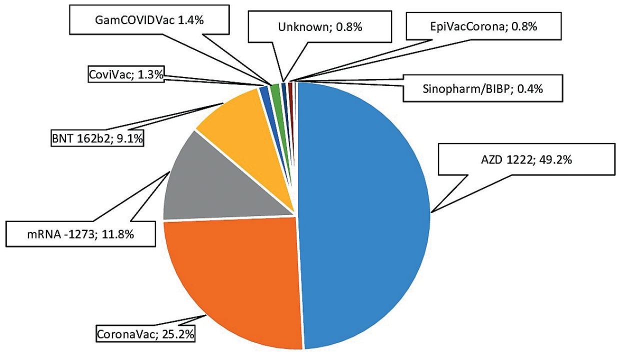

Figure 11. Range of preparations used to vaccinate volunteers

Among those immunized with WVV, similar results were obtained (Table 7). The proportion double positive (Nc^+RBD^+) was 93.2% (95% CI: 91.0-94.9). The proportion RBD monopositive was lower (4.5%; 95% CI: 3.1-6.3) compared with that following use of vector vaccines (Table 6). The differences were significant ($p < 0.001$). In contrast, the proportion monopositive for Nc was 1.6% (95% CI: 0.8-2.8). The differences were significant (compared to immunization with vector vaccines) at $p < 0.001$. It can be assumed that the higher 'monopositive for Nc' values when using whole-virion inactivated vaccines is associated with the presence of Nc antigens in their composition.

The third platform group, mRNA-based vaccines, included two preparations: mRNA-1273 and BNT162b2 (Table 8). Analysis drew attention to the smaller share of Nc^+RBD^+ volunteers. The decrease is noticeable, although not significant relative to total seroprevalence in vaccinated volunteers (Table 4).

Analysis to assess the structure of seroprevalence in response to whole-virion vaccines is simply for reference since WVVs contain a full range of antigenic determinants. From this point perspective, it is more

TABLE 3. HUMORAL IMMUNE RESPONSE OF UNVACCINATED VOLUNTEERS (n = 1113)

		Nc Abs status, n, % (95% CI)		Total, n, % (95% CI)
		Nc^+	Nc^-	
RBD Abs status	RBD^+	955 85.8 (83.6-87.7)	98 8.8 (7.2-10.6)	1053 94.6 (93.1-95.8)
	RBD^-	43 3.9 (2.8-5.2)	17 1.5 (0.9-2.4)	60 5.4 (4.1-6.9)
	total	998 89.7 (87.7-91.4)	115 10.3 (8.6-12.3)	1113 (100)

TABLE 4. HUMORAL IMMUNE RESPONSE IN THOSE VACCINATED AGAINST COVID-19 (n = 2540)

		Nc Abs status, n, % (95% CI)		Total, n, % (95% CI)
		Nc+	Nc-	
RBD Abs status	RBD+	2305 90.8 (89.6-91.8)	205 8.1 (7.0-9.2)	2510 98.8 (98.3-99.2)
	RBD-	17 0.7 (0.4-1.1)	13 0.6 (0.3-0.9)	30 1.2 (0.8-1.7)
	total	2322 91.4 (90.3-92.5)	218 8.6 (7.5-9.7)	2540 (100)

Note. Unknown vaccine data excluded.

TABLE 5. STRUCTURE OF VACCINES USED FOR VOLUNTEER IMMUNIZATION

Platform	Vaccine	Individuals vaccinated	Vaccination subtotals	
			n	% (95% CI)
vector	AZD1222	1260	1296	50.6 (48.7-52.5)
	Gam-COVID-Vac	36		
inactivated whole-virion	CoronaVac	644	688	26.9 (25.2-28.6)
	CoviVac	34		
	Sinopharm/BIBP	10		
mRNA	mRNA-1273	302	536	20.9 (19.4-22.6)
	BNT162b2	234		
peptide	EpiVacCorona	20	20	0.8 (0.5-1.2)
unknown*		21	21	0.8 (0.5-1.3)
	Total	2561	2561	100

Note. *, volunteers were unable to indicate the type of vaccine they received.

TABLE 6. STRUCTURE OF SARS-CoV-2 Abs SEROPREVALENCE AMONG VOLUNTEERS IMMUNIZED WITH VECTOR VACCINES (n = 1296)

		Nc Abs status n, % (95% CI)		Total, n, % (95% CI)
		Nc+	Nc-	
RBD Abs status	RBD+	1170 90.3 (88.5-91.8)	115 8.9 (7.4-10.6)	1285 99.2 (89.5-99.6)
	RBD-	4 0.3 (0.08-0.8)	7 0.5 (0.2-1.1)	11 0.8 (0.4-1.5)
	total	1174 90.6 (88.9-92.1)	122 9.4 (7.9-11.1)	1296 (100)

TABLE 7. STRUCTURE OF SARS-CoV-2 Abs SEROPREVALENCE AMONG VOLUNTEERS IMMUNIZED WITH WVV (n = 688)

		Nc Abs status n, % (95% CI)		Total, n, % (95% CI)
		Nc+	Nc-	
RBD Abs status	RBD+	641 93.2 (91.0-94.9)	31 4.5 (3.1-6.3)	672 97.7 (96.2-98.7)
	RBD-	11 1.6 (0.8-2.8)	5 0.7 (0.2-1.7)	16 2.3 (1.3-3.8)
	total	652 94.8 (92.8-96.3)	36 5.2 (3.6-7.2)	688 (100)

TABLE 8. STRUCTURE OF SARS-CoV-2 Abs SEROPREVALENCE AMONG VOLUNTEERS IMMUNIZED WITH mRNA VACCINES (n = 536)

		Nc Abs status n, % (95% CI)		Total, n, % (95% CI)
		Nc+	Nc-	
RBD Abs status	RBD+	475 88.6 (85.6-91.2)	58 10.8 (8.3-13.8)	533 99.4 (98.4-99.9)
	RBD-	2 0.4 (0.05-1.3)	1 0.2 (0.0-1.0)	3 0.6 (0.1-1.6)
	total	477 89.0 (86.0-92.0)	59 11.0 (8.5-14.0)	536 100

analogous to seroprevalence in people who have had natural infection (asymptomatic or overt COVID-19). Noteworthy is a noticeable, although not significantly lower proportion of individuals who are monopositive for Nc Abs following mRNA-based vaccination. This is likely explained by the absence in mRNA vaccines of determinants eliciting production of anti-Nc Abs.

In addition to analysis of seroprevalence by vaccine type (vector, whole-virion, mRNA), vaccine distributions by age and region were assessed (Figures 12, 13).

Of the four major vaccines, AZD1222 was the most commonly used. Peak use of this vaccine occurred in people aged 40 to 59 years. In other words, the active working population was more likely to be vaccinated with the AZD1222 vector vaccine. It was used for vaccination in the age groups 18-29 and 60-69 years significantly less often. Unfortunately, the authors failed to establish the reasons for such selectivity.

A different distribution was noted for the WVV CoronaVac. This preparation was more often used in the age groups 18-29 years and 60+; the others were used much less frequently. Obviously they were an additional, but not decisive, helpful factor influencing collective immunity.

The structure of vaccine type utilization in various Tajik regions and cities was characterized by significant heterogeneity (Figure 13, Table 11S, see Supplementary data). Those in the capital (Dushanbe city) and the Isfara district were more often vaccinated with AZD1222 or CoronaVac; BNT162b2 was significantly less frequently used. In Vahdat district, most of the population was vaccinated with the AZD1222 vector vaccine or mRNA-1273. The leaders in the predominant use of AZD1222 were the Kulob, Tursunzade and Panjakent districts, as well as Khuland and Bokhtar cities. Almost everywhere in the RT, the implementation frequency of other vaccines was much lower.

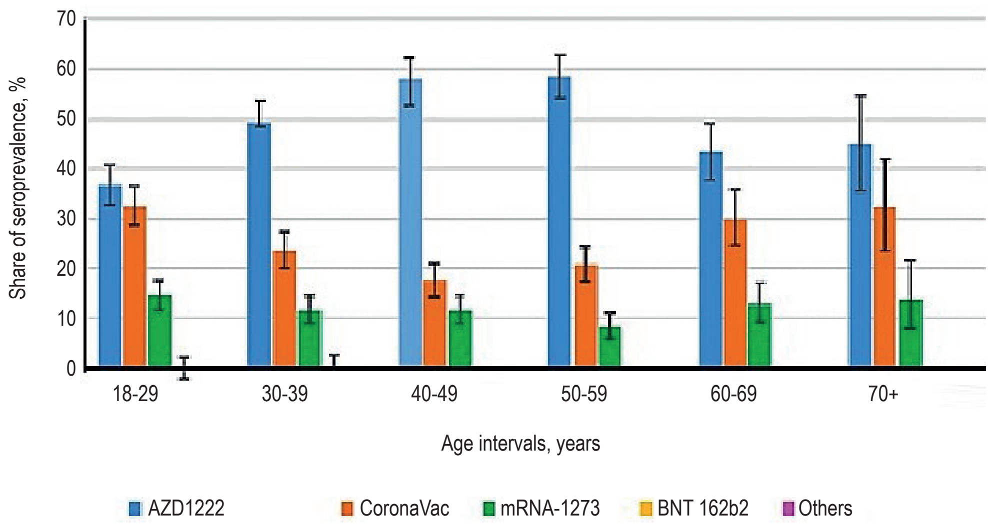

Figure 12. Distribution of vaccines used for immunization by age group (Table 10S, see Supplementary data)

Note. The age group 1-17 years old was excluded from analysis due to the small number of observations (< 0.4%). The legend shows the types of vaccines used (Figures 12, 13). Other refers to any other vaccines (see Table 5).

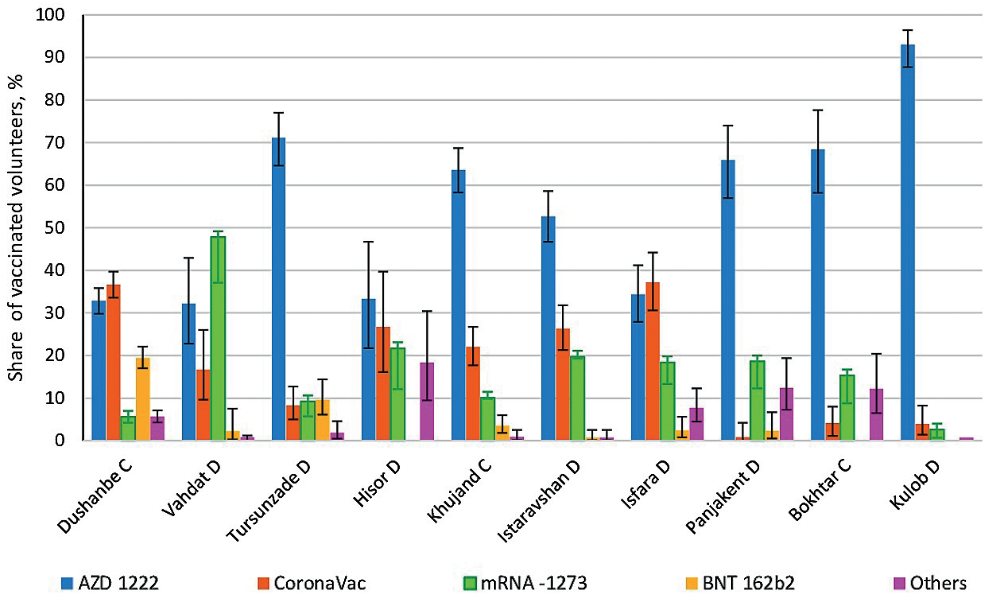

Figure 13. Distribution of vaccines used for immunization in Tajik districts (D) and cities (C)
Note. Black vertical lines are 95% confidence intervals.

Statistical analysis of the seroprevalence of Abs to the two main SARS-CoV-2 antigens revealed almost absolute herd immunity to the pathogen. A significant role in this achievement was played by the vaccines used in the RT. Eventually, they made it possible to reach a total seroprevalence of 99.5% (95% CI: 99.1-99.7). The outcome obtained convincingly confirms the effectiveness of the COVID-19 mass vaccination deployed among the population of the RT.

Discussion

The Republic of Tajikistan, as global data show [12, 18], is a regional leader in overcoming the COVID-19 pandemic. Considering that since the end of February 2022 there have been no registered cases of overt COVID-19 in the country, the epidemic situation can be qualified as favorable. A significant factor, that had a decisive influence in overcoming the COVID-19 pandemic, was undoubtedly mass vaccination in the country. It was launched in accordance with the Emergency COVID-19 Project, with support by the World Bank [7]. As of 05/19/2022, 91.3% of Tajik residents had completed vaccination (received 2 doses), undoubtedly due to the mass vaccination campaign.

This value was clearly reflected in the seroprevalence structure of the surveyed cohort of volunteers recruited from different Tajik regions (Figure 5). When analyzing the age structure of seroprevalence, it is worth noting a very high proportion of individuals seropositive for Nc and RBD Abs, ranging from 87-99% (Figure 2). In addition, there was a significantly lower Nc seroprevalence among children and young people aged 18-19 years, alongside significantly higher levels among those aged 70^{+} years. Interestingly, a similar situation was noted in bordering Kyrgyzstan [19]. In a number of Russian regions, predominant seroprevalence among children aged 1–17 years was noted, yet with reduced levels in volunteers aged 70^{+} [24, 31]. As for the proportion of seropositive individuals (RBD, OS), an almost absolute seroprevalence level of 97-99% was seen here (Figure 2).

With increasing serum concentration interval, quantitative analysis of Nc Abs distribution showed a shift from a 2^{nd} order polynomial (in the region 5 to 10% seropositivity, Abs range 17-31 BAU/mL) to a direct linear regression (tgα = 0.40), ranging from 17.1% (95% CI: 13.2 -21.6) among children (aged 1-17 years) to 22.3% (95% CI: 21.0-23.4) in those aged 70^{+} (Figure 3).

Different dynamics were observed with quantitative analysis of the distribution of RBD Abs seropositivity (Figure 4). The proportion RBD^{+} volunteers in the range 26.6 to 450 BAU/mL decreased linearly in the age intervals from 1 year to 70^{+} years. With an increase in the proportion of individuals with RBD Abs levels > 450 BAU/mL, the trend transformed upward, and the regression changed from linear to 2^{nd} order polynomial. This can likely be explained by longer overall lifetime contact with pandemic and seasonal coronaviruses in adults and the elderly compared with children. The Nc Abs distribution dynamics among people of different ages also supports the likelihood of such an assumption. However, this is still only a hypothesis that requires additional evidence.

The study was conducted in different Tajik geographic regions, with the exception of the Gorno-Badakhshan Autonomous Region. We assessed the influence of region of residence on the level of seroprevalence (Nc, RBD, OS). The results did not show a clear geographical zoning, although some individual features were noted in a number of areas (Figures 5, 14). When ranking regions by Nc seroprevalence, the lowest level was determined to be among residents of Khujand and Bokhtar cities; the highest was in Hisor district. Ranking by seroprevalence did not reveal geographic patterns. For example, the already noted city of Khujand is located in the north of the country, and the city of Bokhtar is in the south.

On the other hand, correspondence analysis (Figure 7) showed a high correlation between seropositivity frequency and districts (Isfara, Vahdat, Panjakent, Hisor) where the maximum shares of Nc Abs seropositivity were found. A low correlation was seen with Khujand city, where seropositivity, as indicated above, was lowest. However, it was not possible to identify any regional differences regarding seropositivity groups RBD and OS. In all cases, the measured indicators varied from 94.7% to 100%; any existing differences were not significant. Finally, even the minimum Nc seroprevalence in Khujand city was 83.4% (95% CI: 79.4-86.9), higher than the postulated threshold for cessation of epidemic processes [26, 28].

When assessing the influence of professional factors, heterogeneity was noted due to the distribution of volunteers by professional group. The largest number of volunteers in the cohort belonged to the group medical workers (Figure 7). Seropositivity values in this profession were: 91.8% (95% CI: 90.3-93.1) for Nc; 98.8% (95% CI: 98.2-99.3) for RBD; and 99.7% (95% CI: 89.4-100) for OS. For OS, differences were significant at ($p < 0.001$) relative to Nc and RBD. This result was expected since healthcare professionals are the most likely to come into contact with COVID-19 patients. It is no coincidence that medical personnel, especially those in infectious disease departments or hospitals, are a risk group for SARS-CoV-2 nosocomial infection frequency [10, 17]. The smallest proportion Nc seropositive was noted in the groups 'state + military employees' and 'manufacturing + agriculture + transport'. As for seropositivity groups RBD and OS, it varied from 93.8% (95% CI: 89.2-96.9) to 100.0% (Figure 9). This position was confirmed by correspondence analysis (Figure 10), which did not reveal a significant relationship between SARS-CoV-2 seroprevalence and occupation. The overall value of the χ^2 index of the performed correspondence analysis was 15.7416 ($p < 0.4712$).

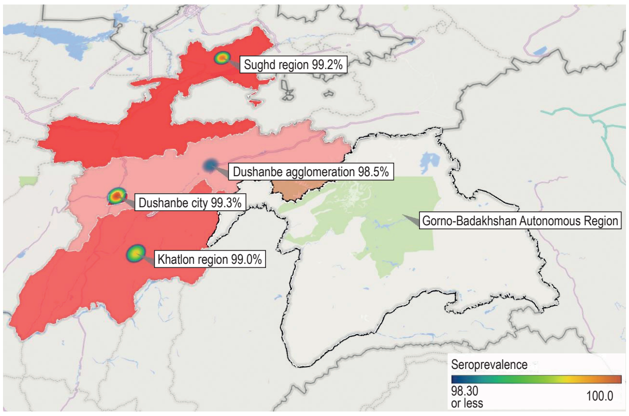

Figure 14. Heat map of seroprevalence levels in the surveyed Tajik regions

Note. Studies were not conducted in the Gorno-Badakhshan Autonomous Region. The seroprevalence scale is shown in the lower right corner.

The proportion of unvaccinated seropositive volunteers with no history of manifest COVID-19 (i.e., seropositive asymptomatic) was 92.8% (95% CI: 91.0-94.3). The largest shares of such individuals were found among volunteers in the age groups 1-17 (> 97%), 18-29 (> 97%), and among the elderly aged 70^+ (~100%) (Figure 10). The smallest number of asymptomatic [seropositive] volunteers was found among 50-49 years old, their proportion was 85%. Considering that this group included only unvaccinated volunteers without a history of confirmed COVID-19, it can be reasonably argued that asymptomatic forms of infection are widespread in the Republic. These may serve as an important component of the mechanism behind the formation of high collective immunity to SARS-CoV- 2.

An additional factor contributing to the almost complete cessation of COVID-19 incidence in the population during the second half of 2022 was, of course mass vaccination. The cumulative level of collective humoral immunity in the entire cohort was 99.1% (95% CI: 98.8-99.4). More specifically (Table 3), the shares were: 89.2% (95% CI: 88.2-90.2) for double positive (Nc^+RBD^+); 1.6% (95% CI: 1.2-2.1) for Nc monopositive; and 8.3% (95% CI: 7.4-9.2) for RBD monopositive. Such a high figure, of course, requires further analysis and interpretation.

Considering that 44.9% of the population were not vaccinated, we initially estimated the level of humoral immunity in this volunteer category (Table 4). Overall seropositivity in this group was 98.4% (96% CI: 97.6-99.1); differences with the herd immunity score in the entire cohort (Table 3) were not significant. A possible source of such a high seroprevalence could be COVID-19 convalescents. However, their share in the cohort was only 9.8% (95% CI: 8.8-10.8).

This is probably insufficient to significantly affect OS among unvaccinated volunteers. As such, it is logical to assume that the main reason for this phenomenon may be wide dissemination of asymptomatic infection among the Tajik population, including volunteers.

The high seropositivity in the unvaccinated Tajik population represents an important, yet auxiliary, component of herd immunity. The main role belongs to specific vaccination. As already emphasized, authorities carried out the important step of mass vaccination.

Something similar was done in Israel, using the BNT162b2 (mRNA) vaccine [6]. As of April 2021, 4,709,335 people (> 71% of the pop.) had completed vaccination in Israel [9]. It was an unprecedented action that gave hope for the elimination of COVID-19 in at least one country. However, after a short period of time, data on cases of disease among those vaccinated with BNT162b2 appeared [2]. According to the source, as early as 1-10 days after vaccination, 22 healthcare workers (of 4081 immunized) developed COVID-19. When the Delta variant appeared in Israel, the number of cases of overt infection among vaccinated individuals increased by 2 to 3-fold [5].

Unlike Israel, where only BNT162b2 was used, the RT used a tactic of mass immunization using vaccines from all major platforms (Table 6). To a certain extent, such usage was involuntary. Tajik medical authorities used vaccines received from international organizations and individual countries as assistance. Nonetheless, the variety gave the best result in terms of durable herd immunity.

When assessing seroprevalence among vaccinated volunteers (Table 5), the results practically did not differ from the humoral immunity level in general (Table 3). Seroprevalence among vaccinated individuals was 99.5% (95% CI: 99.1-99.7); differences from the total cohort were not significant. Among vaccines used in the RT, the most widespread was AZD1222. Its share, together with another vector vaccine Gam-COVID-Vac (Sputnik V, Sputnik Light), was 51.4% (95% CI: 49.5-53.4). The inactivated WVV family (CoronaVac, CoviVac) ranked second in terms of distribution, with a 27.3% share (95% CI: 25.6-29.1). Third place was taken by mRNA preparations (mRNA-1273, BNT162b2), whose contribution was 21.3% (95% CI: 19.7-22.9). The vaccine classes used, regardless of their prevalence, caused comparable levels of herd immunity among the population (Tables 7-8, not significant): vector – 99.4% (95% CI: 98.9-99.8); whole-virion – 99.3% (95% CI: 98.3-99.8); and vaccine mRNA – 99.8% (95% CI: 99.0-100).

Thus, it can be argued that the simultaneous or sequential use of preparations created on three main platforms during mass vaccination made it possible to achieve almost absolute immunity to SARS-CoV-2. In this regard, a detailed analysis of vaccine usage distribution by age, regional, and occupational factors did not bring any surprises. The largest number of people immunized with vector vaccines was noted among the able-bodied population aged 30 to 59 years (Figure 12). Whole-virion inactivated vaccines were also mainly received by able-bodied persons, albeit in a broader age range beginning younger (18 to 59 years). Messenger RNA preparations were distributed much less frequently, mainly in the same age intervals.

The smallest proportion vaccinated (any preparation) was noted among people aged 70+, probably due to contraindications in the group. Children aged 1-17 years were immunized only in isolated cases (any vaccine). Nuances of vaccine distribution by region were noted (Figure 13). In all Tajik territories, a prevalence of vector vaccines was noted. In Dushanbe city only, most individuals received a whole-virion inactivated vaccine, which was unexpected.

Conclusion

In summarizing our analysis of herd immunity among the Tajik population, we can make a cautious assumption that one of the likely factors in the formation of highly robust herd immunity may have been the simultaneous use of several vaccines produced on different platforms. The distribution among the population of the widest possible set of antigenic determinants made it possible to form the most diverse set of antibodies. This formed an impediment to spread of the pathogenic virus. Of course, such a hypothesis would not even be plausible without the conditions formed through the mass immunization campaign for the population undertaken by the authorities of the Republic of Tajikistan. A unique combination of social and biological factors made it possible to achieve maximum immunity to SARS-CoV-2, thus preventing further development of the epidemic process.

Conflict of interest: none.

Author contributions

AVP, NDJ – study planning; MMR, TAA – study organization; SDV, MMM, BTK – collection and primary processing of biomaterial;

AMM, ESA – organization of sample transportation; IVD, OVZ – laboratory study of biomaterial; VAI – database formation; AAK – statistical analysis; VSS, TAA, ESA – analysis of data received, writing and editing of the text; ESR – translation and editing of text.

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Supplementary data

TABLE 1S. VOLUNTEER QUESTIONNAIRE

Personal information:

1. Surname
2. Name
3. Middle name
4. Gender
5. Region and district of residence
6. Since what year have you been living in this region
7. Address of registration in the region according to the passport
8. Date of birth
9. Name of the parent or legal representative of the volunteer under 18
10. Your phone
11. Your e-mail
12. Field of activity
13. Place of work. position. type of activity

Special questions

1. Have you been given a PCR test for SARS-CoV-2? Specify result and date.
2. Have you been diagnosed with COVID-19? When was the diagnosis made? Was it complicated by pneumonia?
3. The presence of symptoms of acute respiratory infections on the date of filling out the questionnaire: Runny nose. cough. fever. other symptoms. Date of symptom onset.
4. Presence of chronic diseases: list
5. Have you had family or work contact with people with COVID-19? Specify a date.
6. Indicate where you are on the date of filling out the questionnaire:
   – In the hospital
   – Quarantined under observation
   – In quarantine at home
   – At home (I follow the announced regime)
   – I continue to work
7. Have you left the country in the last 3 months? Specify the country and date of return.
8. Have you traveled to other regions of the country in the last 3 months? Indicate from which region the return was and the date of return.
9. Have you taken immunomodulatory drugs since January 2020? Specify one immunomodulator from the pop-up list. How long?
10. Smoking (No/Yes/Quit)
11. Have you been vaccinated against COVID-19? The name of the vaccine. Date of first injection. Date of second injection
    11a. Reactions to the vaccine. indicate the reaction
    11b. Have you had a PCR test for COVID-19 after vaccination? Specify result and date
    11c. Have you been tested for antibodies to COVID-19 after vaccination? Specify result and date

Consent to participate in the study and the processing of personal data.
Consent to send the results of the study to the specified e-mail.
Date of filling out the Questionnaire (day. month. year)

TABLE 2S. POPULATION OF REGIONS CONTRIBUTING TO THE VOLUNTEER COHORT

Region	Population			Number of volunteers	Share of the region's population, % (95% CI)
	Total persons	Of them			
		Urban	Rural		
Dushanbe city	948,800	948,800	–	1,368	0.14 (0.14-0.15)
Vahdat district	352,000	62,300	289,700	137	0.04 (0.03-0.05)
Tursunzade district	312,400	58,400	254,000	283	0.09 (0.08-1.10)
Hisor district	315,500	42,600	272,900	82	0.03 (0.02-0.03)
Khujand city	196,400	196,400	-	404	0.21 (0.19-0.23)
Istaravshan district	282,200	60,900	221,300	373	0.13 (0.12-0.15)
Isfara district	281,200	60,700	220,500	372	0.13 (0.12-0.15)
Panjakent district	304,200	42,500	261,700	156	0.05 (0.04-0.05)
Bokhtar city	124,400	124,400	–	243	0.20 (0.17-0.22)
Kulob district	216,700	103,600	113,100	256	0.12 (0.11-0.13)
Overall	3,333,800	1,700,600	1,736,800	3,674	0.11 (0.11-0.11)

Note. The total population of the RT was 9,838,400 as of 10/01/2022.

TABLE 3S. DISTRIBUTION OF PARTICIPANTS BY AGE

Age group, years		Examined	
		n, persons	share, %
1-17		328	8.9
subgroup	1-6	30	9.2
	7-13	128	39.0
	14-17	170	51.8
18-29		761	20.7
30-39		733	20.0
40-49		632	17.2
50-59		648	17.6
60-69		408	11.1
70+		164	4.5
Overall		3674	100

TABLE 4S. DISTRIBUTION OF VOLUNTEERS BY ACTIVITY

Activity	Examined	
	n, persons	share, %
Medicine	1481	40.3
Unemployed	739	20.1
Pensioners	256	7.0
Pupils	278	7.6
Students	230	6.3
Education	205	5.6
Other	177	4.8
Office workers	74	2.0
Business	71	2.0
Government service	42	1.2
Science	39	1.1
Agriculture	18	0.5
Manufacturing	12	0.4
Transport	12	0.4
Military service	9	0.3
Creation	4	0.1
Preschoolers	27	0.8
total:	3674	100.0

TABLE 5S. VOLUNTEER SEROPREVALENCE BY AGE

Age group, years	Total, persons	Nc		RBD		OS	
		Overall	% (95% CI)	Overall	% (95% CI)	Overall	% (95% CI)
1-17	328	288	87.8 (83.8-91.1)*	306	93.3 (90.0-95.7)	322	98.2 (96.1-99.3)
18-29	761	668	87.8 (85.2-90.0)*	739	97.1 (95.7-98.2)	753	98.9 (97.9-99.5)
30-39	733	678	92.5 (90.3-94.3)*	717	97.8 (96.5-98.7)	727	99.2 (98.2-99.7)
40-49	632	588	93.0 (90.8-94.9)*	622	98.4 (97.1-99.2)	631	99.8 (99.1-100.0)
50-59	648	591	91.2 (88.7-93.3)*	640	98.8 (97.6-99.5)	646	99.7 (98.9-100.0)
60-69	408	370	90.7 (87.4-93.3)*	401	98.3 (96.5-99.3)	404	99.0 (97.5-99.7)
70+	164	156	95.1 (90.6-97.9)	159	96.9 (93.0-99.0)	161	98.2 (94.7-99.6)
total:	3674	3339	90.9 (89.9-91.8)	3584	97.5 (97-98)	3644	99.2 (98.9-99.4)

Note. *, differences with the data in the RBD or OS columns are statistically significant.

TABLE 6S. QUANTITATIVE DISTRIBUTION OF Nc Abs LEVELS AMONG VOLUNTEERS OF DIFFERENT AGE GROUPS

Age group, years	Total persons	Nc Abs Range, BAU/mL									
		17-31		32-124		125-332		333-666		> 667	
		n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
1-17	328	35	10.7 (7.6-14.5)	84	25.6 (21.0-30.7)	62	18.9 (14.8-23.6)	51	15.5 (11.8-19.9)	56	17.1 (13.2-21.6)
18-29	761	60	7.9 (6.1-10.0)	221	29.0 (25.8-32.4)	148	19.5 (16.7-22.4)	136	17.9 (15.2-20.8)	103	13.5 (11.2-16.2)
30-39	733	55	7.5 (5.7-9.7)	201	27.4 (24.2-30.8)	140	19.1 (16.3-22.1)	148	20.2 (17.3-23.3)	134	18.3 (15.6-21.3)
40-49	632	30	4.8 (3.2-6.7)	167	26.4 (23.0-30.1)	106	16.7 (13.9-19.9)	133	21.0 (17.9-24.3)	152	24.1 (20.8-27.6)
50-59	648	33	5.1 (3.5-7.1)	117	18.1 (15.2-21.2)	93	14.3 (11.7-17.3)	138	21.3 (18.2-24.7)	210	32.4 (28.8-36.2)
60-69	408	33	8.1 (5.6-11.2)	87	21.3 (17.4-25.6)	69	16.9 (13.4-20.9)	72	17.6 (14.1-21.7)	109	26.7 (22.5-31.3)
70⁺	164	10	6.1 (3.0-10.9)	40	24.4 (18.3-31.7)	29	17.7 (12.1-24.4)	23	14.0 (9.1-20.3)	54	32.9 (25.8-40.7)
total:	3674	256	7.0 (5.4-7.8)	917	25.0 (23.6-26.4)	647	17.6 (16.4-18.8)	701	19.1 (17.8-20.4)	818	22.3 (21.0-23.6)

TABLE 7S. QUANTITATIVE DISTRIBUTION OF Nc Abs LEVELS AMONG VOLUNTEERS OF DIFFERENT AGE GROUPS

Age group, years	Total persons	RBD Abs Range, BAU/mL					
		22.6-220		221-450		> 450	
		n	% (95 CI)	n	% (95% CI)	n	% (95% CI)
1-17	328	94	28.7 (23.8-33.9)	102	31.1 (26.1-36.4)	110	33.5 (28.4-38.9)
18-29	761	185	24.3 (21.3-27.5)	228	30.0 (26.7-33.3)	326	42.8 (39.3-46.4)
30-39	733	119	16.2 (13.6-19.1)	188	25.7 (22.5-29.0)	410	55.9 (52.2-59.6)
40-49	632	73	11.5 (9.2-14.3)	113	17.9 (15.0-21.1)	436	69.0 (65.2-72.6)
50-59	648	57	8.8 (6.7-11.2)	102	15.8 (13.0-18.8)	481	74.2 (70.7-77.6)
60-69	408	55	13.5 (10.3-17.2)	67	16.4 (13.0-20.4)	279	68.4 (63.6-72.9)
70⁺	164	15	9.1 (5.2-14.6)	24	14.6 (9.6-21.0)	120	73.2 (65.7-79.8)
Overall	3674	598	16.3 (15.1-17.5)	824	22.4 (21.1-23.8)	2162	58.8 (57.2-60.4)

TABLE 8S. SARS-CoV-2 Abs SEROPOSITIVITY AMONG VOLUNTEERS, BY SURVEYED REGION

City (C) or Districts (D)	Total persons	Seropositivity Group					
		Nc		RBD		OS	
		n	Share, % (95% CI)	n	Share, % (95% CI)	n	Share, % (95% CI)
Dushanbe, C	1368	1239	90.6 (88.9-92.1)	1332	97.3 (96.4-98.1)	1359	99.3 (98.7-99.7)
Vahdat, D	137	131	95.6 (90.7-98.4)	134	97.8 (93.7-99.6)	136	99.3 (97.8-100.0)
Tursunzade, D	283	249	88.0 (83.6-91.5)	275	97.2 (94.5-98.8)	279	98.5 (96.4-99.6)
Hisor, D	82	80	97.6 (91.5-99.7)	79	96.3 (89.7-99.2)	81	98.8 (93.4-100.0)
Khujand, C	404	337	83.4 (79.4-86.9)	395	97.8 (95.8-99.0)	399	98.8 (97.1-99.6)
Istaravshan, D	373	351	94.1 (91.2-96.3)	369	98.9 (97.3-99.7)	372	99.7 (98.5-100.0)
Isfara, D	372	355	95.4 (92.8-97.3)	363	97.6 (95.5-98.9)	368	98.9 (97.3-99.7)
Panjakent, D	156	151	96.8 (92.7-99.0)	154	98.7 (95.5-99.8)	155	99.4 (96.5-100.0)
Bokhtar, C	243	213	87.6 (82.8-91.5)	230	94.7 (91.0-97.1)	239	98.4 (95.8-99.5)
Kulob, D	256	233	91.0 (86.8-94.2)	253	98.8 (96.6-99.8)	255	99.6 (97.8-100.0)
Overall	3674	3339	90.9 (89.9-91.8)	3584	97.5 (97.0-98.0)	3644	99.2 (98.8-99.4)

TABLE 9S. DISTRIBUTION OF SEROPOSITIVE VOLUNTEERS BY ACTIVITY

Occupation	Examined people		Nc Abs		RBD Abs		Overal seroprevalence	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Civil Service + Army	51	1.4 (1.1-1.8)	43	84.3 (71.7-93.0)	50	98.0 (89.6-100.0)	50	98.0 (89.6-100.0)
Industry + agriculture + transport	42	1.1 (0.8-1.5)	36	85.1 (74.5-94.6)	41	97.6 (87.4-99.9)	41	97.6 (87.4-99.9)
Business	71	2.0 (1.5-2.4)	62	87.3 (77.3-94.0)	69	97.2 (90.2-99.7)	71	100
Children+scoolars	305	8.3 (7.4-9.2)	270	88.5 (84.4-91.9)	287	94.1 (90.8-96.5)	301	98.7 (96.7-99.6)
Other	177	4.8 (4.2-5.6)	158	89.3 (83.8-93.4)	166	93.8 (89.2-96.9)	172	97.2 (93.5-99.1)
Students	230	6.3 (5.5-7.1)	208	90.4 (85.9-93.9)	224	97.4 (94.4-99.0)	226	98.3 (95.6-99.5)
Unemployed	739	20.1 (18.8-21.4)	671	90.8 (88.5-92.8)	716	96.9 (95.4-98.0)	732	99.1 (98.1-99.6)
Education	205	5.6 (4.9-6.4)	188	91.7 (87.1-95.1)	204	99.5 (97.3-100.0)	205	100
HealthWorkers	1481	40.3 (38.7-41.9)	1359	91.8 (90.3-93.1)	1464	98.8 (98.2-99.3)	1478	99.7 (89.4-100.0)
Office workers	74	2.0 (1.6-2.5)	68	91.9 (83.2-97.0)	70	94.6 (86.7-98.5)	73	98.6 (92.7-100.0)
Retired people	256	7.0 (6.2-7.8)	236	92.2 (88.2-95.2)	250	97.7 (95.0-99.1)	252	98.4 (96.1-99.6)
Science + creativity	43	1.2 (0.8-1.6)	40	93.0 (80.9-98.5)	43	100	43	100
Overall	3674	100	3339	90.9 (89.9-91.8)	3584	97.5 (97.0-98.0)	3644	99.2 (98.8-99.4)

TABLE 10S. DISTRIBUTION OF VACCINES USED, BY AGE GROUP

Age group, years	Exami-ned	Vaccinated		Vaccine Used									
				AZD1222#		CoronaVac#		mRNA-1273#		BNT 162b2#		Others#*	
		n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
1-17$	328	11	3.4 (1.7-5.9)	3	27.3 (6.0-61.0)	3	27.3 (6.0-61.0)	2	18.2 (2.3-51.8)	2	18.2 (2.3 -51.8)	1	9.1 (0.2-41.3)
18-29	761	554	72.8 (69.5-75.9)	203	36.6 (32.6-40.8)	188	33.9 (30.0-38.1)	80	14.4 (11.6-17.7)	46	8.3 (6.1-10.9)	37	6.7 (4.8-9.1)
30-39	733	552	75.3 (72.1-78.5)	273	49.5 (45.2-53.7)	130	23.6 (20.1-27.3)	64	11.6 (9.0-14.6)	50	9.1 (6.8-11.8)	35	6.3 (4.5-8.7)
40-49	632	510	80.7 (77.4-83.7)	296	58.0 (53.6-62.4)	89	17.5 (14.3-21.0)	59	11.6 (8.9-14.7)	48	9.4 (7.0-12.3)	18	3.5 (2.1-5.5)
50-59	648	520	80.3 (77.0-83.3)	304	58.5 (54.1-62.7)	108	20.8 (17.4-24.5)	43	8.3 (6.1-11.0)	55	10.6 (8.1-13.5)	10	1.9 (0.9-3.5)
60-69	408	305	74.8 (70.3-78.9)	132	43.3 (37.6-49.1)	91	29.8 (24.8-35.3)	39	12.8 (9.3-17.1)	28	9.2 (6.2-13.0)	15	4.9 (2.8-8.0)
70+	164	109	66.5 (58.7-73.6)	49	45.0 (35.4-54.8)	35	32.1 (23.5-41.7)	15	13.8 (7.9-21.7)	5	4.6 (1.5-10.4)	5	4.6 (1.5-10.4)
Overall	3674	2561	69.7 (68.2-71.2)	1260	49.2 (47.3-51.1)	644	25.2 (23.5-26.9)	302	11.8 (10.6-13.1)	234	9.1 (8.1-10.3)	121	4.8 (4.0-5.6)

Note. $, data for child subgroups (1-17 years old) are not presented due to an insufficient number of observations; #, calculation of the proportion of persons vaccinated with a specific vaccine is relative to the column 'Vaccinated'; *, combined results of immunization with others (Gam-COVID-Vac, CoviVac, EpiVacCorona).

TABLE 11S. DISTRIBUTION OF SEROPREVALENT VOLUNTEERS BY PLACE OF RESIDENCE

Cuty (C) or District (D)	Examined	Include vaccinated		AZD		CoronaVac		mRNA1273		BNT 162b2		Others	
		n	% (95%CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Dushanbe C	1368	973	71.1 (68.7-76.5)	319	32.8 (29.8-35.8)	356	36.6 (33.6-39.7)	54	5.6 (7.2-7.2)	189	19.4 (17.0-22.1)	55	5.7 (4.3-7.3)
Vahdat D	137	90	65.7 (57.1-73.6)	29	32.2 (22.8-42.9)	15	16.7 (9.6-26.0)	43	47.8 (37.1-59.6)	2	2.2 (0.3-7.8)	1	0.8 (0.2-4.5)
Tursunzade D	283	218	77.0 (71.7-81.8)	155	71.7 (64.6-77.0)	18	8.3 (5.0-12.7)	20	9.2 (5.7-13.8)	21	9.6 (6.1-14.1)	4	1.8 (0.5-4.6)
Hisor D	82	60	73.2 (62.2-82.4)	20	33.3 (21.7-46.7)	16	26.7 (16.1-39.7)	13	21.7 (12.1-34.2)	0	0	11	18.3 (9.5-30.4)
Khujand C	404	346	85.6 (81.8-88.9)	220	63.6 (58.3-68.7)	76	22.0 (17.7-26.7)	35	10.1 (7.2-13.8)	12	3.5 (1.8-6.0)	3	0.9 (0.2-2.5)
Istaravshan D	373	285	76.4 (71.8-80.6)	150	52.6 (46.7-58.6)	75	26.3 (21.3-31.8)	56	19.7 (15.2-24.7)	2	0.7 (0.1-2.5)	2	0.7 (0.1-2.5)
Isfara D	372	207	55.7 (50.4-60.8)	71	34.3 (27.9-41.2)	77	37.2 (30.6-44.2)	38	18.4 (13.3-24.3)	5	2.4 (0.8-5.6)	16	7.7 (4.5-12.3)
Panjakent D	156	129	82.7 (75.8-88.3)	85	65.9 (57.0-74.0)	1	0.8 (0.02-4.20)	24	18.6 (12.3-26.4)	3	2.3 (0.5-6.7)	16	12.4 (7.3-19.4)
Bokhtar C	243	98	40.3 (31.1-46.8)	67	68.4 (58.2-77.4)	4	4.1 (1.1-10.1)	15	15.3 (8.8-24.0)	0	0	12	12.2 (6.5-20.4)
Kulob D	256	155	60.6 (54.3-66.6)	144	93.0 (87.7-96.4)	6	3.9 (1.4-8.2)	4	2.6 (0.7-6.5)	0	0	1	0.7 (0.02-3.5)
Overall	3674	2561	69.7 (68.2-71.2)	1260	49.2 (47.3-51.1)	644	25.2 (23.5-26.9)	302	11.8 (10.6-13.1)	234	9.1 (8.1-10.3)	121	4.8 (4.0-5.6)