Original research

Dynamics of the development of the epidemic of coronavirus infection and assessment of population immunity to SARS-COV-2 in the territory of the Kyrgyz Republic

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Abstract

Objective: The aim of this study was to assess the dynamics of the development of the coronavirus infection epidemic and their relationship with the formation of population immunity to the SARS-CoV-2 virus among the population of the Kyrgyz Republic.

Methods: The seroepidemiological study is population-based, prospective, cross-sectional, stratified by five age categories and was conducted in all nine geographical regions of the Kyrgyz Republic. Primary health care (PHC) organizations were selected by random sampling method and a list of people from each PHC was used to randomly select participants. All respondents were included in the study based on their prior informed consent. Participants were interviewed about age, gender, present symptoms of disease, seeking health care and hospitalization. The study materials were sera and questionnaire data of those who consented to the study.

Results: Seroprevalence among population of the Kyrgyz Republic as a whole was in the first round -30.8% and in the second round -71.2%. The study of the seroprevalence rate by age showed that the lowest rates were found among children younger than 9 years: during the first round - (16.5 (1.4)%), in the second round - (51.4 (1.9)%). There was also an increase in the proportion of seropositive individuals in all regions. By region, seroprevalence in the first round ranged from 13.0% (9.7-16.3) to 62.7% (59.2-69.2), in the second round from 63.9 to 77.8%.

In the first round of the study 925/1446 (64.0%) (95% CI 61.5-66.5) seropositive individuals had symptoms of COVID-19, and in the second round 1696/3372 or 50.3% (48.6-52.0), respectively. According to the results of all study rounds, the proportion of seeking medical care among the seropositive increases in parallel with the increasing age, so in the first round it ranged from 10.0 to 27.5% and in the second round from 6.2 to 37.5%.

Conclusion: With the increasing prevalence of coronavirus infection, seroprevalence to SARS-CoV-2 virus increased in parallel, so that from July 2020 to February 2021 it increased by 2.3-fold, from 30.8% to 71.2%. By February 2021, 28.8% of the population remained susceptible to coronavirus infection. Among children aged 0-9 years, only 23.8% had symptoms of coronavirus infection, while in adults over 65 years of age- 60.3% had symptoms, which is 2.5 times higher than in children. Due to increased awareness of the population on prevention of coronavirus infection in the second round of the study, the percentage of seeking medical care increased by 3.6% compared to the first round (25.4% vs. 21.8%). Also, with the increasing possibility of hospitalization in the healthcare system of Kyrgyz Republic, the proportion of hospitalized patients increased by 4.6% (10.1% vs. 5.5%).

Key words: coronavirus infection, SARS-COV-2, seroepidemiological study, morbidity, population immunity, seropositivity

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Introduction

At the end of 2019, humanity faced a new biological threat, when the first case of a new severe pneumonia with an unclear etiology was registered in the Chinese city of Wuhan (1,2). On January 30, 2020, the World Health Organization (WHO) declared a public health emergency of international concern (3). Lightning-fast global spread of the new pathogen, frequent cases of a severe course of disease, often ending with a fatal outcome, served as a justification for the WHO declaration of the beginning of a pandemic(4).

Despite preventive measures to prevent the importation of this infection in the Kyrgyz Republic, on March 18, 2020, three citizens who returned from a small hajj from Saudi Arabia were diagnosed with COVID-19 (5).

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Graphical abstract

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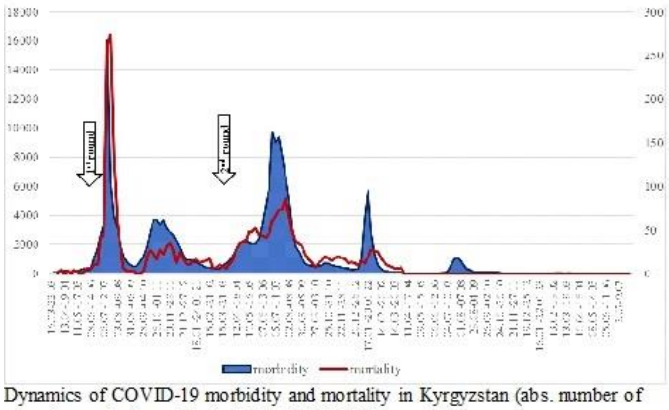
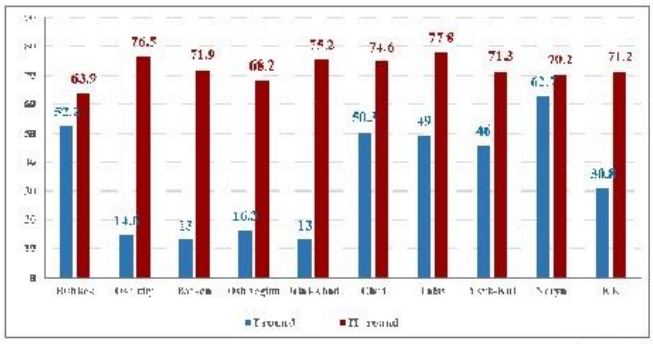
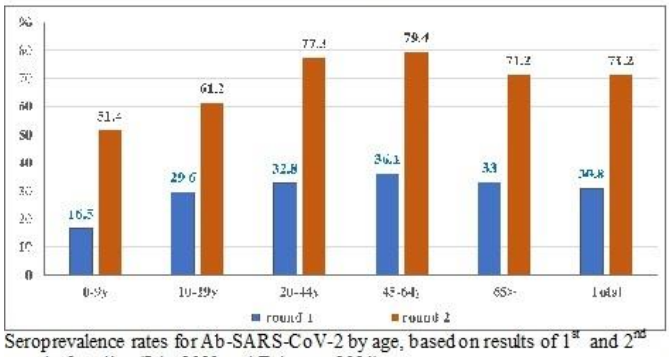


Dynamics of COVID-19 morbidity and mortality in Kyrgyzstan (abs. number of cases by weeks from March 2020 to 30.07.2023)



Seroprevalence rates for Ab-SARS-CoV-2 by age, based on results of 1st and 2nd round of studies (July 2020 and February 2021)



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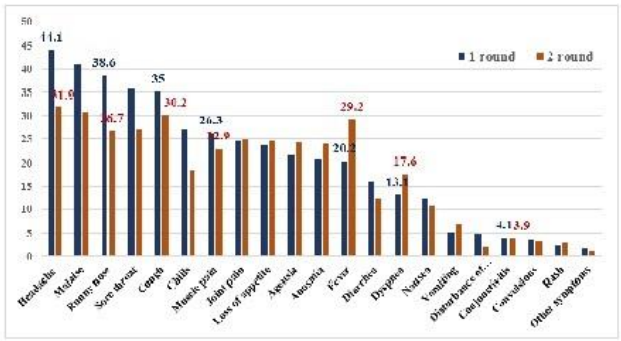

Proportion of symptomatic individuals among seropositive individuals in 1st and 2nd round of the study (July 2020 and February 2021)

Later on, during 3 months sporadic incidence of up to 100 cases was registered on the territory of the Kyrgyz Republic, and only from the 25th week of 19.06.2020 the number of infected people started to increase continuously. From the moment of registration of the first COVID-19 cases in the Republic, the emergency regime and state of emergency were introduced (6, 7). Due to the need to restore economic stability, economically significant facilities began to open in stages from 10 May 2020. The activities of public transport and facilities related to food security and nutrition of the population have been partially resumed. At the end of June 2020, the anti-epidemic measures among the population weakened and mass events, wedding celebrations and wakes began to be held, which caused a sharp increase in the incidence of disease (8).

Throughout 2020, the disease occurred in two waves. The first wave of morbidity, rather high, was observed in all regions of the country in the period from June to mid-August. Duration of the first wave was 65 days from 19.06. to 22.08.2020 and the peak of cases was registered on 29 weeks 160,626 cases of SARS-CoV-2. The number of infected persons during the entire period of the wave was 40,232. The second, longer (100 days) wave started at the end of September and peaked in early November at 45 weeks 3,941 cases. A total of 35,526 cases were registered during the second wave. By July 2021, the incidence of the disease was widespread throughout the territory of the Republic, with 554.8 cases per 100,000 population, and the number of deaths totalled 933, with a mortality rate of -2.6% (Fig. 1) (5).

To assess the true prevalence of COVID-19, the process of formation of post-infectious humoral immunity, to forecast the development of the epidemiological situation, to identify the features of the epidemic process, as well as to plan measures for specific and non-specific prevention of the disease, two rounds of a seroepidemiological study were conducted in 2020-2021 to study population immunity to the SARS-CoV-2 coronavirus (9-13).

The purpose of this study is to assess the dynamics of the development of the coronavirus infection epidemic and their relationship with the formation of population immunity to the SARS-CoV-2 virus among the population of the Kyrgyz Republic.

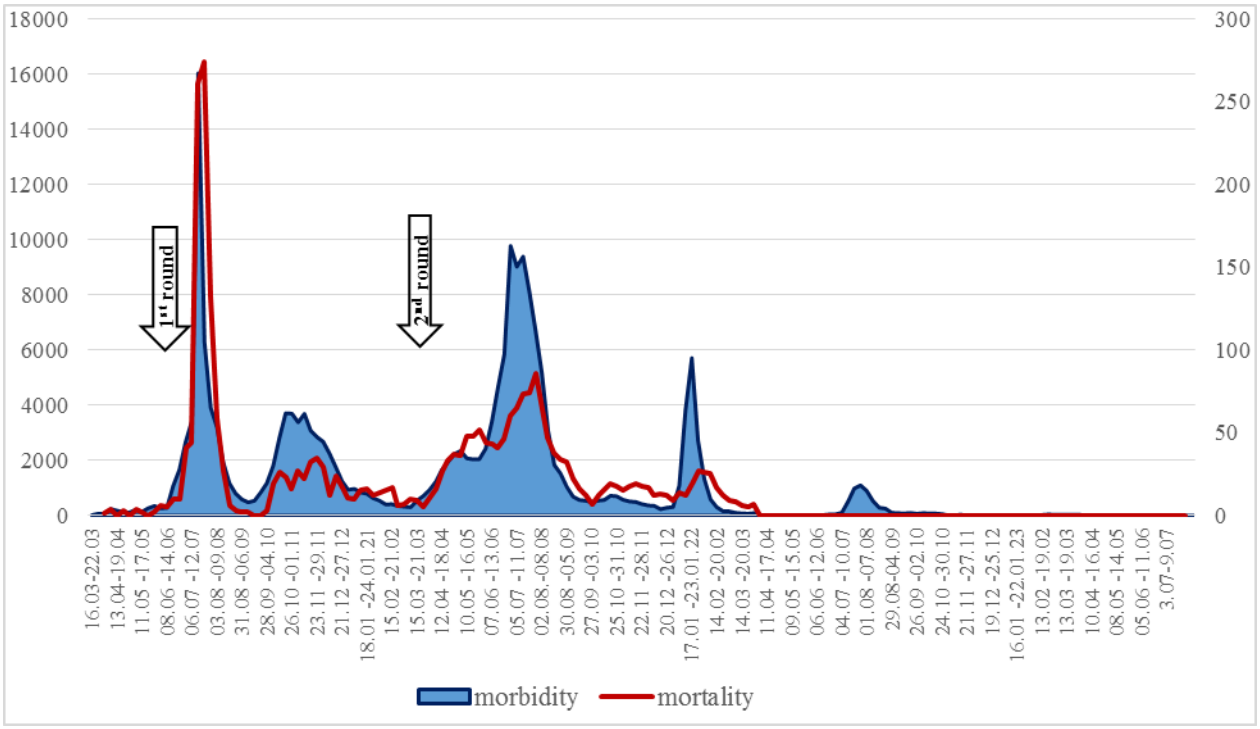

Figure 1. Dynamics of COVID-19 morbidity and mortality in Kyrgyzstan (absolute number of cases by weeks from March 2020 to 30.07.2023)

Methods

Study design and population

The seroepidemiological study is population-based, prospective, cross-sectional, stratified by five age categories and conducted in all nine geographical regions of the Kyrgyz Republic. The study is designed to provide data on the main epidemiological and serological patterns of SARS-CoV-2 virus spread.

The study material was serologic and epidemiological data of the persons who consented to the study, as well as COVID-19 reporting data from public health organizations.

The studies were conducted with technical assistance from WHO within the framework of a program to assess population immunity to SARS-CoV-2 in the population of the Kyrgyz Republic.

The selection of participants for the study was carried out by random sampling, medical organizations of primary health care (PHC) were selected in all 9 regions of the country. From the list of the population assigned to the selected PHC organizations, participants were randomly recruited to participate in the survey. Participants were interviewed about age, gender, symptoms of the disease, healthcare seeking behavior, hospital admission and frequency of disease symptoms manifestation.

The population, registered in the electronic health system in the country, were used as the sampling frame, where as of January 1, 2020, total of 6,456,515 people were registered. Health insurance is universal, and all citizens are registered in the e-health system (Tables 1 and 2).

The sample size will be calculated using the on-line statistical formula at:

http://www.openepi.com/Menu/OE_Menu.htm

For the sample size calculation, we hypothesized 50% i.e. unknown prevalence of antibodies in the general population. The estimated population size for this sero-prevalence survey is **384** individuals:

n =(DEFF*Np (1-p)) /((d2 / Z21- α / 2 * (N-1) + p * (1-p))

Where:

n = sample size

N = population = 6,456.515

p = Hypothesized % frequency of outcome factor in the population = 50%+/-5

d = Confidence limits as % of 100 (absolute +/- %) = 5%

D = Sample/design effect (for cluster surveys) = 1.

If we account for non-response rate of 25% than the total sample size would be 384+25%= 480 participants.

Table 1. Population of Kyrgyzstan by age groups and regions, according to the system of E- health records as of 01.01.2020.

Regions	Age Groups					Total population size (absolute number)	Fraction/ Share of population
	0-9	10-19	20-44	45-64	65 +		
Bishkek City	226569	133621	423247	195532	61611	1040580	16.1
Osh City	71840	46343	125310	50660	11840	305993	4.7
Batken region	138156	90423	199578	82111	20977	531245	8.2
Osh region	344896	245352	504353	209183	51174	1354958	21.0
Jalal-Abad region	298054	219282	468071	194421	46764	1226592	19.0
Chui region	216976	143094	342779	186726	60934	950509	14.7
Talas region	64785	53004	92212	42644	12751	265396	4.1
Issyk-Kul region	109007	88736	174917	92100	28147	492907	7.6
Naryn region	66220	58216	99781	48961	15157	288335	4.5
Total	1536503	1078071	2430248	1102338	309355	6,456,515	100.0

Table 2. Proportion of population of Kyrgyzstan by region and age for determining the sample for seroepidemiological study (1.01.2020)

Regions	Age Groups					Total population size	Selected group
	0-9	10-19	20-44	45-64	65+		
Bishkek City	21,8	12.8	40.7	18.8	5.9	100	699
Osh City	+23.5	15.1	41.0	+16.6	3.9	100	206
Batken region	26.0	17.0	37.6	15.5	3.9	100	357
Osh region	+25.5	18.1	37.2	15.4	3.8	100	911
Jalal-Abad region	24.3	17.9	38.2	15.9	3.8	100	825
Chui region	22.8	15.1	36.1	19.6	6.4	100	639
Talas region	24.4	20.0	34.7	16.1	4.8	100	178
Issyk-Kul region	22.1	18.0	35.5	18.7	5.7	100	331
Naryn region	23.0	20.2	34.6	17.0	5.3	100	194
Total	23.8	+16.7	37.6	17.1	4.8	100	4340

1. Given the lack of true prevalence of SARS CoV-2 virus in the regions, "level of accuracy of the estimate", countries equated the expected incidence rate to 50%.
2. Confidence interval/limits) entered as 5,0%.
3. In the columns "Sample/Design Effect" and "Clusters" – we indicated the value "1". As a result, the sample size for each region was 384 people. Given that during the study some people may refuse to participate, some may not participate fully, some may fill out the questionnaire incompletely or illegibly, etc., some information will have to be excluded from the analysis. Considering these aspects, when calculating the sample, it is customary to increase its size by 15-25% of the original size/estimate, therefore, accordingly, we get: 384 x 25% = 480 people (Table 3).

The sample size was calculated based on the proportion of the population in each age group. The selection of persons for the study was carried out from the list of the assigned population by age groups.

The selection of individuals for the purpose of the study was done using a stepwise systematic selection method. The sampling step was carried out according to the formula K = N/n, where N is the size of the age group, n is the number of people selected in each age group.

For example, the age group 65 + made 1000 people in the area, served by PHC health care organization. The sample for study in this age group should be 24 people, which is 5% in accordance with the share of this age group in the total population in the serviced area.

Next, we calculated the sampling step using the formula: 1000 (population of a given age group): 24 (estimated number for the study) = 42 (every forty-second person in this age group should be included in the study). The choice of the district of each region (there are 9 in total) was carried out by identifying the largest number of reported cases of COVID-19 (14).

Table 3. Number of samples by eligible groups and age groups (N=4820)

Regions	Age Groups					Total Population Size	Health Workers
	0-9	10-19	20-44	45-64	65+		
Bishkek City	152	90	284	131	41	699	77
Osh City	48	31	84	34	8	206	23
Batken region	93	61	134	55	14	357	39
Osh region	232	165	339	141	34	911	101
Jalal-Abad region	200	147	315	131	31	825	91
Chui region	146	96	230	126	41	639	71
Talas region	43	36	62	29	9	178	20
Issyk-Kul region	73	60	117	62	19	331	37
Naryn region	45	39	67	33	10	194	21
Total	1033	725	1634	741	208	4340	480

Inclusion criteria: All individuals identified for recruitment into the investigation, irrespective of age, irrespective of acute or prior COVID-19 infection.

Individuals who refused to give informed consent or had a contraindication to venipuncture were not included in the study. Instead, the next respondent of similar gender and age on the assigned list of the family medicine center was included.

Ethics: All respondents were included in the study on the basis of their prior informed consent. Respondents were provided with an information notice about the processing of their personal data within the survey in accordance with national requirements. Prior to the start of the study, an Ethical Committee opinion was obtained that the study is not in conflict with international ethical practices.

Variables

The study material was serologic and epidemiological data of the persons who consented to the study, as well as COVID-19 reporting data from public health organizations.

SARS-CoV-2 testing

Laboratory testing was carried out on the basis of the Republican Scientific and Practical Center for Quality Control of Laboratory Diagnostics of Infectious Diseases at the National Institute of Public Health of the Ministry of Health of the Kyrgyz Republic by ELISA method using the test system "SARS-CoV-2-Ab ELISA WANTAI PRC" to determine total antibodies (IgM, IgG) to SARS-CoV-2.

Protocol of the study

The first round was conducted in June 2020 according to the results of the questionnaire for serologic analysis was selected 4691 people, the second round was conducted 7 months later, from the first round of the study February 2021 examined 4735 people. The total cohort size was 9426 individuals. In each region, a cohort of volunteers was stratified into 5 age groups:

-0–9 age (1-round n =720; 2-round n =662)
-10–19 age (1-round n =575; 2-round n =822)
-20–44 age (1-round n =1840; 2-round n =1738)
-45–64 age (1-round n =1341; 2-round n =1322)
-65 and more (1-round n =209; 2-round n =191).

Statistical analysis

Statistical analysis of the data was carried out using the methods of variation statistics in the Excel program. Calculation of the prevalence of SARS-CoV-2 antibodies with a 95% confidence interval (CI) was carried out among the studied population by age, gender, regions and population with and without disease symptoms, seeking healthcare and/or hospitalized by the frequency of manifestation of disease symptoms throughout all stages of the study, correlation relationship between the time of examination and seropositivity.

Results

Seroprevalence among population of the Kyrgyz Republic as a whole amounted in the first round - 30.8% and in the second round-71.2%. According to the results of the second round of seroepidemiological study seroprevalence among the examined individuals in April 2021 was 71.2%, which shows a 2.3-fold increase in the proportion having antibodies to SARS-CoV-2 virus compared to the previous similar study, which was conducted at the end of July 2020.

Compared to the first round of the study, an increase in the proportion of seropositive individuals was noted in all age groups. In the first round of the study, seroprevalence by age groups ranged from 16.5 to 36.1%. The study of the seroprevalence level by age showed that the lowest rates were found among children under 9 years of age: during the first round it amounted to (16.5 (1.4)%), in the second round - (51.4 (1.9)%). In both rounds of the study, the indicators of all other age groups older than 9 years were almost same. In the second round the highest seroprevalence rates 77.3 (1.0)% and 79.4 (1.1)% were observed in socially active population groups from 20 to 64 years of age, who had a high risk of contact with asymptomatic COVID-19 patients and infected COVID-19 patients. Seroprevalences in different age groups of the population had statistically significant differences ($p<0.001$) except for age 65 and older (Table 4).

Table 4. Seroprevalence rates for Ab-SARS-CoV-2 by age. based on results of 1st and 2nd round of studies (July 2020 and February 2021)

Age Group, years	1st round				2nd round			
	Examined	Positive	95% CI	p	Examined	Positive	95% CI	p
0-9	726	120	16.5 (13.8-19.2)	< 0.001	662	340	51.4 (47.6 - 55.2)	< 0.001
10-19	575	170	29.6 (25.9-33.3)	< 0.001	822	503	61.2 (57.9 - 64.5)	< 0.001
20-44	1840	603	32.8 (30.7-34.9)	< 0.001	1738	1343	77.3 (75.3 - 79.3)	< 0.001
45-64	1341	484	36.1 (33.5-38.7)	< 0.001	1322	1050	79.4 (77.2 - 81.6)	< 0.001
≥65	209	69	33.0 (26.6-39.4)	< 0.1	191	136	71.2 (64.8 –77.6)	< 0.1
Total	**4691**	**1446**	**30.8 (29.5-32.1)**	**< 0.001**	**4735**	**3372**	**71.2 (69.9 - 72.5)**	**< 0.001**
Male	1480	403	27.2 (24.8-29.4)	< 0.001	1469	940	64.0 (61.5-66.5)	< 0.001
Female	3211	1043	32.5 (31.0-34.2)	< 0.001	3266	2432	74.5 (73.0-76.0)	< 0.001

A similar increase in the proportion of seropositive individuals was noted in all regions. By region, seroprevalence in the first round ranged from 13.0% (9.7-16.3) to 62.7% (59.2-69.2). The lowest seropositivity rates were in the Southern regions of the country. During the second round of study, the percentage of detection of seropositive samples was higher than in the first round, ranging from 70.2 to 77.8%. Seropositivity in many regions did not statistically significantly differ ($p>0.05$) from the Republican indicator (71.2 (0.7)), except for Bishkek, Talas region and Jalal-Abad region (Fig.2).

A direct average correlation ($r=0.598$) between the time of examination and the level of seropositivity among the examined population was established; the later the examination was conducted, the higher the level of seropositive results for Ab-SARS-CoV-2 (Fig. 3).

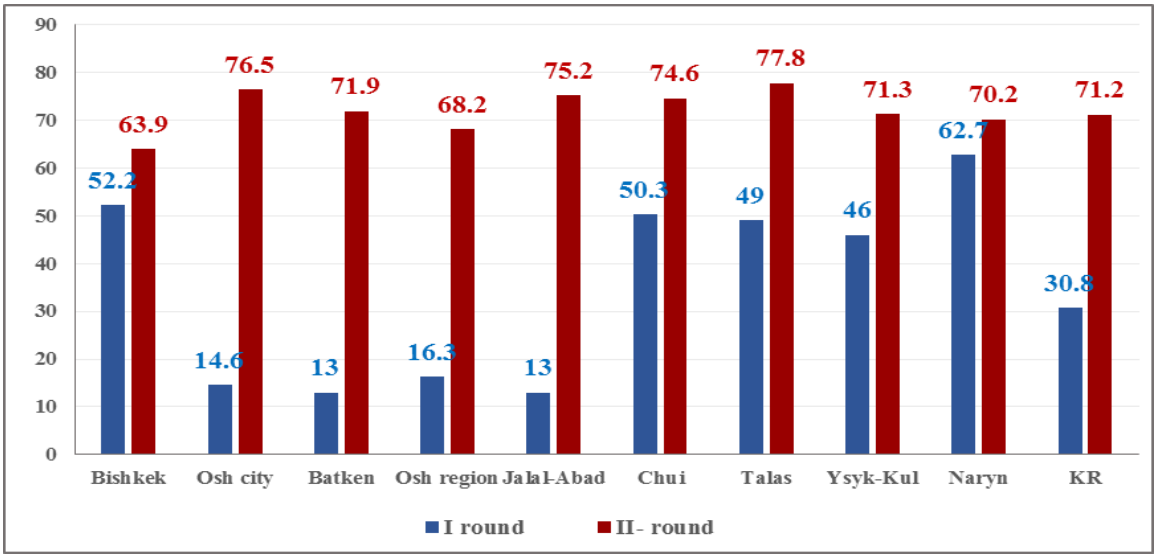

Figure 2. Seroprevalence rates for Ab-SARS-CoV-2 by age, based on results of 1st and 2nd round of studies (July 2020 and February 2021)

KR- Kyrgyz Republic

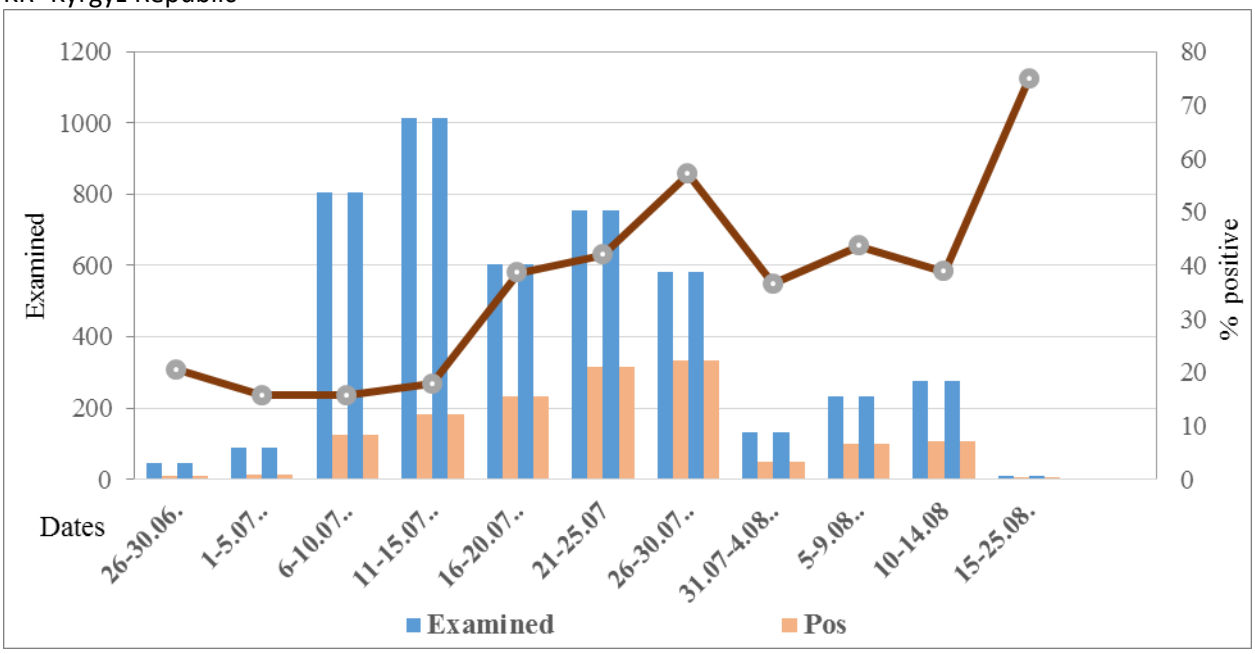

Figure 3. Analysis between the time of blood collection and seropositivity of examined individuals (July 2020, N= 4691)

Pos- positive

When analyzing the epidemiological and clinical data obtained, it was found that not all seropositive individuals had symptoms of coronavirus infection. In the first round of the study, out of 1446 seropositive individuals, 925 64.0% (61.5-66.5) had symptoms of COVID-19, and in the second round out of 3372 individuals 1696 - 50.3% (48.6-52.0) had symptoms, respectively. The rate of symptoms in seropositive individuals in the second round decreased by 21.5% compared to the data of the first round of the study (50.3 vs. 64.0%), which is in line with the trends of disease severity indicators in the Kyrgyz Republic.

The proportion of symptomatic individuals increased in parallel with increasing age both in the first round (45.0 to 71.0%) and in the second round (23.8 to 63.5%).

In both rounds of the study, a comparative analysis of the differences in the proportion of symptoms among seropositive individuals in different age groups was performed. According to the results of the analysis, at the age of 0-9 years, the symptoms of coronavirus infection were less (p<0.001) and at the age of 20-44 years, the symptoms were more (p<0.001) than the average statistical indicators for the Republic (Table 5).

Table 5. Analysis of symptomatic coronavirus infection among seropositive individuals (July 2020 and February 2021)

Age group, years	Seropositive with symptoms of COVID-19							
	1st round				2nd round			
	Examined	Pos	95% CI	P	Examined	Pos	95% CI	P
0-9	120	54	45.0 (36.1-53.9)	< 0.001	340	81	23.8 (19.3-8.3)	< 0.001
10-19	170	105	61.8 (54.5-69.1)	< 0.001	503	178	35.4 (31.2-9.6)	< 0.001
20-44	603	415	68.8 (65.1-72.5)	< 0.001	1343	716	53.3 (50.6-6.0)	< 0.001
45-64	484	302	62.4 (58.1-66.7)	< 0.001	1050	667	63.5 (60.6-6.4)	< 0.001
65 and >	69	49	71.0 (60.3-81.7)	< 0.01	136	82	60.3 (52.1-8.5)	< 0.01
Total	**1446**	**925**	**64.0 (61.5-66.5)**	< 0.001	**3372**	**1696**	**50.3 (48.6-2.0)**	< 0.001
Male	401	247	61.6 (56.8-66.4)	< 0.001	940	378	40.2 (37.1-3.3)	< 0.001
Female	1045	678	64.9 (62.0-67.8)	< 0.001	2432	1318	54.2 (52.2-6.2)	< 0.001

A comparative analysis of clinical symptoms and their occurrence among seropositive individuals in both rounds were also carried out. In the comparative analysis among all examined and among seropositive individuals in both rounds, the frequency of occurrence of disease symptoms was not equal. The onset of COVID-19 infection was most often manifested by symptoms of acute respiratory disease of varying severity. As the results of the study show, at the first round among seropositive patients the following symptoms were frequently encountered: headache (44.1%), malaise (41.1%), runny nose (38.6%), sore throat (35.6%), etc., which are typical for coronavirus infection. In the second round, the frequency of symptoms significantly decreased, which shows that the disease was mild compared to the first round (Fig. 4).

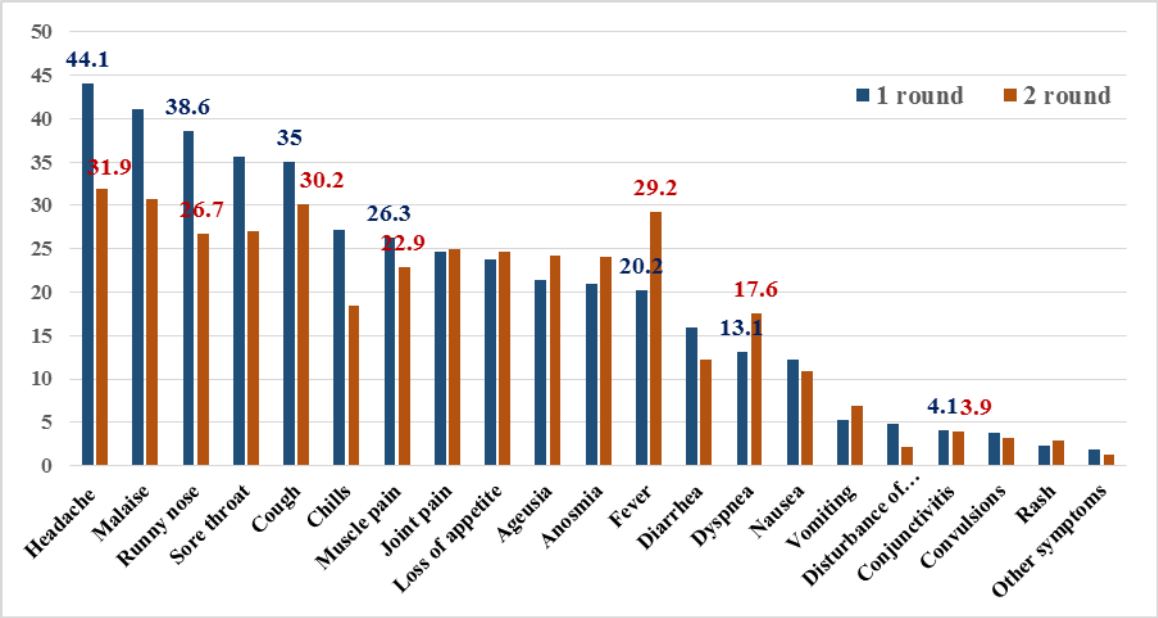

Figure 4. Proportion of symptomatic individuals among seropositive individuals in 1st and 2nd round of the study (July 2020 and February 2021)

The results of both rounds of the study show that with increasing age, the proportion of people seeking medical care grows in parallel in the first round ranged from 10.0 to 27.5 %, and in the second from 6.2 to 37.5%. Overall, the proportion of people seeking medical care increased by 16.5% compared to the first round of the study (25.4 vs. 21.8%). The proportion of hospitalized patients among seropositive individuals also increased by 83.6% (Table 6 and 7).

Table 6. Analysis of seeking medical care among seropositive individuals (July 2020 and February 2021)

Age group, years	Seeking medical care among seropositive individuals							
	1st round				2nd round			
	Examined	Pos	95% CI	p	Examined	Pos	95% CI	p
0-9	120	12	10.0 (4.6-15.4)	< 0.001	340	21	6.2 (3.6-8.8)	< 0.001
10-19	170	27	15.9 (10.4-21.4)	< 0.001	503	35	7.0 (4.8-9.2)	< 0.001
20-44	603	140	23.2 (19.2-26.6)	< 0.001	1343	360	26.8 (24.4-29.2)	< 0.001
45-64	484	117	24.2 (20.4-28.0)	< 0.001	1050	388	37.0 (34.1-39.9)	< 0.001
65 and >	69	19	27.5 (17.0-38.0)	< 0.1	136	51	37.5 (29.4-45.6)	< 0.001
Total	**1446**	**315**	**21.8 (19.7-23.9)**	**< 0.001**	**3372**	**855**	**25.4 (23.9-26.9)**	**< 0.001**
Male	401	85	21.2 (17.2-25.2)	< 0.001	940	189	20.1 (17.5-22.7)	< 0.001
Female	1045	230	22.0 (19.5-24.5)	< 0.001	2432	665	27.3 (25.5-29.1)	< 0.001
Pos - positive								

Table 7. Analysis of hospitalizations among seropositive individuals (July 2020 and February 2021)

Age group, years	Hospitalized among seropositive individuals							
	1st round				2nd round			
	Examined	Pos	95% CI	p	Examined	Pos	95% CI	p
0-9	120	2	1.7 (0.6-4.0)	< 0.001	340	0	0 (0-0)	< 0.001
10-19	170	5	2.9 (0.4-5.4)	< 0.001	503	4	0.8 (0-1.6)	< 0.001
20-44	603	34	5.6 (3.8-7.4)	< 0.001	1343	132	9.8 (8.2-11.4)	< 0.001
45-64	484	35	7.2 (4.9-9.5)	< 0.001	1050	183	17.4 (15.2-19.7)	< 0.001
65 and >	69	4	5.8 (0.3-11.3)	< 0.001	136	23	16.9 (10.6-23.2)	< 0.001
Total	**1446**	**80**	**5.5 (4.3-6.7)**	< 0.001	**3372**	**342**	**10.1 (9.1-11.1)**	< 0.001
Male	401	25	6.2 (3.1-7.5)	< 0.001	940	742	7.9 (6.2-9.6)	< 0.001
Female	1045	55	5.3 (3.9-6.7)	< 0.001	2432	268	11.0 (9.8-12.2)	< 0.001
Pos - positive								

Discussion

The epidemiological situation of the new coronavirus infection on the territory of the Kyrgyz Republic developed two months later than in other countries of the world. Registration of the first cases of COVID-19 was noted on March 18, 2020, further spreading throughout the republic.

The situation changed after the closure of the state border and the introduction of a number of anti-epidemic measures in the country, and as a result, there was no sharp increase in the incidence. The first maximum incidence rate was reached by the 27th week (June 29-July 05, 2020), when 6261 new cases of COVID-19 were registered (incidence rate 97.0‰). An average, 526 cases were detected per day. Starting from the 34th week (August 17-23, 2020), there was a decrease in the incidence to 100 cases of the weekly rate (5).

The dynamics of COVID-19 morbidity in the Republic is characterized by a two-wave structure. The first wave of coronavirus infection is associated with rapid spread of infection among the population in the summer period of 2020. In the first wave, the peak value of the number of infected people in the territories of the Republic was observed on the 29th week (July 13-19, 2020) with the registration of 16026 patients (21.7 ‰). In the whole Republic, the weekly dynamics of detection of new COVID-19 cases was characterized by a gradual increase from week 25 to week 34 (Fig. 1).

The next rise of morbidity started from 24.09.2020 to 01.01.2021 year with a peak of 3941 cases in the 45th week (November 2-8, 2020). The incidence rate for the whole period was 550.5 ‰. As of 01.07.2021, 126395 cases of COVID-19 were registered in the Republic. The total incidence rate per 100,000 population amounted to 1937.5. There were total 2009 deaths with confirmed diagnosis of COVID-19, mortality rate -1.6%, mortality rate - 30.8‰.

At the peak of the epidemic in July 2020 (30323 cases) and June-July 2021 (20274 to 37889 cases), the B variant of SARS-CoV-2 coronavirus was circulating.

According to the data obtained, the Indian variant (B.1.617.2, Delta) predominates in the samples collected in June-August 2021. Results of the study taken in June-July 2021, there were variants “British” (B.1.1.7, Alpha, 4 samples) and “South African” (B.1.351, Beta,1 sample), but these were no longer found in the August 2021 samples. The data indicate a coincidence with the global trend of the dominance of the Delta variant, which has caused a new wave of COVID-19 cases in the world (15).

Analysis of published data on COVID-19 incidence shows that the dynamics of coronavirus infection in each country has its own characteristics. This is due to many factors related to the level of economic development, the structure of health care, the speed and scope of restrictive measures taken by the government, the health and mentality of society as a whole, and other factors (16).

The results of the second round of population-based age-stratified seroepidemiological study of coronavirus 2019 (COVID-19) infection in the Kyrgyz Republic show that seroprevalence among the examined persons in the regions for the presence of antibodies against SARS-CoV-2 virus for the month of April was 71.2%. This shows increased the proportion of persons with antibodies by 2.3 times compared to the previous similar study, which was conducted at the end of July 2020 and seroprevalence was 30.8%. An increase in the proportion of seropositive individuals was noted in all age groups and regions. Vaccination in the Kyrgyz Republic started from March 29, 2021, therefore herd immunity is determined by post-infectious immunity.

In the first round of the study (July 2020), the analysis of seropositive samples detection by region showed that in the Southern regions of the country (Osh, Batken, Jalalabad regions and Osh city) the percentage of seropositive samples detection was low, ranging from 13 to 16.3% and statistically sharply different from the national indicator of 30.8% (95% CI 29.5-32.1). This is explained by the fact that these samples were collected in late June and early July 2020, i.e. before the first wave of the epidemic rise in the country. In the Northern regions (Chui, Naryn, Issyk-Kul, Talas regions and Bishkek city) of the country seroprevalence rates at the 1st round were significantly higher than in the South of the country and ranged from 46.0 to 62.7%. The high level of seroprevalence was due to the fact that the collection of analyses was conducted in the second half of July 2020, i.e. during the peak period of the rise in the incidence of COVID-19. It should also be noted that the rise in incidence in the Northern regions began 2-3 weeks earlier than in the South of the country.

In the second round seroprevalence in the Southern regions ranged from 68.2 to 76.5%, and in the northern regions from 63.9% to 77.8%. It should be noted that in contrast to the result of the first round of the study, in the second round seroprevalence in many Southern and Northern regions did not statistically significantly differ ($p>0.05$) from the republican indicator (71.2 (0.7)), insignificant differences were in Bishkek (63.9(1.7)), Talas (77.8)3.0)) and Jalal-Abad (75.2(1.4)) regions.

According to literature data, incidence rates and seropositivity in cities were higher than in rural areas. The high incidence rates and seropositivity of coronavirus infection in Bishkek city is due to the higher density of the population (6,806 personskm^2) compared to the republican (52 persons/km^2), Chui (42.9 persons/km^2) and Osh (42.4 persons/km^2) regions (17). And also the high incidence rate in Bishkek city and Chui oblast is presumably associated with high levels of population migration with other countries and within the country (Fig. 5).

An analysis of the results of seroprevalence among age groups of the population shows that as the time of the pandemic spread across the regions, there was a parallel increase in seroprevalence. The increase in seroprevalence was observed in all age groups, regardless of region. Seroprevalence in all age groups in first round ranged from 16.5 to 36.1%, second round 51.4-79.4%.

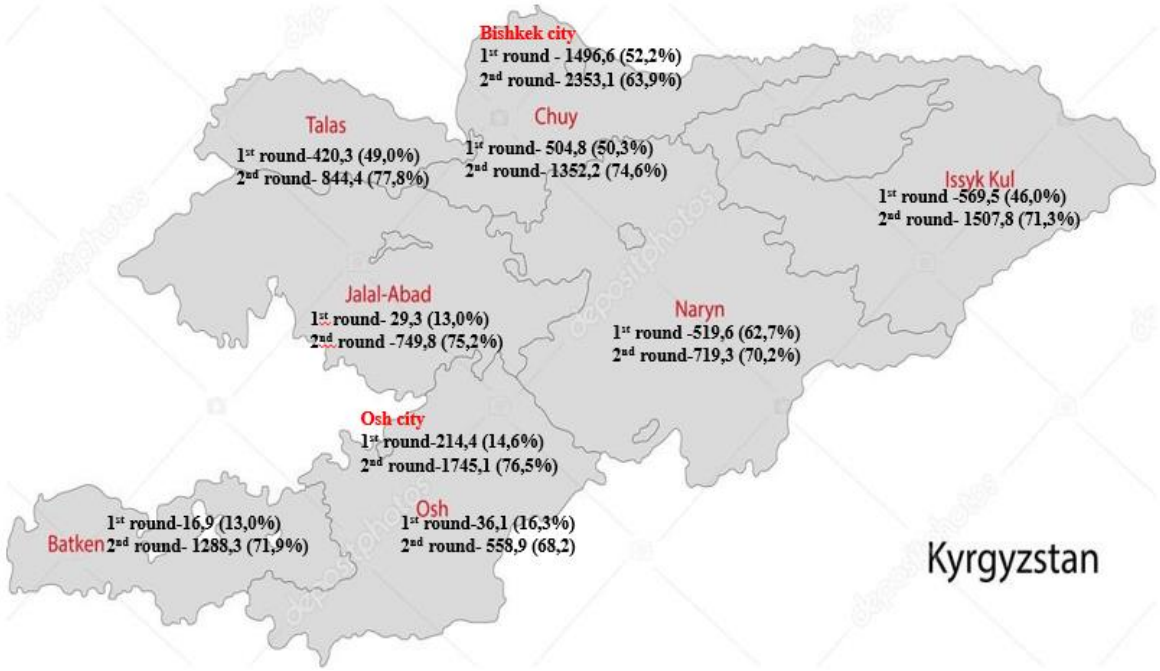

Figure 5. Incidence rates and seropositivity by regions (July 2020 and February 2021)

The result of the study showed that seroprevalence in different age groups of the population (except age 65 and above) had statistically significant differences ($p<0.001$). The seroprevalence rates in both rounds were particularly lowest among children under 9 years of age: at first round -16.5%, second round - 51.4%. One of the reasons for the lower index of seropositivity in children aged 0-9 years was due to the restrictive measures of online education of primary school children, which corresponds to the literature description of other studies (18, 19). In both rounds of the study, the highest antibody prevalence rates were observed in the socially active age groups from 20 to 44 years (32.8% and 77.3%) and from 45 to 64 years (36.1% and 79.4%) in almost all regions of the Kyrgyz Republic.

The analysis of morbidity of similar periods has shown that intensive morbidity indicators for the similar period has increased by 2,4 times, the morbidity indicators for the Republic on 1.08.2020 was 578,7 and on 1.04.2021 - 1373,3. That proves that the proportion of people with antibodies against SARS-CoV-2 increases in parallel with the growth of coronavirus infection morbidity rate. The higher the incidence of COVID-19 in cities/districts at the time of sampling, the higher the level of seropositive results for Ab SARS-CoV-2 among the population and vice versa. High correlation ($r=0.702$) ($p<0.05$) was established between the level of the COVID-19 incidence rate in the regions and the level of seropositive results for Ab SARS-CoV-2 among the population.

In both rounds of the study, it was found that some of the seropositive individuals had no symptoms of coronavirus infection. Symptom prevalence in seropositive individuals in the second round of the study tended to decrease, in general, compared with the results of the first round, decreased by 21.5% (64.0% and 50.3%), which corresponds to the trends in the severity of the disease in the Kyrgyz Republic. The proportion of people with symptoms in both rounds of the study was higher in the older age groups. At the ages of 20-44 years (68.8% and 53.3%) and 45-64 years (62.4% and 63.5%), symptoms were more common ($p<0.001$) than the national average.

A comparative analysis of differences in the proportion of symptoms among seropositive individuals in different age groups showed that in both rounds of the study, coronavirus infection symptoms were less frequent in 0-9 year old (45.0% and 23.8%). This suggests that among children aged 0-9 years, when infected with SARS-CoV-2 virus more often than in other ages, the symptoms of the disease were not manifested or imperceptibly manifested. Globally, children have been shown to account for 1-5% of all symptomatic cases of COVID-19 (20).

The most common symptoms in patients with COVID-19 are fever, chills, headache, muscle pain, dry cough, fatigue, and shortness of breath. Patients also often complain of sore throat, partial or complete loss of smell and/or taste, nausea and vomiting, diarrhea, and runny nose (21).

The analysis of two rounds of our study showed that among seropositive individuals, the frequency of occurrence of the symptoms of the disease tended to decrease, so headache occurred in the 1st round in 44% of persons, in the 2nd round 31.9%, the same indicators were for sore throat (33.8% and 27.1%), runny nose (35.7% and 26.7%), cough (31.8% and 30.2%), fever (46.7% and 29.2%) etc. The results are consistent with other studies where it was noted that SARS-CoV-2 infected individuals may be asymptomatic or have mild to severe disease (22).

According to the results of two rounds of the study, among seropositive individuals, with increasing age, the proportion of people seeking medical care increased in parallel, so in the 1st round the number of children aged 0-9 years who applied for medical care was 10.0% and among people aged 65 and older it was 27.5%, in the 2nd round respectively 6.2 and 37.5%.

Overall, the rate of seeking medical care in 1st round was 21.8%, in 2nd round 25.4%. In the 2nd round there was a 16.5% increase compared to the 1st round of the study (25.4 vs. 21.8%), which indicates increased awareness of the population on prevention of coronavirus infection and increased ability of the healthcare system to receive patients with COVID-19 symptoms.

In the analysis, the proportion of hospitalized persons among seroprevalent was 5.5% and 10.1%. The increase in the proportion of hospitalized persons in the 2nd round of 83.6%, in our opinion, is due to the ability of the healthcare system of the Kyrgyz Republic to hospitalize all patients in need. In the Republic from May 2020 to April 2021, more than 3500 beds were additionally created for hospitalization of patients diagnosed with COVID-19.

Study limitations

When sampling into age categories, children under 18 years of age were not separately divided were included in the 10-19 years age group. The obtained seroprevalence rates in the settlements where seroepidemiological studies were conducted cannot be applied to the general population of the Republic, as well as to the regions as a whole. When developing the study protocol, it was planned to apply the results obtained to estimate the prevalence of coronavirus infection in the general population. When settlements in the regions were selected for this study, the incidence rates in these settlements did not exceed the statistical average for the Republic and the regions. But morbidity rates in all settlements, where the seroepidemiological study was conducted in April 2021 was higher than the average Republican and average regional rates, so we believe that the obtained data on seroprevalence to SARS-CoV-2 virus is slightly higher than in the whole country and in separate regions.

Conclusions

The epidemiological situation on coronavirus infection was characterized by rapid spread throughout the Kyrgyz Republic with periodic ups and downs similar to the global situation. During 2020-2021, three waves of COVID-19 pandemic were noted. With the increasing prevalence of coronavirus infection, seroprevalence to SARS-CoV-2 increased in parallel, from July 2020 to February 2021 increased by 2.3-fold, from 30.8% to 71.2%. By February 2021, 28.8% of the population remained susceptible to coronavirus infection. The presence of symptoms in seropositive individuals in the second round decreased by 21.5% compared to the first round of the study, which is in line with the trends in disease severity indicators. Among children aged 0-9 years, only -23.8% had symptoms of coronavirus infection, while 60.3% of adults older than 65 years had symptoms, which is 2.5 times higher than in children. The presence of symptoms of coronavirus infection among seropositive individuals in the second round was 13.7% lower than in the first round of the study and amounted to 50.3% versus 64.0%. Due to increased awareness of the population on prevention of coronavirus infection in the second round of the study, the percentage of seeking medical care increased by 3.6% compared to the first round (25.4% vs. 21.8%). Also, with the increasing possibility of hospitalization in the healthcare system of Kyrgyz Republic, the proportion of hospitalized patients increased by 4.6% (10.1% vs. 5.5%).

Ethics: Informed consent was obtained from patients before all procedures and study protocol was approved by institutional Ethics Committee
Peer-review: External and internal
Conflicts of interest: None to declare
Authorship: Zh.N.N., Z.Sh.N., T.E.K., K.K.R. equally contributed to study and manuscript preparation.

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