DOI: https://doi.org/10.17816/EID628868

Проявления эпидемического процесса и клинико-эпидемиологические характеристики пациентов в раннем периоде эпидемии COVID-19 в России

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АННОТАЦИЯ

Обоснование. Пандемия COVID-19 стала серьёзным вызовом всему человечеству и нанесла значительный социальный и экономический ущерб большинству стран. Для наиболее объективной оценки эпидемиологических и клинических особенностей новой коронавирусной инфекции необходимо проведение исследований, основанных на большом объёме данных о пациентах, выявленных в разные периоды эпидемии на всей территории Российской Федерации.

Цель исследования — определить основные проявления эпидемического процесса и клинико-эпидемиологические особенности взрослых пациентов с COVID-19, обнаруженные в первый и второй периоды подъёма и спада заболеваемости новой коронавирусной инфекцией в России.

Материалы и методы. В исследование были включены пациенты в возрасте ⩾18 лет с подтверждённым диагнозом COVID-19, выявленные в периоды с 02.03.2020 по 30.06.2020 (*n*=286 205) и с 01.11.2020 по 31.01.2021 (*n*=1 655 022) на территории 85 субъектов РФ.

Результаты. На раннем этапе эпидемии COVID-19 в России с помощью критерия Вальда–Вольфовица выделены 2 периода подъёма и спада заболеваемости: март–август 2020 года и сентябрь 2020 года – май 2021 года. Медиана возраста пациентов с COVID-19 в первый период составила 50,0 [37–62] лет, во второй — 52,0 [39–64] года; доля лиц женского пола — 55,5 и 60,1% соответственно. Распределение пациентов по тяжести течения заболевания в первый и второй периоды составило: лёгкое — 63,0 и 74,4%; среднетяжёлое — 29,0 и 20,1%; тяжёлое — 4,9 и 3,5%; крайне тяжёлое — 3,1 и 2,1% соответственно. В первый период в структуре заболевших преобладали лица в возрастной группе 50–59 лет (20,5%), во второй — 60–69 лет (20,5%). Медиана длительности периода от появления симптомов до установления диагноза составила 4 дня в оба периода, медиана длительности течения заболевания — 16,0 [12–21] и 13 [10–17], медиана длительности госпитализации — 15,0 [12–20] и 13,0 [10–18]. Частота госпитализаций — 48,4 и 25,6% в первый и второй периоды, доля пациентов в отделениях реанимации и интенсивной терапии — 7,8 и 10,3%, переводов на искусственную вентиляцию легких — 5,6 и 7,7% соответственно. В оба периода медиана возраста умерших составила 73 [66–82] года, при этом в возрастных группах 30–39, 40–49, 50–59 и 60–69 лет доля мужчин среди умерших была выше. Наличие одного и более хронических заболеваний, а также мужской пол увеличивали вероятность летального исхода (ОШ=10,2 и ОШ=1,3 в первый период; ОШ=16,0 и ОШ=1,6 во второй период соответственно).

Заключение. В раннем периоде эпидемии COVID-19 в России, связанном с распространением дикого штамма SARS-CoV-2 и генетически близкородственных линий, обнаружены отличия в проявлениях эпидемического процесса и клинико-эпидемиологических характеристиках пациентов. Во втором периоде на фоне более высоких показателей заболеваемости и смертности по сравнению с первым периодом наблюдалось снижение частоты тяжёлого и крайне тяжёлого течения COVID-19, снижение частоты и длительности госпитализаций, но отмечалось незначительное увеличение доли пациентов, проходивших лечение в отделениях реанимации и интенсивной терапии, и частоты переводов на искусственную вентиляцию лёгких.

Ключевые слова: эпидемиология; SARS-CoV-2; заболеваемость; госпитализация; смертность.

Как цитировать:
Фомичева А.А., Пименов Н.Н., Комарова С.В., Уртиков А.В., Сахаутдинов А.Р., Стрелкова Д.А., Неклюдова Г.В., Рачина С.А., Авдеев С.Н., Чуланов В.П. Проявления эпидемического процесса и клинико-эпидемиологические характеристики пациентов в раннем периоде эпидемии COVID-19 в России // Эпидемиология и инфекционные болезни. 2024. Т. 29, № 2. С. 92–107. DOI: https://doi.org/10.17816/EID628868

Рукопись получена: 07.03.2024 **Рукопись одобрена:** 08.04.2024 **Опубликована online:** 18.04.2024

DOI: https://doi.org/10.17816/EID628868

Manifestation of epidemic process, clinical and epidemiological characteristics of adult patients in the early period of the COVID-19 epidemic in Russia

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ABSTRACT

BACKGROUND: The COVID-19 pandemic became a challenge and caused significant social and economic damage to most countries. For the most objective assessment of the epidemiological and clinical features of COVID-19 during different periods of the epidemic, studies based on a large volume of data on patients identified throughout the Russian Federation are necessary.

AIM: To analyze the epidemic process and clinical and epidemiological features of adult patients with COVID-19 identified during the first and second periods of the rise and decline in the incidence of COVID-19 in Russia.

MATERIALS AND METHODS: This study included patients aged ⩾18 years with a confirmed diagnosis of COVID-19 and identified in the periods from March 2, 2020, to June 30, 2020 (*n*=286,205) and from November 1, 2020, to January 31, 2021 (*n*=1 655 022), in Russia.

RESULTS: At the early stage of the COVID-19 epidemic in Russia, two periods of the rise and fall in incidence were noted: March–August 2020 and September 2020–May 2021, using the Wald–Wolfowitz test. The median age of the patients with COVID-19 in the first and second periods were 50.0 [37–62] and 52.0 [39–64] years, respectively, and women accounted for 55.5 and 60.1% of the patients, respectively. The distributions of patients according to disease severity in the first and second periods were as follows: mild, 63.0 and 74.4%; moderate, 29.0 and 20.1%; severe, 4.9 and 3.5%; extremely severe, 3.1 and 2.1%, respectively. In the first and second periods, cases were dominated by patients aged 50–59 years (20.5%) and 60–69 years (20.5%), respectively. In both periods, the median duration from the onset of symptoms to diagnosis was 4 days, the median disease durations were 16.0 [12–21] and 13 [10–17], and the median duration of hospitalization were 15.0 [12–20] and 13.0 [10–18]. The hospitalization rates were 48.4 and 25.6% in the first and second periods; transfer rates to the ICU, 7.8 and 10.3%; and invasive mechanical ventilation rates, 5.6 and 7.7%, respectively. In both periods, the median age at death was 73 [66–82] years, with a higher proportion of men aged 30–39, 40–49, 50–59, and 60–69 years. The presence of one or more chronic diseases, as well as male sex, increased the likelihood of death (odds ratio = 10.2 and 1.3 in the first period; odds ratio = 16.0 and 1.6 in the second period).

CONCLUSIONS: In the early period of the COVID-19 epidemic in Russia, related to the spread of the wild strain of SARS-CoV-2 and genetically closely related variants, the manifestations of the epidemic process and clinical and epidemiological characteristics of patients varied. In the second period with higher incidence and mortality rates than the first period, the frequency of severe and extremely severe COVID-19 and the frequency and duration of hospitalizations decreased; however, the frequency of transfers into the intensive care unit and artificial lung ventilation slightly increased.

Keywords: epidemiology; SARS-CoV-2; incidence; hospitalization; mortality.

To cite this article:
Fomicheva AA, Pimenov NN, Komarova SV, Urtikov AV, Sakhautdinov AR, Strelkova DA, Nekludova GV, Rachina SA, Avdeev SN, Chulanov VP. Manifestation of epidemic process, clinical and epidemiological characteristics of adult patients in the early period of the COVID-19 epidemic in Russia. *Epidemiology and Infectious Diseases.* 2024;29(2):92–107. DOI: https://doi.org/10.17816/EID628868

Received: 07.03.2024 **Accepted:** 08.04.2024 **Published online:** 18.04.2024

BACKGROUND

In December 2019, the first cases of pneumonia caused by the novel coronavirus SARS-CoV-2 were diagnosed in China [1]. The first case of SARS-CoV-2 infection outside China was reported on January 13, 2020, in Thailand, and SARS-CoV-2 rapidly spread worldwide [2]. On January 30, 2020, the World Health Organization (WHO) declared the outbreak of the novel coronavirus infection as a public health emergency of international concern, and on March 11, 2020, WHO declared the outbreak a pandemic [3, 4]. In February 2020, the disease caused by the novel coronavirus was officially called COVID-19 [5].

The first two cases of COVID-19 in Russia were recorded on January 31, 2020, among Chinese citizens. Anti-epidemic measures were implemented to prevent the entry and spread of COVID-19, including strengthening the sanitary and quarantine control regime at Russian state border crossing points, medical surveillance or isolation of persons returning from China, laboratory examination of persons with suspected infection, and strengthening disinfection[1].

The first case of COVID-19 among Russian citizens was recorded on March 2, 2020, in a man who had recently returned from Italy. Thereafter, the incidence of COVID-19 aggressively increased, with more than 2,500 cases and 9 deaths from the new coronavirus infection in 75 Russian individuals by March 31, 2020. The intensity of the epidemic process of COVID-19 in Russia was the lowest during the first spring–summer period compared with the subsequent periods. The increase in incidence in 2020–2021 began in megacities and subsequently spread across the federal districts [6].

SARS-CoV-2 is distinguished by a remarkable variability. At the outset of 2020, the original "Wuhan strain" of SARS-CoV-2 was prevalent globally. However, following March of that year, a strain containing the initial phenotypically significant mutation, D614G, emerged and superseded the previous strain. Nevertheless, these changes did not significantly impact the severity of the disease [7]. The period of dominance of these strains was followed by a pandemic phase, during which the "variants of concern" spread. These variants exhibited higher infectivity and virulence than previous strains. The Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2) variants were identified in late 2020. The Omicron variant (B.1.1.529) was first identified in November 2021 [8].

A review of the clinical and demographic characteristics of patients with COVID-19 at the early stage of the pandemic (before the emergence of the SARS-CoV-2 Delta variant) in different countries has revealed that age, sex, and comorbidities can influence the course of infection and its outcome. In particular, a higher risk of adverse outcomes was observed in males and the older population [11, 12]. Moreover, the risk of severe course and need for artificial ventilation (AV) was higher among individuals with hypertension and other cardiovascular diseases, diabetes mellitus, respiratory diseases, obesity, and tobacco dependence [13–15]. However, in Russia, studies on the characteristics of patients with COVID-19 were limited to certain cities or regions or conducted in certain cohorts of patients.

This study aimed to conduct a comparative analysis of the clinical and epidemiological characteristics of adult patients with COVID-19 identified during the initial and subsequent phases of the rise and decline in the incidence of the novel coronavirus infection in Russia.

MATERIALS AND METHODS

Statistical analysis examined the morbidity and mortality rates associated with the novel coronavirus infection in 2020–2021. The data used in this study were obtained from the online resource "stopcoronavirus.rf."

The boundaries of periods of morbidity dynamics were determined by estimating growth/decline rates and statistically evaluating the differences in COVID-19 morbidity levels using the Wald–Wolfowitz criterion.

The study included patients aged ⩾18 years with laboratory-confirmed diagnoses (ICD-10 code U07.1) detected on the territory of 85 individuals in Russia from March 2, 2020, to June 30, 2020 (the first period of the rise and fall of morbidity, *n*=286,205), and from November 1, 2020, to January 31, 2021 (the second period of the rise and fall of morbidity, *n*=1,655,022). Anonymized data were obtained from the COVID-19 patient registry, which is a repository of information on individuals infected with SARS-CoV-2. The study assessed and compared demographic (sex and age) and clinical and epidemiologic characteristics in the study cohorts.

The following clinical and epidemiologic patient characteristics were assessed:

- Severity of the diseases course
- Frequency of hospitalizations
- Frequency of transfers to the intensive care unit (ICU)
- Proportion of patients requiring AV
- Duration of the period from onset of symptoms to detection of the disease
- Duration of the course of the disease (from diagnosis to outcome)
- Duration of hospitalization
- Comorbidities
- Outcomes

[1] Resolution of the Chief State Sanitary Doctor of the Russian Federation dated January 24, 2020, no. 2 "On additional Measures to Prevent the Importation and Spread of New Coronavirus Infection Caused by 2019-nCoV". Available at: https://www.rospotrebnadzor.ru/upload/iblock/2b1/postanovlenie-ot-24.01.2020-_2-koronovirusnaya-infektsiya.pdf; Resolution of the Chief State Sanitary Doctor of the Russian Federation, dated January 31, 2020, no. 3 "On Additional Sanitary and Anti-Epidemic (Preventive) Measures to Prevent the Importation and Spread of a New Coronavirus Infection Caused by 2019-nCoV". Available at: https://rospotrebnadzor.ru/upload/iblock/312/postanovlenie-ot-31.01.2020-_3-o-poroved.-dopoln.-meropr.-po-koron.-virusn.-infekts..pdf

The proportions of patients treated in the ICU and transferred to the AV were calculated among hospitalized patients.

The severity of the disease course was established in accordance with the current version of the Temporary Methodological Recommendations "Prevention, Diagnosis, and Treatment of Emerging Coronavirus Infection (COVID-19)" of the Russian Ministry of Health.

Statistical analysis of the data was performed using the IBM SPSS V20.0 program. The categorical variables were described using frequencies and quantitative variables using the median and interquartile intervals. The statistical significance of the differences between the variables was determined using the Mann–Whitney U test and χ^2 criteria at the accepted level of statistical significance of p <0.05. Additionally, the odds ratio (OR) with 95% confidence intervals (CI) was calculated.

RESULTS

Dynamics of the epidemic process in the early period of the COVID-19 epidemic in russia

During the COVID-19 pandemic, changes in the dynamics of morbidity were observed in Russia, as in other countries, characterized by several periods of rise and fall ("waves"). During the initial phase of the epidemic in Russia, which coincided with the dissemination of the wild strain of SARS-CoV-2 and genetically related variants, two periods of elevated morbidity were identified. This was obtained by determining the reliability of differences between the periods using the Wald–Wolfowitz criterion (p <0.05) (Fig. 1).

The initial period encompassed a 6-month duration (March–August 2020). During this period, the morbidity rate exhibited a fluctuating pattern, with an increase observed from March to April 2020 and a subsequent decline from June to August 2020. The maximum value of the incidence rate in this period was 204.8 cases per 100,000 population (May 2020), whereas the minimum value was 1.6 cases per 100,000 population (March 2020). In this period, the maximum values of the mortality rate were recorded subsequent to the peak of the incidence rate, occurring in June and July 2020 (3.2 cases per 100,000 population).

The second period of morbidity rise and decline lasted for 9 months (September 2020–May 2021). The rise in morbidity was recorded from September to December 2020 and the decline from January to April 2021. In May 2021, a slight increase was noted in morbidity (+2.5%); however, no significant differences were found between the incidence rates in April and May 2021 (p ⩾0.05). The maximum incidence rate during the second period of the rise and fall of incidence was 590.8 cases per 100,000 population (December 2020), whereas the minimum was 123.8 cases per 100,000 population (September 2020). Concurrently, the month with the highest mortality rate coincided with the month with the highest incidence rate (December 2020), with a mortality rate of 11.7 cases per 100,000 population. The lowest mortality rate was observed in October 2020 (5.0 cases per 100,000 population).

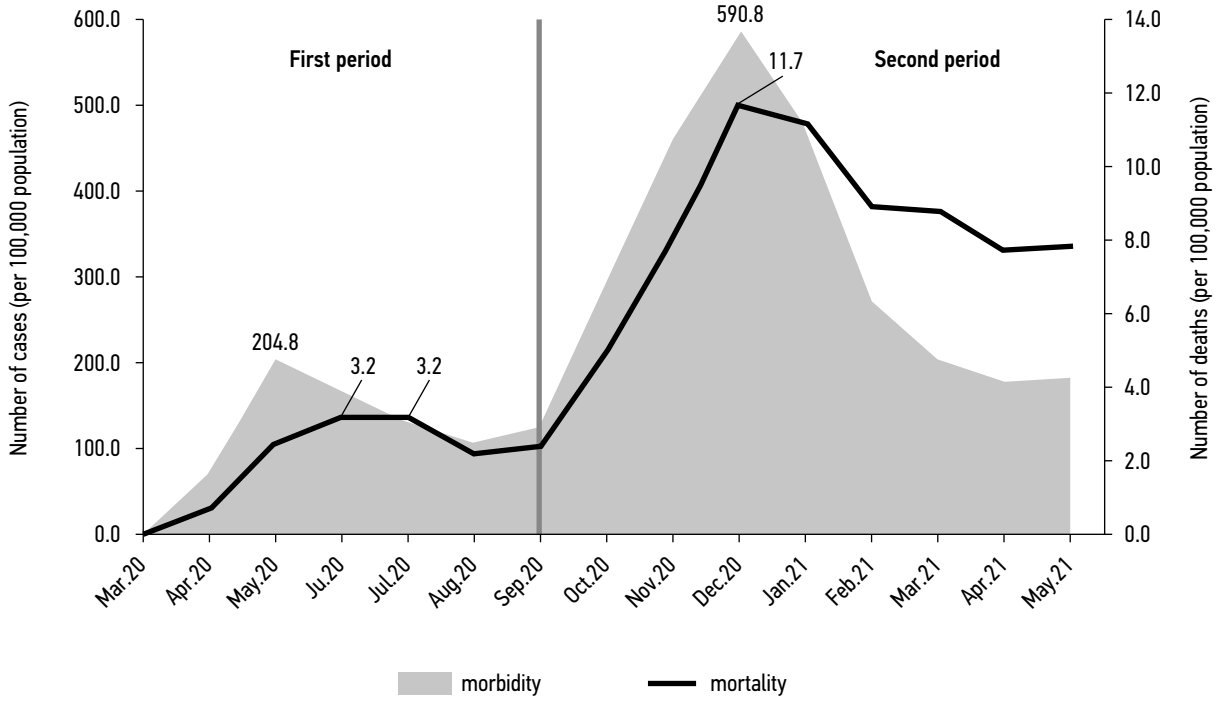

Fig. 1. Dynamics of COVID-19 incidence and mortality in the early period of the epidemic of a new coronavirus infection in Russia (Wald–Wolfowitz test, p <0.05).

Clinical and epidemiologic characteristics of patients with COVID-19 during the first phase of the rise and subsequent decline in the incidence of novel coronavirus infection in Russia

The median age of adult patients with COVID-19 during the initial surge in incidence in Russia was 50 (37–62) years. Of these patients, 55.5% were females. The largest proportion of patients was represented by the age group 50–59 years (20.5%), and the smallest was the age group 18–29 years (11.1%) (Table 1).

Upon analysis of the sex distribution of patients, the most pronounced differences were observed in the age group >70 years (p <0.05) (Fig. 2).

Majority (63.0%) of patients exhibited mild severity of the disease. In the youngest age group (18–29 years), the proportion of patients with mild forms of the disease was 81.6%, and 0.1% of patients in this age group experienced an extremely severe form of COVID-19. However, in older age groups, an increase was observed in the frequency of severe and extremely severe courses of the disease (Fig. 3). The frequency of extremely severe disease was higher in male (3.5%) than in female (2.7%) patients (p <0.05).

The median duration of the disease course from diagnosis to outcome was 16 (12–21) days. The median duration from symptom onset to diagnosis was 4 (1–8) days.

The frequency of hospitalizations was 48.4%. The median duration of hospitalization was 15 (12–20) days. Among hospitalized COVID-19 patients, 53.1% of the patients had a moderate disease course (Fig. 4). Majority of hospitalized patients were between the ages of 60 and 69 (22.0%), with a smaller proportion between the ages of 18 and 29 (7.9%) (p <0.05). The median age of hospitalized patients was 56 (42–67) years.

The proportion of patients treated in the ICU was 7.8%. Males (51.4%, p <0.05; OR=1.2; 95% CI: 1.2–1.3) and individuals aged ⩾70 years (55.0%, p <0.05) were admitted to the ICU more frequently. The proportion of patients with one or more comorbidities among those treated in the ICU was 77.9% (OR=5.6; 95% CI: 5.3–5.9). The highest frequency of transfers to the ICU was observed among patients with oncologic, endocrine, and cardiovascular diseases (20.9%, 19.2%, and 16.4%, respectively; p <0.05).

The proportion of patients requiring AV was 5.6%, and the rate of transfer to ventilator was higher among males (6.1% vs. 5.1%, p <0.05; OR=1.2; 95% CI: 1.2–1.3). Individuals aged ⩾70 years accounted for 52.8% of patients connected to a ventilator (p <0.05). Furthermore, 80% of patients had one or more comorbidities (p <0.05; OR: 6.2; 95% CI: 5.9–6.6). The proportion of patients requiring AV was highest in the groups of patients with oncologic, endocrine, and cardiovascular diseases (15.3%, 15.2%, and 12.2%, respectively; p <0.05).

Overall, 25.8% of patients diagnosed with COVID-19 during the initial period of the disease's rise and fall exhibited at least one comorbid disease (Table 1). Among comorbid patients, 78.4% were hospitalized, and the hospitalization rate among patients without comorbidities was 38.1% (p <0.05). The most frequent hospitalization rates were observed in patients with cardiovascular (30.5%) and endocrine (11.5%) diseases.

The median age of the deceased was 73 years (64–83 years). Patients aged ⩾70 years constituted the majority of the deceased (59.8%), whereas the smallest proportion was represented by the age group 18–29 years

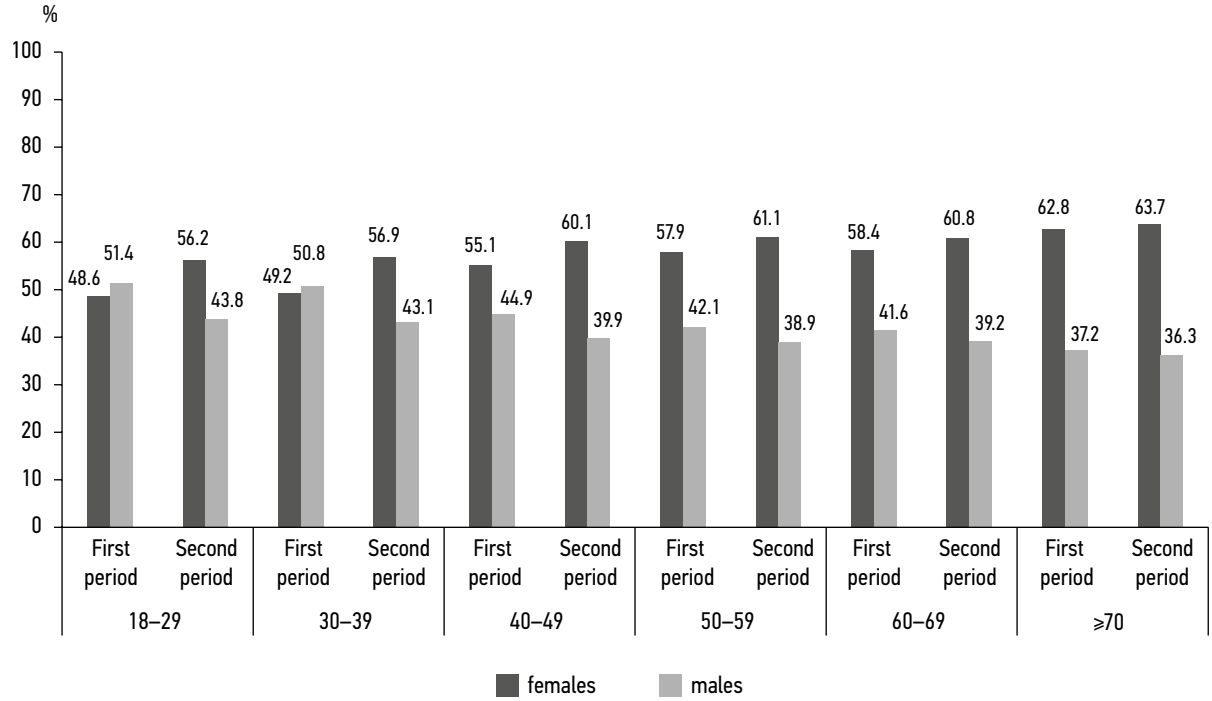

Fig. 2. Age and sex structure of patients with COVID-19 in the first and second waves of COVID-19 in Russia (chi-squared test, p <0.05).

Table 1. Demographic and clinical characteristics of patients in the first and second waves of COVID-19 in Russia

Indicators	First period (March to August 2020)	Second period (September 2020 to May 2021)	*p*
Sex (male/female), %	44.5 / 55.5	39.9 / 60.1	⩽0.001
Age of patients, median, years	50.0 [37–62]	52.0 [39–64]	<0.05
Age groups of patients, %			⩽0.001
18–29 years	11.1	9.4	
30–39 years	18.5	17.6	
40–49 years	18.9	18.3	
50–59 years	20.5	19.4	
60–69 years	17.8	20.5	
⩾70 years	13.1	14.9	
Severity of the disease, %			⩽0.001
Mild course	63.0	74.4	
Moderate course	29.0	20.1	
Severe course	4.9	3.5	
Extremely severe course	3.1	2.1	
Comorbidities, %	25.8	20.0	⩽0.001
Cardiovascular diseases	18.3	15.0	
Endocrine diseases	6.5	5.7	
Respiratory diseases	3.6	2.4	
Oncological diseases	2.0	1.3	
Tuberculosis	0.1	0.1	
HIV infection	0.2	0.1	
Other	5.4	4.9	
Duration of the period from the onset of symptoms to diagnosis, median, days	4.0 [1–8]	4.0 [2–7]	⩾0.05
Duration of the disease (from diagnosis to outcome), median, days	16.0 [12–21]	13.0 [10–17]	<0.05
Duration of hospitalization, days	15.0 [12–20]	13.0 [10–18]	<0.05
Frequency of hospitalizations, %	48.4	25.6	⩽0.001
Sex of those hospitalized, male / female, %	47.1 / 52.9	43.4 / 56.6	<0.05
Age of those hospitalized, median, years	56.0 [42–67]	64.0 [54–72]	<0.05
Proportion of patients treated in the intensive care unit, %	7.8	10.3	⩽0.001
Frequency of transfers to artificial ventilation, %	5.6	7.7	⩽0.001
Sex of the deceased, male/female, %	51.2/48.8	50.6/49.4	⩾0.05
Age of the deceased, median, years	73 [64–83]	73 [66–82]	⩾0.05

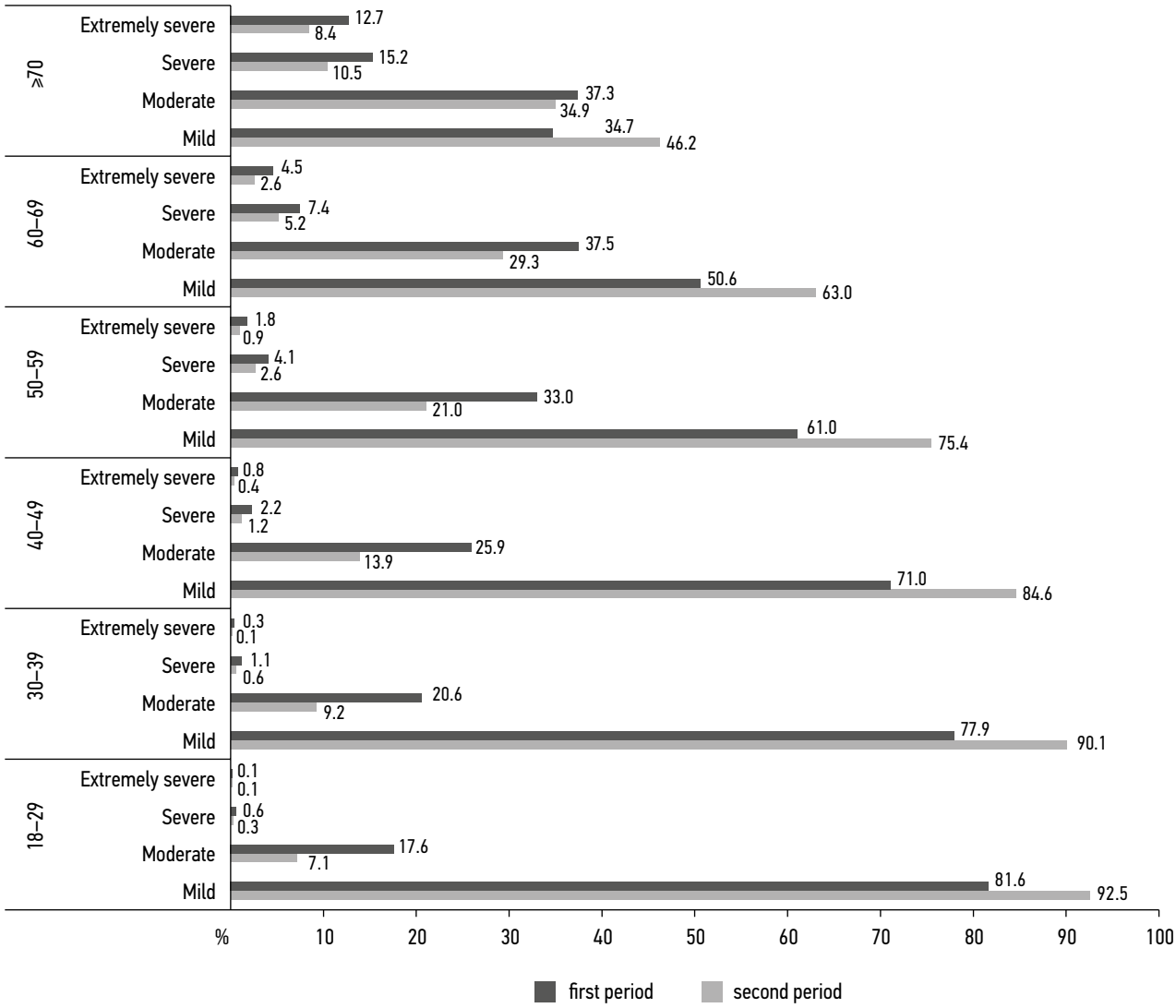

Fig. 3. COVID-19 severity in various age groups in the first and second waves of COVID-19 in Russia (chi-squared test, p <0.05).

(0.4%) (p <0.05). In 57.5% of the patients who died, the disease was extremely severe. The probability of death was higher in males (OR=1.3; 95% CI: 1.3–1.4; p <0.05). Figure 5 shows the age–sex structure of patients who died of COVID-19. Patients with comorbidities were significantly more likely to die compared with patients without comorbidities (OR=10.2; 95% CI: 9.8–10.6; p <0.05). Among the deceased patients with comorbidities, the highest incidence of fatal outcomes was observed in the group with cardiovascular and endocrine pathologies (64.5% and 26.2%, respectively).

Clinical and epidemiologic characteristics of patients with COVID-19 during the second phase of the rise and the subsequent decline in the incidence of novel coronavirus infection in Russia

In the second period of the increase and subsequent decrease in the incidence of COVID-19 in Russia, the average age of adult patients was 52 (39–64) years, and the proportion of females in the structure of patients was 60.1%. The highest incidence of the disease was observed in the 60–69 age group (20.5%), and the lowest incidence was observed in the 18–29 age group (9.4%). In all age groups, the disease was recorded more frequently in females: from 56.2% in the 18–29 age group to 63.7% in the ≥70 age group (p <0.05) (Fig. 2).

Majority of patients (74.4%) exhibited mild disease, whereas the most severe form of the disease was observed in the smallest number of patients (2.1%) (Table 1). The severity of the disease increased with age. The proportion of patients with an extremely severe disease course increased from 0.1% in the age group 18–29 years to 8.4% among patients in the age group ≥70 years (p <0.05). Conversely, in the 18–29 age group, most patients (92.5%) exhibited mild disease, and only 46.2% of patients aged ≥70 years exhibited mild disease (p <0.05) (Fig. 3).

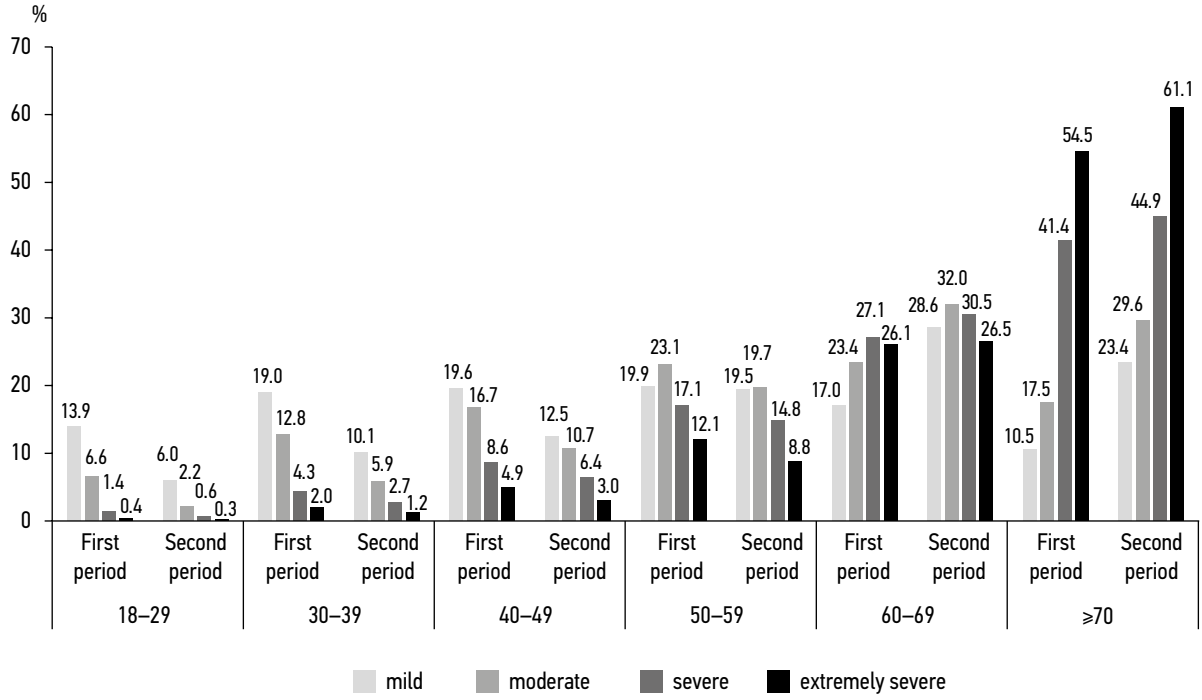

Fig. 4. COVID-19 severity in various age groups of hospitalized patients during the first and second waves of COVID-19 in Russia (chi-squared test, p <0.05).

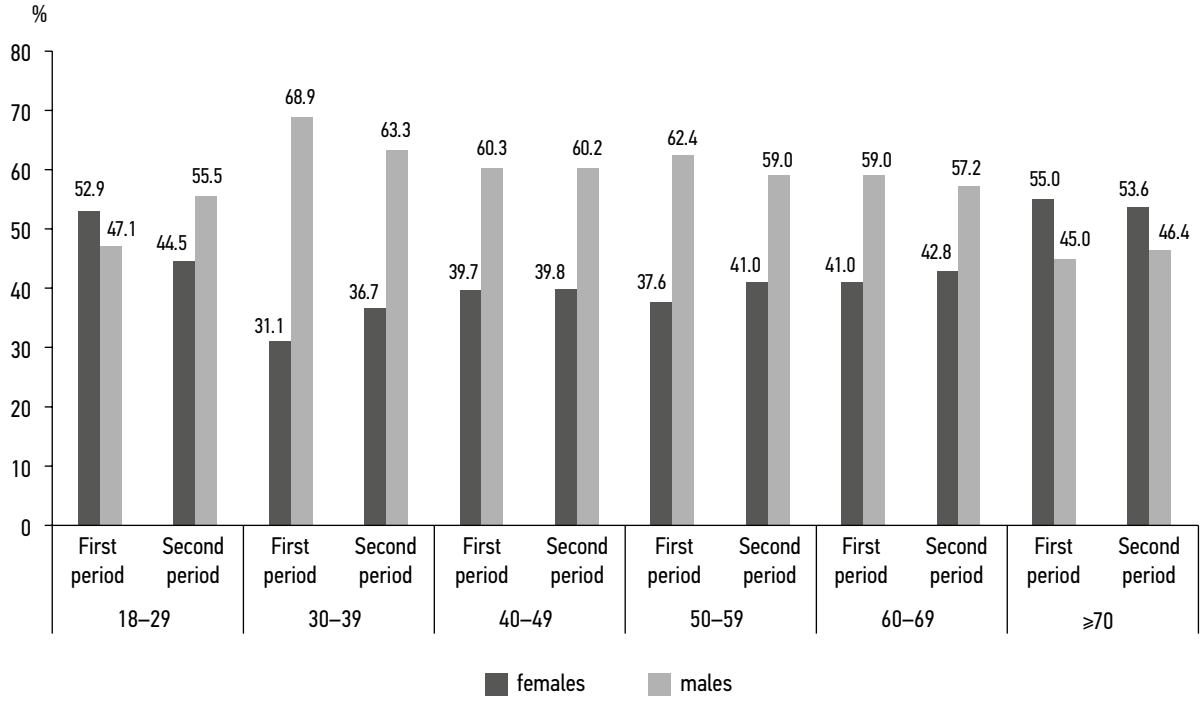

Fig. 5. Age and sex structure of deceased patients with COVID-19 in the first and second waves of new coronavirus infection in Russia (chi-squared test, p <0.05).

The median duration of the disease from diagnosis to outcome was 13 days (10–17 days), and the duration of the period from symptom onset to diagnosis was 4 days (2–7 days).

During the second peak period, 25.6% of patients with COVID-19 were hospitalized. Of these, 61.9% had a moderately severe disease course (Fig. 4). The median period of hospitalization was 13 (10–18) days. Among those hospitalized, a larger proportion of patients were in the ≥70 age group (33.1%), whereas a smaller proportion (2.4%) were in the 18–29 age group (p <0.05). The median age of those hospitalized was 64 (54–72) years.

The proportion of patients treated in the ICU during the study period was 10.3%. Of these, 50.6% were males (OR=1.4; 95% CI: 1.3–1.4) and 60.5% were aged ⩾70 years (p <0.05). Among patients transferred to the ICU, 80.6% had one or more comorbidities (OR=4.0; 95% CI: 3.9–4.1). The highest rate of hospitalization in the ICU was observed among patients with cancer, HIV infection, and endocrine diseases (21.1%, 17.5%, and 17.3%, respectively; p <0.05).

The proportion of patients requiring AV was 7.7%. Of these, 50.8% were males (OR=1.4; 95% CI: 1.3–1.4). The ⩾70 age group had the highest proportion of patients transferred to the ventilator (59.5%, p <0.05). One or more comorbidities were observed in 81.7% of patients on AV (OR=4.2; 95% CI: 4.0–4.3). The groups of patients with oncologic and endocrine diseases had the highest proportion of patients on AV (15.8 and 13.6%, respectively; p <0.05).

During the second period of the rise and fall of morbidity, the proportion of patients with at least one comorbidity was 20.0% (Table 1). Among comorbid patients, majority (68.9%) were hospitalized, in contrast to non-comorbid patients (14.9%) (p <0.05). The incidence of hospitalization among patients with COVID-19 and cardiovascular or endocrine disease was 43.0% and 17.6%, respectively (p <0.05).

The median age of the patients who died was 73 (66–82) years. Individuals aged ⩾70 years constituted the majority of the deceased (63.7%, p <0.05). In all age groups, except for ⩾70 years, a greater proportion was observed among males (Fig. 5). Among those who died, the smallest proportion (1.1%) was observed in patients with a mild disease course, whereas the largest proportion (58.8%) was observed in patients with an extremely severe course (p <0.05). The probability of death was significantly higher in patients with one or more comorbidities (OR=16.0; 95% CI: 15.7–16.3; p <0.05) and in males (OR=1.6; 95% CI: 1.54–1.59). Among the patients who died, 69.0% and 29.6% had concomitant cardiovascular and endocrine disease, respectively.

DISCUSSION

A study of the dynamics of COVID-19 morbidity at the initial stage of the epidemic in Russia (from 2020 to the first half of 2021) revealed two periods of rise and decline in morbidity, with an increase in the intensity of the epidemic process in the second period. During these periods, fluctuations in the mortality rate from COVID-19 were noted, which were delayed compared to the dynamics of morbidity in both periods.

A comparison of the obtained results with those from other countries revealed differences in the dynamics and intensity of epidemic processes. In China, the first two periods of rise and decline in morbidity were observed from December 2019 to April 2020 (peak: February 13, 2020, with 13,026 cases) and from June to August 2020 (peak: July 30, 2020, with 276 cases) [16]. A clinical and epidemiological analysis of patients who became ill during the initial rise and subsequent decline in incidence in China revealed a male predominance (57%–73%). Majority of patients were aged 30–79 years (86.6%) (median: 49 years). The majority of cases exhibited mild disease courses (80.9%) [17].

In Russia, during the periods of the first and second rise and decline in COVID-19 incidence, majority of patients were females (55.5% and 60.1%, respectively). Despite the significant differences in the sex structure among patients with COVID-19 in Russia, the ratio of males and females can be considered comparable.

A comparative analysis of the demographic characteristics of patients with COVID-19 in the early stages of the epidemic in the United States, Italy, Sweden, and South Africa revealed a striking similarity in the proportion of female patients, with a prevalence of 51.3%, 54.1%, 59.0%, and 57.4%, respectively [19–21]. In contrast, the proportion of females was lower in France, Brazil, and Nigeria (44%, 43%, and 35%, respectively) [22–24]. The role of sex as a risk factor for the disease remains controversial. This indicator may reflect the demographic structure of the general population or demographic and socioeconomic factors. In some countries, healthcare is less accessible to females owing to social and financial constraints [25]. Moreover, males less likely seek medical care and tend to postpone visiting a doctor until the symptoms of the disease progress [26].

In Russia, during the initial and subsequent periods of the rise and decline in the incidence of COVID-19, the highest proportion of cases occurred in individuals aged 50–59 years and 60–69 years, respectively. Conversely, the 18–29 age group had the lowest proportion of cases. Leong et al. divided countries into three categories based on the age group with the highest proportion of cases: persons aged 20–39 years old (Canada, Chile, Germany, New Zealand, Portugal, South Korea, Turkey, and the United States), those aged 50–59 years (Peru and South Africa), and those aged ⩾80 years (Italy, the Netherlands, and the United Kingdom) [27]. These differences may be attributed to varying age structure of the population, testing methodologies, and socioeconomic factors.

In both the first and second periods of the rise and decline in the incidence of COVID-19 in Russia, majority of patients exhibited a mild course of the disease. In the second period, the proportion of such patients was higher by 11.4%, and the frequency of severe and extremely severe courses of the disease decreased by 1.4% and 1.0%, respectively. During both analyzed periods, the severity of the disease course tended to increase with age. The disease course was milder in the youngest age groups than in the older age groups, indicating the high importance of preventive measures in this group.

During the second period of morbidity increase, there was a decrease in the median duration of the disease (by 3 days, on average) and hospitalization (by 2 days, on average). The median duration from symptom onset to diagnosis remained at 4 days. Those infected with SARS-CoV-2 who are in the incubation period or asymptomatic significantly contribute to the continuation of the epidemic, despite being unaware

of their role as sources of infection [28]. At the end of the incubation period and in the first days of the disease, a person infected with SARS-CoV-2 is at the greatest risk to others [29], and from the onset of symptoms to diagnosis, active case detection and timely testing of contact persons are crucial anti-epidemic measures.

In comparison to the first period, the frequency of hospitalizations in Russia decreased by 1.9 times. This decline may be associated to modifications in the approach to the provision of medical care to patients with COVID-19. The changes introduced by the order of the Ministry of Health of Russia, dated October 23, 2020, no. 1140n, to the order of the Russian Ministry of Health, dated March 19, 2020, no. 198n, titled, "On The Temporary Procedure for Organizing the Work of Medical Organizations for the Implementation of Measures to Prevent and Reduce the Risks of Spread of the Novel Coronavirus Infection (COVID-19)" permitted outpatient treatment of patients with a moderate or severe disease course under isolation conditions, provided that they did not belong to a risk group.

Significant alterations in the indications for hospitalization were reflected in the composition of hospitalized patients. In the second period of the COVID-19 morbidity surge, the proportion of hospitalized patients in the 60–69 and 70 years age groups increased by 8.7% and 13.1%, respectively. Conversely, the proportion of patients aged 18–60 years among hospitalized patients decreased in all age groups within this range. In the United States and Denmark, older individuals were hospitalized more frequently during the early period of the epidemic [30, 31]. However, in countries such as China and India, the demographic profile of hospitalized patients was notably skewed toward younger individuals [1, 32]. In India, the largest proportion of hospitalized patients was represented by individuals aged 20–29 years. This can be attributed to both the demographic structure of the population (mean age: 28.4 years; proportion of the population >65 years: 6.2%) and influence of restrictive measures.

Additionally, during the second period, a 1.8-fold decrease was noted in the proportion of patients with a mild course of the disease among those hospitalized (from 30.8% to 16.7%), whereas the proportion of patients with an extremely severe disease course increased (from 6.3% to 8.0%). In Denmark and Japan, an increase in the proportion of patients with a mild disease course was observed among those hospitalized during the second peak of incidence [30, 33].

In Russia, the incidence of fatal outcomes among hospitalized patients increased by 2.6% compared to the first period of the rise and decline in morbidity. However, in other countries, particularly in the United States, Japan, and Denmark, the incidence of fatal outcomes decreased in the second period [30, 31, 33]. This discrepancy may be attributable to alterations in the modalities of medical care and disease prevention, the unequal distribution of the disease burden across healthcare systems, and the expanded coverage of the population with COVID-19 testing.

The hospitalization rate in the ICU during the first phase of the study was 7.8%, and the ventilator use rate was 5.6%. The results of a study conducted in China in early 2020 demonstrated that the rate of hospitalizations in ICU and proportion of patients on ventilators were 6.2% and 3.1%, respectively, among patients with comorbidities (3.8% and 1.6%, respectively). These rates were slightly lower than those observed among patients with COVID-19 in the first period in Russia [18]. In the second period, in Russia, an increase was noted in the rate of transfer to ICU and AV, up to 10.3% and 7.7%, respectively. However, a study conducted in New York demonstrated a 15% reduction in the risk of hospitalization in ICU in the second period [31]. Moreover, a reduction in the rate of transfer to the ICU during the second period of the rise and decline was observed among hospitalized patients in Japan (from 11.8% to 6.1%) and Denmark (from 15.9% to 3.9%) and among elderly hospitalized patients in the Netherlands (from 10.9% to 8.3%) [30, 33, 34]. In contrast, in Iran, where the third period of the rise and decline in COVID-19 incidence coincided with the second period in Russia, the rate of transfer to the ICU in the third period was higher (18.8%) compared with the first and second periods (14.7% and 17.6%, respectively) [35].

The results of the present study indicated that a significant proportion of patients with COVID-19 had one or more comorbidities (25.8% in the first and 20.0% in the second periods of morbidity). Furthermore, 50% of these patients were hospitalized, which may be related to the more severe course of the disease in this group of patients and requirements of regulatory documents governing the mandatory hospitalization of persons with chronic diseases. The study conducted at the Central Clinical Hospital of the Russian Academy of Sciences did not identify any significant differences in the age of patients with COVID-19. The authors attributed this to the fact that the study considered the age imbalance in contrast to previously published studies [36].

In the context of comorbidities among patients with COVID-19 in Russia, both in the first phase of the pandemic and subsequently, cardiovascular diseases (18.3% and 15.0%, respectively) and endocrine disorders (6.5% and 5.7%, respectively) were the most prevalent, aligning with the findings of studies conducted in the United States and China [37, 38].

The study results indicate that the majority of the deceased were males, with the exception of the age group ≥70 years. Additionally, in the first period, the majority of the deceased were males, with the exception of those aged 18–29 years. The higher share of females in the structure of the deceased of the older age group may be due to natural reasons. According to the Federal State Statistics Service, as of January 1, 2022, the number of females per 1,000 males of the corresponding age group in Russia increased with age. This was observed to be from 944 in the 0–4 age group to 2,324 in the ≥70 age group [39]. The results of this analysis are consistent with those of other studies, which have indicated a higher risk of mortality from COVID-19

among males [15, 40]. However, in some countries, including Canada and the Netherlands, the differences in the incidence of fatal outcomes from new coronavirus infection between female and male patients were not statistically significant. Conversely, in countries such as India, Italy, Peru, Portugal, South Korea, the United Kingdom, and the United States, the proportion of deaths was significantly higher in males than in females [27]. The higher incidence of severe cases and adverse outcomes of COVID-19 among males can be explained by differences in the expression of angiotensin-converting enzyme type 2 receptors; levels of sex hormones (higher levels of androgens and lower levels of estrogens), which influence the functioning of the immune system (higher production of type 1 interferons, T- and B-cells); and the presence of bad habits [11, 41].

An increased number of deaths from COVID-19 were observed in groups at high risk of developing severe disease [27, 42]. A study conducted among patients with COVID-19 in Iran between February and April 2020 demonstrated an increased risk of mortality with age (by 5% with a 1-year increase in age), sex (males exhibited a 45% higher risk of mortality), and the presence of comorbidities (45% higher risk) [10].

Despite the significant differences between age groups in the structure of COVID-19 cases in Russia both in the first and second periods of the epidemic, the percentage ratio of these groups indicates a comparable contribution to the epidemic process of all age groups of the adult population of the country.

Presumably, the epidemic had a significant impact on population groups that did not seek medical care owing to the mild course of the disease, low motivation for treatment, or other reasons. This highlights the importance of extending preventive measures to the entire population, with a focus on vulnerable groups, as the risk of adverse outcomes is significantly higher for the elderly and those with chronic diseases. Furthermore, the significance of prompt diagnosis of infection and examination of contact persons should be emphasized, given the considerable time lag between the onset of symptoms and diagnosis of COVID-19. Moreover, the epidemiological and clinical characteristics of patients with COVID-19 should be analyzed at the population level during subsequent periods of rising and falling incidence in Russia to study the impact of new virus variants on the course of the disease and structure of patients.

CONCLUSIONS

In the initial phase of the COVID-19 pandemic in Russia, two distinct periods of morbidity were identified: from March to August 2020 and September 2020 to May 2021. These periods were associated with the spread of the wild strain of SARS-CoV-2 and its genetically closely related variants. In the second period in Russia, an increase was noted in the incidence of COVID-19 and mortality from the new coronavirus infection. Concurrently, there was an increase in the proportion of mild forms of the disease, a decrease in the frequency of hospitalizations and duration of illness and hospitalization, and an increase in the proportion of patients treated in the ICU and transferred to ventilators, compared to the first period. The analysis enabled the identification of specific risk factors, including older age, male sex, and presence of chronic diseases, particularly those affecting the cardiovascular and endocrine systems.

ADDITIONAL INFORMATION

Funding source. The research was supported by grant No. 24-45-00060 of the Russian Science Foundation (jointly with the National Natural Science Foundation of China (NSFC), project No. 72361137562) "Theoretical Modeling, Simulation and Capacity Building of Sino-Russian Medical Surge Response System in the Perspective of Complex Networks".

Competing interests. The authors declare that they have no competing interests.

Authors' contribution. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work. A.A. Fomicheva — study concept and design, collection and processing of material, statistical analysis, writing the text; N.N. Pimenov — study concept and design, writing the text, article editing; S.V. Komarova — collection and processing of material, article editing; A.V. Urtikov — collection and processing of material, statistical analysis; A.R. Sakhautdinov, D.A. Strelkova — text editing; G.V. Nekludova, S.A. Rachina, S.N. Avdeev — text editing, scientific consulting; V.P. Chulanov — study concept and design, scientific consulting, text editing.

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