MONITORING THE SPREAD OF COVID-19 ACROSS TUBERCULOSIS PATIENTS IN MOSCOW

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The COVID-19 pandemic necessitated making timely managerial decisions when providing medical care to patients with tuberculosis (TB). The study aimed to develop a system for monitoring of TB combined with COVID-19 and estimate the prevalence of COVID-19 among TB patients, along with the efficacy of the measures applied. A registry of TB/COVID-19 patients was developed based on the Barclay-SV Medical Database Management System. It was used to perform comparative analysis of the information about 1837 patients with active TB forms and confirmed COVID-19 for two periods of the pandemic, 2020–2021 and 2022–2023, and against the data on all new TB cases and TB relapses registered in Moscow in 2020–2023: 7812 and 1243 individuals respectively, from the TB surveillance registries, excluding those identified posthumously. The socio-demographic structure of patients with TB/COVID-19 co-infection identified in 2020–2023 did not change and corresponded to that of TB patients. In the second period analyzed, mild COVID-19 cases were registered more often (60.9% vs. 41.6%; $p < 0.01$), the share of moderate COVID-19 cases decreased from 48.2% to 20.6% ($p < 0.01$), and the share of severe cases decreased from 6.4% to 4.9% ($p = 0.19$). In 2022–2023, the share of individuals with COVID lung damage decreased from 45.1% to 17.6%, while the number of cases of COVID upper respiratory tract lesion increased from 47.1% to 64.5% ($p < 0.05$). The fact of having HIV infection, CAD and hypertension, kidney and genitourinary diseases increased the chance of developing COVID-19 by TB patients 1.5–2-fold, and disseminated pulmonary tuberculosis, caseous pneumonia, lung tissue destruction and bacterial excretion increased it 1.4–1.6-fold. The registry made it possible to control routing of TB/COVID-19 patients, as well as treatment outcomes: the total share of individuals cured reached 90.1%.

Keywords: monitoring, novel coronavirus infection, SARS-CoV-2, tuberculosis, tuberculosis/COVID-19 co-infection, tuberculosis epidemiological monitoring system

Author contribution: Kotova EA, Belilovsky EM — developing the method, literature review, manuscript writing, editing; Sumarokova EV — data acquisition and analysis, developing the method, literature review, manuscript writing, editing; Monchakovskaya ES — statistical data processing.

Compliance with ethical standards: retrospective processing of the registry data did not involve personal information

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Received: 11.12.2024 **Accepted:** 15.01.2025 **Published online:** 11.02.2025

DOI: 10.24075/brsmu.2025.003

МОНИТОРИНГ РАСПРОСТРАНЕНИЯ COVID-19 СРЕДИ БОЛЬНЫХ ТУБЕРКУЛЕЗОМ В МОСКВЕ

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Пандемия COVID-19 вызвала необходимость принятия своевременных управленческих решений при оказании медицинской помощи больным туберкулезом (ТБ). Целью работы было создание системы мониторинга ТБ, сочетанного с COVID-19, и проведение оценки распространения COVID-19 среди больных ТБ и эффективности проводимых мероприятий. Разработан регистр больных ТБ, сочетанным с COVID-19, на основе Системы управления базами медицинских данных «Барклай-СВ». С его помощью проводили сравнительный анализ информации о 1837 больных активными формами ТБ с подтвержденной COVID-19 по двум периодам пандемии: 2020–2021 гг. и 2022–2023 гг. и в сравнении с данными обо всех впервые выявленных больных и рецидивах ТБ, зарегистрированных в г. Москве в 2020–2023 гг.: 7812 и 1243 человека соответственно из регистров систем эпидемиологического мониторинга ТБ, исключая выявленных посмертно. Социально-демографическая структура больных сочетанной инфекцией ТБ/COVID-19, выявленных в 2020–2023 гг., не менялась, соответствовала этому параметру у больных ТБ. Во втором анализируемом периоде случаи легкого течения COVID-19 регистрировали чаще (60,9% против 41,6%; $p < 0,01$), доля случаев среднетяжелого течения COVID-19 снизилась с 48,2% до 20,6% ($p < 0,01$), тяжелого течения — с 6,4% до 4,9% ($p = 0,19$). Доля лиц с ковидным поражением легких без дыхательной недостаточности в 2022–2023 гг. уменьшилась с 45,1% до 17,6%, при росте случаев ковидного поражения верхних дыхательных путей с 47,1% до 64,5% ($p < 0,05$). Наличие ВИЧ-инфекции, ИБС и гипертонической болезни, болезней почек и мочеполовой системы в 1,5–2 раза увеличивало шанс проявления COVID-19 у больных ТБ, а диссеминированный ТБ легких, казеозная пневмония, наличие деструкции легочной ткани и бактериовыделения — в 1,4–1,6 раза. Регистр позволил осуществлять контроль маршрутизации пациентов ТБ/COVID-19, а также результаты лечения: доля излеченных в совокупности достигла 90,1%.

Ключевые слова: мониторинг, новая коронавирусная инфекция, SARS-CoV-2, туберкулез, сочетанная инфекция туберкулез/COVID-19, система эпидемиологического мониторинга туберкулеза

Вклад авторов: Е. А. Котова, Е. М. Белиловский — разработка метода, обзор литературы, написание статьи, редактирование; Е. В. Сумарокова — сбор и обработка материала, разработка метода, обзор литературы, написание статьи, редактирование; Е. С. Мончаковская — статистическая обработка материала.

Соблюдение этических стандартов: ретроспективную обработку данных регистра вели без использования персональной информации

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Статья получена: 11.12.2024 **Статья принята к печати:** 15.01.2025 **Опубликована онлайн:** 11.02.2025

DOI: 10.24075/vrgmu.2025.003

The pandemic of novel coronavirus infection (COVID-19) has become an example of the rise of a serious challenge for public health system having a rather limited exposure time. On March 11, 2020, the World Health Organization declared the beginning of the pandemic of the disease assigned the name COVID-19, and on May 5, 2023 declared the end of the pandemic [1–3]. The sheer scale of the influence of novel infection on public health system, arrangement of medical care, and economy requires not only timely response through temporary rearrangement of methods to deal with population and patients, but also arrangement of the temporary system for control and monitoring of the efficacy of the measures applied with continuous assessment of the epidemic process manifestations aimed at using the data for development of temporary methodological guidelines on prevention, diagnosis, and treatment of the disease, timely amendment of the latter, and prediction of the epidemiological situation development.

Moscow was among the first cities of the Russian Federation to face COVID-19. On March 2, 2020, the first disease case was reported in the capital, and red alert was declared as early as on March 5 [4, 5]. The main objective was to prevent the blast load on Moscow's healthcare system and avoid the scenario when the hospitals are overwhelmed and healthcare professionals do not have time to provide care to patients.

In April 2020, the Clinical Committee that included senior external experts of the Moscow Government Department of Health and chief physicians of municipal hospitals repurposed for treatment of patients with COVID-19 was established. The following goal was set for specialists: to promptly develop a clinical protocol for diagnosis of novel coronavirus infection (COVID-19) in patients undergoing inpatient treatment in medical institutions of Moscow [6]. A Protocol for treatment of patients with tuberculosis combined with novel coronavirus infection was developed at the Moscow Research and Clinical Center for Tuberculosis Control of the Moscow Government Department of Health (hereinafter, MRCCTC or Center).

In MRCCTC including two multidisciplinary clinics (Clinic No. 1, Clinic No. 2) and 9 branches in administrative districts of Moscow, beds were repurposed for COVID-19 patients. Beds in the Clinic No. 2 were used for inpatient treatment of patients with the combined infection (tuberculosis and COVID-19). Beds in two branches of the Center (in the South-Eastern and North-Western districts of Moscow) were used for treatment of patients with tuberculosis and mild novel coronavirus infection, as well as for observation of patients, who had contacted COVID-19 patients, and novel coronavirus infection convalescents in different time periods [7–9].

Under conditions of the developing pandemic of novel coronavirus infection, it became necessary to promptly develop and implement the system for monitoring of measures to detect and treat COVID-19 in patients with tuberculosis, which could ensure timely analysis of the epidemiological situation with the combined TB/COVID-19 infection and control of patient routing [10].

Today, one of the country's most well-developed tuberculosis surveillance systems (TBSS) functions in the city, which is used to acquire, process, and analyze the case-based data on detection, treatment and follow-up of TB patients for almost 25 years based on the scientifically grounded information structures that remain versatile and stable enough over a long time [11].

In Moscow, TBSS is based on the flexible Barclay-SV Medical Database Management System (MDBMS) allowing one to promptly develop and modify (if necessary) the information structure of the registries with arrangement of data entry, processing, and analysis.

During the pandemic the question arose about the need to create a temporary registry for monitoring of combined tuberculosis/COVID-19 infection and control over the effectiveness of the measures applied with the timely retrospective analysis of data on the patients having tuberculosis combined with COVID-19. The study aimed to promptly develop a system for monitoring of tuberculosis combined with COVID-19, analyze the spread of novel coronavirus infection among tuberculosis patients, and assess the effectiveness of the anti-epidemic measures applied.

METHODS

The temporary registry of patients with tuberculosis combined with novel coronavirus infection (TB/COVID-19) was developed based on the flexible Barclay-SV MDBMS (developed by MRCCTC together with Elecard-Med LLC, certificate of state registration of software No. 2019661941 dated 12.09.2019, Russian software registry entry No. 21931 dated 20.03.2024) [11]. The Barclay-SV MDBMS, in which the Moscow tuberculosis surveillance system registries are implemented, has a built-in designer of configurations (tasks or information structures) with the automated construction of input data entry forms and a report designer.

In the registry created, which was modified a limited number of times during the pandemic, as the regulatory documents and the COVID-19 patient management algorithm changed, in 2020–2023 the data were acquired on 2171 patients (2473 records), which included both information about the patients with active tuberculosis forms and the confirmed diagnosis of COVID-19 and the records of patients, in whom the diagnosis of tuberculosis was not confirmed based on the assessment results, and patients clinically cured of tuberculosis and transferred to the dispensary supervision group III [12, 13].

The analysis included information about 1837 patients with active forms of tuberculosis and the confirmed diagnosis of COVID-19 (2102 records), who were admitted to Moscow COVID hospitals for the first time, including cases when tuberculosis/COVID-19 was identified posthumously, or underwent outpatient treatment due to novel coronavirus infection (64 cases).

To compare patients having active tuberculosis forms and concomitant COVID-19 and those, in whom no novel coronavirus infection was detected, information was taken about all new cases and tuberculosis relapses reported in Moscow in 2020–2023: 7812 and 1243 individuals, respectively, from the city's TBSS registries, excluding those identified posthumously.

In accordance with the Temporary Guidelines on Prevention, Diagnosis, and Treatment of Novel Coronavirus Infection (COVID-19), approved by the Ministry of Health of the Russian Federation [1], Clinical Protocols for diagnosis of novel coronavirus infection (COVID-19) in patients undergoing inpatient treatment in medical institutions of the state public health system of Moscow [6], in 2020–2023 in Moscow, novel coronavirus infection (COVID-19) was diagnosed at the MRCCTC using the direct etiological laboratory diagnosis methods (SARS-CoV-2 RNA detection by polymerase chain reaction (PCR), as well as SARS-CoV-2 antigen detection by immunochromatographic assay (ICA) performed when assessing nasopharyngeal and oropharyngeal smears, regardless of clinical manifestations), indirect etiological diagnosis methods (detection of patients' serum immunoglobulins M, G (IgM and IgG) by immunochemistry methods), instrumental diagnosis method — computed tomography (CT) of lungs.

Immunological testing of the patients' serum was performed at the laboratory of the Center using the reagent

kits for identification of IgM and IgG antibodies against the SARS-CoV-2 strain by immunochemoluminescence assay in clinical samples using the CL analyzers for in vitro diagnosis (Shenzhen Mindray Bio-Medical Electronics Co., Ltd.; China, Mindray Medical Rus LLC). The coefficient used to recalculate the data obtained in BAU/mL was 1.32.

The registry data were analyzed using the chi-squared test and parametric statistical methods. Information about tuberculosis patients having and not having COVID-19 was compared using multiple logistic regression analysis.

RESULTS

During the COVID-19 pandemic, since March 2020, the Barclay-SV MDBMS was used in Moscow to implement monitoring of COVID-19 incidence among tuberculosis patients; the following was controlled when performing monitoring:

– information about the disease detection and diagnosis (dates, detection methods);

– patient routing;

– dynamic changes in assessment results (complete blood counts, D-dimer, anti-HIV, HBs Ag, anti-HCV, RW, PCR and ICA tests for COVID-19, serum IgM and IgG, chest radiography);

– ongoing COVID-19 treatment;

– COVID-19 treatment outcomes.

Information structure of the registry included the following:

– heading part with the main identification data on the patient;

– basic information about the patient: job/educational institution, position, actual residence address, permanent residence address, population category, nationality, social and professional background, information about COVID-19 vaccination;

– information about COVID-19 registration: dates of suspicion and confirmation of the diagnosis; confirmation methods; date of the emergence of clinical symptoms and description of the symptoms; data of seeking medical care due to symptoms of novel coronavirus infection; name of the medical institution the patient had contacted; information about the COVID-19 clinical variants and manifestations, disease severity; concomitant disorders; fact of contacting a COVID-19 patient; initial assessment results; treatment prescribed; measures in the outbreak of infection;

– complete blood counts, D-dimer levels; results of tests for COVID-19 (up to 15) with the automated comparison with normal IgM and IgG levels;

– information about routing specifying the names of medical institutions, where the patient was treated (up to six), specifying the admission ways and final COVID bed-days;

– COVID-19 treatment outcomes with saved information about the data of the last COVID-19-positive smear, achieving smear negativity, and overall COVID-19 treatment outcome;

– basic information about tuberculosis, including the patient's group based on medical history, data on detection, and the diagnosis results.

The Certificate of state registration No. 2022623380 dated 02.12.2022 was obtained for the registry structure and the database "Registry of Patients with Tuberculosis Combined with COVID-19 Registered in Moscow".

Due to temporary nature of the task, the database was developed as a pilot project, separately from the tuberculosis patient registry functioning in Moscow within the framework of TBSS.

The use of the Barclay-SV MDBMS as a basis made it possible to modify the registry data structure during operation, to promptly update the questionnaire and reports with the emergence of new diagnosis, treatment, and prevention methods, to clarify COVID-19 clinical variants and manifestations, and to classify the disease based on severity.

The analysis of the data of patients with tuberculosis combined with COVID-19 registered over four years of the pandemic (2020–2023) by MRCCTC was performed based on the information entered in the registry.

Here are the results of processing the data on 1837 patients, among them 699, 449, 542, and 147 patients, respectively, got COVID-19 in 2020–2023. Hospital readmissions due to COVID-19 were reported for 222 patients (265 hospital readmissions: 51, 77, 112, and 25, respectively in the specified period), which in a number of cases resulted from re-detection of SARS-CoV-2 after achieving negative nasopharyngeal and oropharyngeal smears within the course of the same case of novel coronavirus infection.

One of the data processing goals was to conduct the analysis of changes in the course of novel coronavirus infection under conditions of COVID-19 epidemiological situation changing throughout 4 years based on the registry data. The specified time period was conditionally divided into two 2-year periods: the period of the pandemic development — 2020–2021 and the period of its decline — 2022–2023.

Table 1 provides information about the methods for COVID-19 detection and diagnosis in patients with tuberculosis and confirmed coronavirus infection, who were admitted to the city's COVID beds at least once. The data are provided on the number of patients, in whom novel coronavirus infection was detected primarily by laboratory testing (while CT could also be performed), on the number of patients, in whom the diagnosis of COVID-19 was confirmed based on chest CT (while laboratory testing was also performed), and, finally, on the number of patients, in whom the diagnosis was established based on both CT and laboratory testing results.

The results show significant ($p < 0.01$) changes in predominant methods for detection of novel coronavirus infection over the last two years of monitoring (2022–2023) compared to the first two years of the COVID-19 pandemic (2020–2021): the role of laboratory methods in detection of novel coronavirus infection became overwhelming.

The registry data were used to implement control over routing and the ways of admission of the patients with tuberculosis combined with novel coronavirus infection to the COVID beds deployed at the MRCCTC. Admission to the hospital via ambulance took place in 43.8% of cases, scheduled admission — in 38.8% of cases, transfer from other medical institutions involving the use of sanitary transport — in 13.8% of cases, while in 3.6% of cases the admission ways were different.

Almost one fifth of TB/COVID-19 patients (20.7% or 377 patients) were admitted to the MRCCTC via non-tuberculosis medical institutions, including non-tuberculosis hospitals (149 individuals), municipal outpatient clinics (93 individuals), infection disease hospitals (121 individuals), research and clinical centers and federal institutions (14 individuals).

According to their medical history, about one third of TB/COVID-19 patients indentified during this period had a confirmed contact with the patients suffering from COVID-19 — 29.4%.

The socio-demographic structure of the patients having combined TB/COVID-19 infection, who were identified in 2020–2023, was rather stable.

Distribution of patients with tuberculosis combined with novel coronavirus infection across the population categories is

Table 1. Methods to detect and diagnose COVID-19 in tuberculosis patients with confirmed coronavirus infection admitted for treatment for the first time (Moscow, 2020–2023)*

Year	2020	2021	2020–2021	2022	2023	2022–2023	Total
Total number of admissions	699	449	942	497	130	689	1837
Laboratory method, including combined with CT, abs.	578	364	942	497	130	627	1569
%	82.7	81.1	82.1	91.7	88.4	91	85.4
Computed tomography, including combined with laboratory methods, abs.	219	214	433	103	31	134	567
%	31.3	47.7	37.7	19	21.1	19.4	30.9
By two methods, abs.	119	137	256	61	17	78	334
%	17	30.5	23.3	11.3	11.6	11.3	18.2
Unspecified detection method	21	8	29	3	3	6	35
%	3	1.8	2.5	0.6	2	0.8	1.9

Note: * — No information was available for 35 patients.

similar to that of tuberculosis patients: slightly less than half or 45.6% were permanent residents (41.7%, 50.7%, 46.2%, and 47.3% in 2020–2023, respectively), almost a quarter or 23.8% were residents of other Russian regions (23.3%, 24.2%, 25.3%, and 19.9%, respectively), every seventh person was homeless (16.7%), and every eighth was a foreign citizen (13.9%).

More than a half of TB/COVID-19 patients or 53.1% were jobless and unemployed (56.3%, 50.7%, 51.8%, and 51.4% in 2020–2023, respectively), 16.8% were employed (14.7%, 20.8%, 15.7%, and 17.9% in 2020–2023 respectively), and 14.8% were disabled (13.9%, 14.8%, 15.3%, and 17.1% in 2020–2023, respectively). Others were retirees (11.4%), students (3.1%), and preschool children (0.8%).

More than a half of affected individuals or 54% were incident tuberculosis patients (50.9%, 60.1%, 54.8%, and 63.9% in 2020–2023, respectively), 13.4% had tuberculosis relapses, 9.3% were arriving tuberculosis patients, 21.9% were registered for follow-up as tuberculosis patients before the COVID-19diagnosis.

We compared all new cases and tuberculosis relapses registered in 2020–2023 (excluding those identified posthumously), in which COVID-19 was detected (group 1) or not detected (group 2): 762 and 8293 individuals, respectively.

There were no gender differences in the groups: males accounted for 66.4% and 68.0%, respectively ($p > 0.05$). Patients with TB/COVID-19 were on average older (Fig. 1): the average age in group 1 (with TB/COVID-19) was 44.7 years (95% CI: 43.6–45.8), while in group 2 it was 40.5 years (95% CI: 40.2–40.9), $p < 0.05$.

Table 2 and Fig. 2A and 2B provide the multivariate analysis and multiple logistic regression results for assessment of factors that are statistically related to the presence of COVID-19 in tuberculosis patients, i.e. the probability of the relationship of those with the fact of having novel coronavirus infection exceeds 95% ($p < 0.05$).

The presence of COVID-19 in the tuberculosis patients is associated with a rather large number of individual factors (univariate analysis), such as age over 30 years, fact of having HIV infection, some forms of pulmonary tuberculosis (disseminated, caseous pneumonia), lung tissue destruction and bacterial excretion, as well as the number of concomitant disorders determined by population groups. At the same time, if we take into account the relationship between these factors and apply multivariate analysis, then the following concomitant diseases remain the leading factors most strongly associated with the presence of COVID-19 in tuberculosis patients in terms of statistics: HIV infection, CAD and hypertension, kidney and genitourinary diseases, as well as severe and advanced pulmonary tuberculosis forms.

Thus, among the studied factors associated with tuberculosis, the facts of having disseminated disease forms, caseous pneumonia, bacterial excretion or destruction cavity in the lung show a significant correlation with getting COVID-19. Limited forms of tuberculosis, such as tuberculoma, represent the so-called “protective factors” against COVID-19.

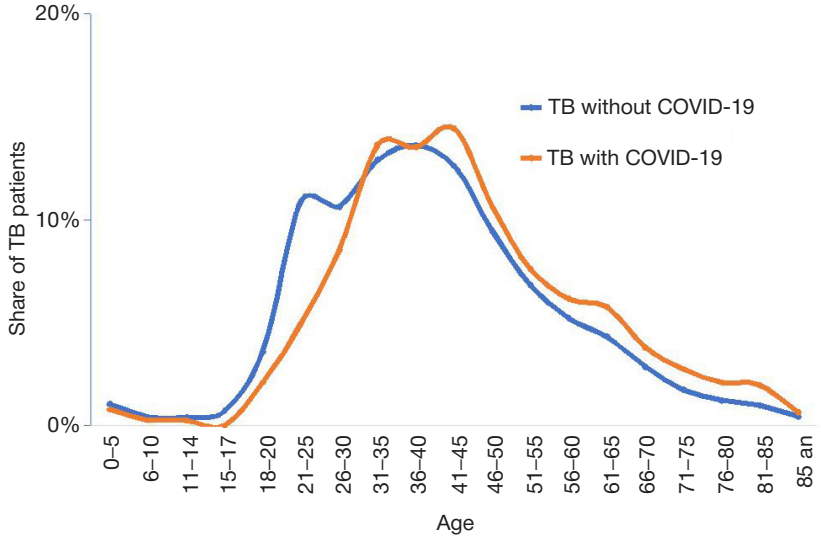

Fig. 1. Age dependence of new tuberculosis cases and tuberculosis relapses depending on the fact of COVID-19 detection (Moscow, 2020–2023)

Table 2. Factors associated with the fact of having COVID-19 in new tuberculosis cases and relapses of tuberculosis (Moscow, 2020–2023). Univaruate and multivariate analysis

Factor	Univariate analysis					Multiple logistic regression
	Number in group 1	Share in group 1, %	Number in group 2	Share in group 2, %	OR (95% CI)	OR (95% CI)
Age under 30 years	127	16.7	2291	27.6	0.52 (0.43–0.64)	$p > 0.05$
HIV infection	225	29.5	1213	14.6	2.45 (2.07–2.89)	1.86 (1.55–2.25)
Disseminated PTB	249	32.7	1479	17.8	2.24 (1.9–2.63)	1.56 (1.3–1.86)
Tuberculoma	11	1.4	459	5.5	0.25 (0.14–0.46)	0.33 (0.18–0.61)
Caseous pneumonia	41	5.4	196	2.4	2.35 (1.66–3.32)	1.72 (1.19–2.47)
Lung tissue destruction	377	49.5	2946	35.5	1.78 (1.53–2.06)	1.41 (1.19–1.67)
Bacterial excretion	401	52.6	2670	32.2	2.34 (2.01–2.72)	1.62 (1.36–1.91)
Diabetes mellitus	51	6.7	370	4.5	1.53 (1.13–2.08)	$p > 0.05$
COPD	92	12.1	646	7.8	1.63 (1.29–2.05)	$p > 0.05$
CAD and hypertension	90	11.8	538	6.5	1.93 (1.52–2.45)	1.84 (1.44–2.37)
Alcohol abuse	33	4.3	232	2.8	1.57 (1.08–2.28)	$p > 0.05$
Drug addiction	22	2.9	102	1.2	2.39 (1.5–3.81)	$p > 0.05$
Diseases of the kidneys and genitourinary system	25	3.3	122	1.5	2.27 (1.47–3.52)	1.78 (1.14–2.79)
Liver and gallbladder diseases	44	5.8	301	3.6	1.63 (1.18–2.25)	$p > 0.05$
Employee	60	7.9	852	10.3	0.75 (0.57–0.98)	$p > 0.05$
Retired person	93	12.2	679	8.2	1.56 (1.24–1.96)	$p > 0.05$
Permanent resident	409	53.7	3422	41.3	1.65 (1.42–1.91)	1.19 (1–1.42)
Homeless person	94	12.3	685	8.3	1.56 (1.24–1.97)	$p > 0.05$
Feign citizen	113	14.8	2711	32.7	0.36 (0.29–0.44)	0.59 (0.46–0.75)

Note: group 1 — TB/COVID-19 patients, group 2 — newly diagnosed patients with tuberculosis and relapses of tuberculosis that have not been added to the TB/COVID-19 registry. PTB — pulmonary tuberculosis, CAD — coronary artery disease, COPD — chronic non-specific lung diseases.

The analysis of information about patients with tuberculosis combined with COVID-19, who were entered in the registry, has shown significant differences in clinical manifestations and immune status of these patients in the initial and final 2-year periods of the pandemic.

Table 3 provides the results of testing for immunoglobulins M (IgM) and G (IgG) obtained when the TB/COVID-19 patients sought medical care in 2020–2023. These data can show the phase of the infectious process course at the time when the patient sought medical care, time since SARS-CoV-2 infection.

Considering provisions of the regulatory documents [1, 6], detection of IgM and IgG levels below normal (1 and 10, respectively) can indicate that less than 7 days have passed since the patient was infected with coronavirus [1, 6, 13–15]; when this IgM level is exceeded and IgG remain within normal (IgM > 1, IgG within normal range) — that there is acute infection, and the patient got infected 1–3 weeks ago [6, 14]; when the levels of immunoglobulins of both classes are elevated — that the infectious process history is 3–10 weeks [15]; when IgM are within normal range and IgG are above normal (IgG ≧ 10, IgM within normal range) — that the patient was exposed to the virus more than 10–12 weeks ago [15].

Comparison of the 2-year periods (2020–2021 and 2022–2023) has shown a significantly reduced share of cases with the IgG and IgM below normal in the second period: 55.4% and 29.3%, respectively ($p < 0.05$), the decrease in the number of cases with the combination, when only IgM are above normal (7.4% and 4.3%, respectively; $p = 0.095$), and a significantly increased share of patients with only IgG above normal: 18.6% and 43.0%, respectively ($p < 0.05$). Furthermore, the results obtained for 616 patients with concomitant HIV infection were similar.

In Moscow, mass vaccination against novel coronavirus infection (COVID-19) was started in December 2020. That is why patients assigned to the last group (IgG ≧ 10, IgM within normal range) also could have elevated IgG levels due to vaccination since 2021. Furthermore, elevated IgG levels can persist for a long time past novel coronavirus infection (about 6 months or more according to different reports) [14, 16, 17].

The findings reflect the pandemic subsides in 2022–2023 and, to some extent, immunization of the population (and therefore tuberculosis patients) due to past contacts with COVID-19 patients and mass vaccination.

The COVID-19 pandemic transformation into routine seasonal infection in 2022–2023 is also evident from the description of clinical symptoms and severity of the course of novel coronavirus infection at the time of case registration.

This registry have been used to monitor the symptoms, course, clinical variants, and manifestations of novel coronavirus infection, disease severity in the registered TB/COVID-19 cases for 4 years (Fig. 3).

While in the first two years of the pandemic dry cough, feeling of tightness in the chest, and decreased sense of smell and taste (significance of the decrease in the share of each symptom; $p < 0.05$), as well as dyspnea ($p = 0.2$) prevailed among the disease symptoms, sore throat and runny nose were more commonly reported during the next two years ($p < 0.05$), i.e. the symptoms of ordinary acute viral infection (Fig. 3A).

Mild COVID-19 cases were significantly more often registered in the last two years (Fig. 3B). The share of those increased from 41.6% to 60.9% ($p < 0.01$), while the share decreased of both moderate (from 48.2% to 20.6% ($p < 0.01$)) and severe (from 6.4% to 4.9% ($p = 0.19$)) COVID-19.

It should be noted that the COVID-19 classification based on severity changed in accordance with the regulatory documents [1]. Initially, there were three degrees: mild, moderate, and severe forms. After Version 5 (08.04.2020) of the

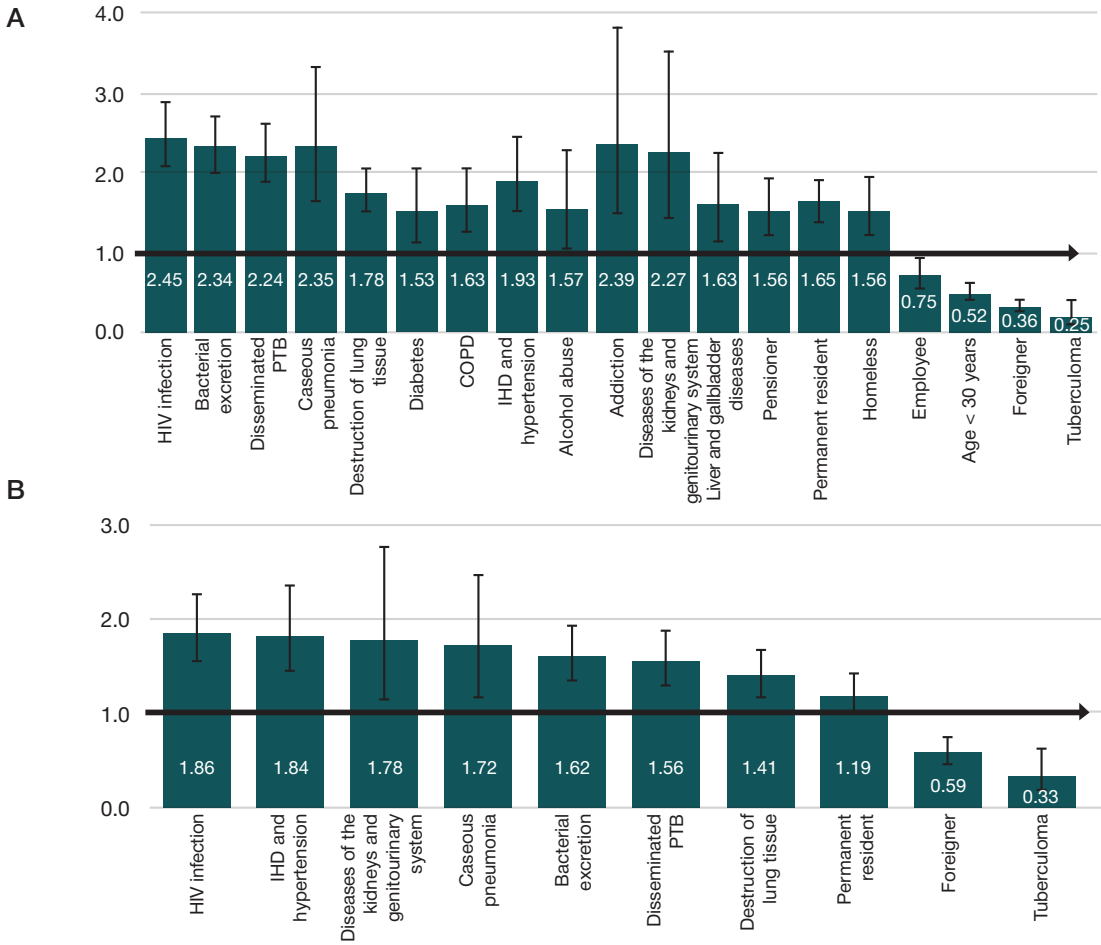

Fig. 2. Factors associated with the presence of COVID-19 in tuberculosis patients, univariate **(A)** and multivariate **(B)** analysis. Odds ratio (OR) of detecting COVID-19 co-infection in the presence of this symptom in a tuberculosis patient or the relationship between this symptom and the fact of having COVID-19 (Moscow, 2020–2023)

Temporary methodological guidelines "Prevention, Diagnosis, and Treatment of Novel Coronavirus Infection (COVID-19)" was issued, the classification became as follows: mild course, moderate course, severe course, extremely severe course.

Furthermore, the decrease in the share of individuals having the COVID lung damage without respiratory failure from 45.1% to 17.6% is reported, along with the growth of the number of cases of COVID upper respiratory tract (URT) lesion: from 47.1% to 64.5% in both cases, $p < 0.05$ (Fig. 3C).

It should be noted that 222 patients, who were readmitted to hospital due to COVID-19 in 2020–2023 had the structure of the clinical variants and severity of novel coronavirus infection similar to that reported for primary hospital admissions during the period of the pandemic subside (2022–2023). The COVID upper respiratory tract lesions at readmission were reported in 62.2% of cases, COVID lung damage without acute respiratory failure (ARF) — in 29.2% of cases, and mild-to-moderate disease course — in 69.8% and 25.0% of cases, respectively. The share of COVID upper respiratory tract lesions and mild disease course was higher at readmission ($p < 0.05$) relative to the data reported for those, who sought medical care for the first time, in whom these indicators were 53.3% and 48.8%, respectively.

The average COVID bed-days of a patient with TB/COVID-19 decreased every year (from 15.5 days in 2020 to 14.4, 12.8, and 10.6 days, respectively, in 2021–2023), which was due not only to the fact that the course of novel coronavirus infection (COVID-19) became milder, but also to the fact that the terms of the COVID–19 convalescent discharge from the COVID bed for isolation changed.

We conducted analysis of the novel coronavirus infection treatment outcomes in the tuberculosis patients undergoing

Table 3. Results of immunoglobulin IgM and IgG tests obtained when detecting COVID-19 in patients with tuberculosis (Moscow, 2020–2023)

Year	Total (examination results are available upon admission)	IgM ≧ 1		IgG ≧ 10		Both are below normal*		IgM >1, IgG normal (<10)**		Both are above normal.***		IgG ≧10 IgM normal (<1)****	
		Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%
2020	218	51	23.4	65	29.8	134	61.5	19	8.7	32	14.7	33	15.1
2021	337	95	28	143	42.5	172	50.7	22	6.5	73	21.5	70	20.6
2022	249	70	28	164	65.6	74	29.6	11	4.4	59	23.6	105	42
2023	7	1	12.5	6	75	1	12.5	0	0	1	12.5	5	62.5
Всего	811	217	26.6	378	46.5	381	46.7	52	6.4	165	20.2	213	26.1

Note: * — no more than 7 days have passed since the infection; ** — acute infection, infection history 1–3 weeks. *** — infection history 3–10 weeks; **** — body's exposure to the virus took place more than 10–12 weeks ago.

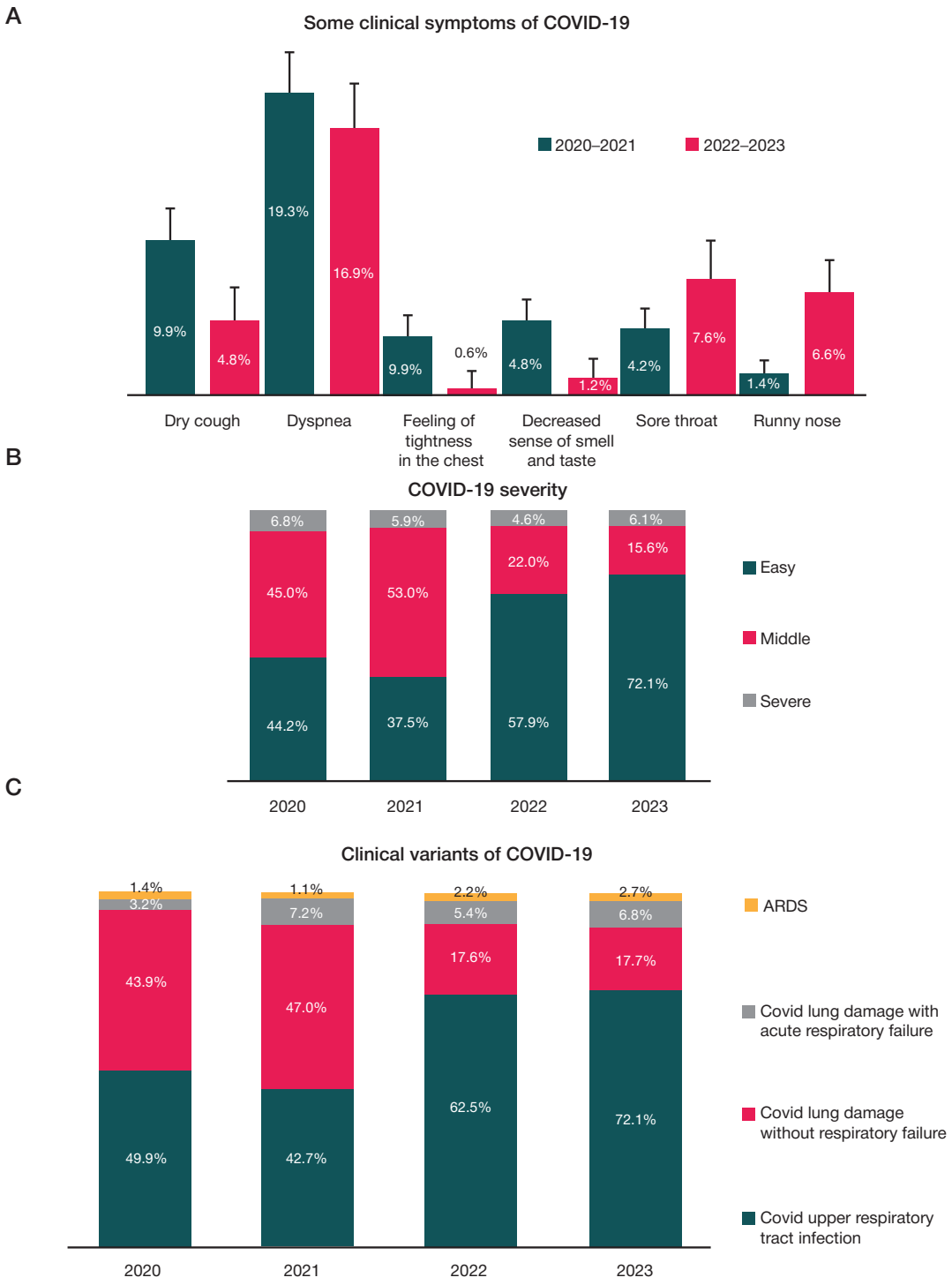

Fig. 3. Results of monitoring the course of COVID-19 in 1837 patients with TB combined with COVID-19, who were admitted for treatment for the first time in 2020–2023 in Moscow. Severe cases also include extremely severe COVID-19 (ARDS or pneumonia with ARF and the need for mechanical ventilation)

treatment in Moscow, primarily occupying COVID beds in hospitals: the share of those cured in 2020–2023 was 84.9% (95% CI: 83.2–86.4%), 5.2% were referred to continue treatment of COVID-19 in outpatient settings, and 9.9% (95% CI: 8.6–11.4%) died. Given the fact that the patients, who had mild coronavirus infection or showed regression of the infection due to treatment, were referred to continue treatment in outpatient settings after discharge from hospital, it can be considered that the total share of the patients with TB/COVID-19 cured is 90.1%.

Three quarters (77.7%) of fatalities were caused by COVID-19, 8.5% (95% CI: 4.9–13.5%) — by HIV infection, and 7.4% (95% CI: 4.9–13.5%) — by tuberculosis. Other causes of death accounted for 6.4%.

DISCUSSION

During the pandemic of novel coronavirus infection the temporary registry of patients having tuberculosis combined with COVID-19 was realized, which ensured the necessary control of information about registration, management and treatment outcomes of the patients.

Successful prompt realization of the TB/COVID-19 temporary registry through efforts of the head anti-tuberculosis

medical institution of the region became possible due to the use of flexible software shell of Barclay-SV MDBMS [11]. The development of this registry represents an example of prompt modification and development of the regional tuberculosis surveillance system in cases of challenges in the form of significant spread of novel hazardous infections. A state certificate was obtained for the registry.

The registry realized made it possible to perform ongoing and retrospective assessment of the structure of affected individuals, determine the factors most strongly statistically associated with the fact of getting novel coronavirus infection in tuberculosis patients, such as concomitant disorders, including HIV infection and pulmonary tuberculosis forms, population groups. Facts of having HIV infection, CAD and hypertension, kidney and genitourinary diseases increased the chance of developing novel coronavirus infection by tuberculosis patients almost 1.5–2-fold (OR = 1.9, 1.8, and 1.8, respectively), and disseminated pulmonary tuberculosis, caseous pneumonia, lung tissue destruction and bacterial excretion increased it 1.4–1.6-fold (OR = 1.6, 1.7, 1.4, and 1.6, respectively).

The registry operation enabled continuous control over the routing of patients, among whom one fifth were transferred to the MRCCTC COVID beds from non-tuberculosis medical institutions, and the treatment outcomes in tuberculosis/COVID-19 patients were as follows: the total share of those cured reached 90.1%.

The information obtained made it possible to assume termination of significant effects of the pandemic on public health system in 2022–2023, which could affect distribution of appropriate resources. The leading clinical symptoms of the infection changed in the last two years of the pandemic, COVID-19 more often progressed to the COVID upper respiratory tract lesion, and the share of cases of COVID lung damage and severe course of novel coronavirus infection was significantly reduced. Immunological testing performed in patients also confirmed the fact of getting out of the pandemic since 2022 and gradual formation of population immunity.

CONCLUSIONS

Prompt arrangement of temporary monitoring of the effects of the novel coronavirus infection pandemic on epidemiology of tuberculosis has demonstrated the necessary flexibility of the regional TBSS. Realization of the registry of patients having the combined tuberculosis/COVID-19 infection in Moscow has enabled prompt and retrospective analysis of data of the patients, control over their routing, treatment outcomes, spread of COVID-19 across tuberculosis patients, and effectiveness of the applied anti-epidemic measures in general.

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