EPIDEMIOLOGY

EPIDEMIOLOGICAL MANIFESTATIONS OF TUBERCULOSIS INFECTION IN THE OMSK REGION: DYNAMICS AND TRENDS

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ABSTRACT

Background. *Tuberculosis (TB) infection remains relevant as one of the leading public health problems in Russia.*
The aim. *To characterize the dynamics and trends of epidemiological manifestations of TB infection in the Omsk region.*
Materials and methods. *An observational descriptive-evaluative epidemiological study was carried out in the Omsk region from 2009 to 2021. The data available in the Federal statistical observation forms NN 7, 8, and 33, and results of the bacteriological study of patients with respiratory TB were analyzed.*
Results. *In the Omsk region, an improvement in the epidemiological situation was observed from 2009 to 2021. It was associated with a decrease in TB prevalence by 3.7 times (from 325.6 to 86.7), mortality – by 5.8 times (from 21.1 to 3.6), incidence – by 2.7 times (from 130.7 to 48.4 per 100,000). At the same time, proportion of microscopy/culture-positive patients infected with multidrug-resistant Mycobacterium tuberculosis strains increased from 9.2 to 29.8 % among all patients, and from 15.5 to 30.6 % among newly diagnosed patients. There was a trend towards an increase in the number of cases with primary extensive drug resistance of M. tuberculosis. The incidence of tuberculosis associated with HIV infection has increased 10 times and reached 15.6 per 100,000 population.*
Conclusions. *In the Omsk region, there is a change in the structure of M. tuberculosis strains with a predominance of multiple and extensive drug resistance along with decrease in TB incidence and mortality. New approaches are needed to organize the system of epidemiological surveillance and control of TB infection.*

Key words: *tuberculosis, incidence, prevalence, drug resistance, M. tuberculosis, HIV infection*

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ЭПИДЕМИОЛОГИЧЕСКИЕ ПРОЯВЛЕНИЯ ТУБЕРКУЛЁЗНОЙ ИНФЕКЦИИ В ОМСКОЙ ОБЛАСТИ: ДИНАМИКА И ТЕНДЕНЦИИ

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РЕЗЮМЕ

Обоснование. *Туберкулёзная инфекция сохраняет свою актуальность как одна из ведущих проблем общественного здравоохранения России.*
Цель исследования: *характеристика динамики и тенденций эпидемиологических проявлений туберкулёзной инфекции на территории Омской области.*
Методы. *Проведено наблюдательное описательно-оценочное эпидемиологическое исследование на территории Омской области за период с 2009 по 2021 г. Исследованы данные статистических отчётных форм № 7, № 8 и № 33, результаты бактериограмм больных туберкулёзом.*
Результаты. *Наблюдалось улучшение эпидемиологической ситуации, связанное с сокращением распространённости туберкулёзной инфекции в 3,7 раза (с 325,6 в 2009 г до 86,7 в 2021 г.), смертности от туберкулёза – в 5,8 раза (с 21,1 до 3,6 на 100 тыс. населения), заболеваемости – в 2,7 раза (с 130,7 до 48,4 случая на 100 тыс. населения). Вместе с тем отмечено изменение структуры случаев инфекции – в контингенте больных туберкулёзом доля бактериовыделителей штаммов Mycobacterium tuberculosis с множественной лекарственной устойчивостью (МЛУ) возросла более чем в 3 раза (с 9,2 до 29,8 %), доля впервые выявленных бактериовыделителей штаммов с МЛУ возросла с 15,5 до 30,6 %. Отмечена тенденция к увеличению количества случаев с первичной широкой лекарственной устойчивостью M. tuberculosis. Заболеваемость туберкулёзом, сочетанным с ВИЧ-инфекцией, возросла в 10 раз (до 15,6 случая на 100 тыс. населения).*
Заключение. *В Омской области наблюдается изменение структуры бактериовыделения с преобладанием множественной и широкой лекарственной устойчивости на фоне тенденции к снижению заболеваемости и смертности населения от туберкулёза. Требуется совершенствование организации системы эпидемиологического надзора и контроля за туберкулёзной инфекцией.*

Ключевые слова: *туберкулёз, заболеваемость, распространённость, лекарственная устойчивость, M.tuberculosis, ВИЧ-инфекция*

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OBJECTIVES

Tuberculosis (TB) infection remains relevant as one of the leading public health problems. Worldwide, about 10 million new cases of tuberculosis have been reported annually in recent years, which were 127 (114–140) cases per 100,000 population in 2020 [1].

The World Health Organization has set a global goal of eliminating tuberculosis by 2035 [2], and efforts to improve the system of tuberculosis care and increase the coverage of the population with measures intended for preventing care and avoiding the spread of tuberculosis have allowed the world community to save an estimated 63 million lives by 2020 [3].

The estimated number of tuberculosis cases in the European Region of the World Health Organization has been consistently decreasing since 2000. The average annual decrease in TB incidence was 5.2 % in the period between 2011 and 2020 and 6.4 % in 2019–2020, which is much higher than the global rate of decrease in TB incidence (1.9 %) and is an example of the fastest rate of decrease worldwide compared to other regions [4].

The epidemiological situation in the Russian Federation has improved significantly, with a significant decrease in the incidence of tuberculosis among the population, which characterises the epidemic situation. However, the increasing number of patients with multidrug-resistant and extensively drug-resistant tuberculosis (MDR/XDR) and HIV infection has an extremely negative impact [5].

Molecular epidemiological studies conducted in Russia during the past 20 years emphasize the special role of the dominant strains of *Mycobacterium tuberculosis* of the Beijing genetic family, which is characterized by a generally strong association with multidrug resistance [6, 7]. The results of a study conducted in the Omsk region made it possible to characterize the genetic diversity of *M. tuberculosis* strains circulating in the region and also to establish the leading role of the Beijing genetic family (65.6 %) [8]. In the population structure of the Beijing *M. tuberculosis* genetic family in the Omsk region, strains of modern sublineage (86.3 %), in particular clusters 94–32 (60.7 %) and B0/W148 (25.0 %) prevailed [7]. Cluster 94–32 strains were characterized by a high level of multidrug resistance (53.8 %). The proportion of ancient sublineage strains was higher than in other regions of Russia and amounted to 13.7 %. Particular clinical relevance has been shown for ancient sublineage strains of genotype Beijing, 52.5 % of which were characterized by pre-extensive and extensive drug resistance [7]. Among the dominant strains of modern Beijing sublineage, the B0/W148 and 94-32 clusters can be observed, in which 33 and 12.4 % of the strains had pre-extensive and extensive drug resistance [8].

Considering the relevance of the co-epidemic processes of tuberculosis and HIV infection, criteria were previously proposed to assess the impact of HIV infection on the development of the tuberculosis epidemic process. Simultaneous development of epidemic processes of tuberculosis and HIV infection, high activity of epidemic processes of both infections with involvement of the general population, as well as positive statistically significant correlations of incidence and prevalence rates indicate the integration of the epidemic processes of HIV infection and tuberculosis and require additional assessment of the quality of preventive and diagnostic measures [9]. Among TB patients combined with HIV infection, the primary MDR rate reached 31.3 % in Russian regions with high HIV prevalence [10, 11]. Among the deceased patients with comorbidities, multidrug resistance represented 40 %, and the efficacy of treatment of such patients was low and did not exceed 7.3 % of patients [10].

The aim of this study aimed to describe the dynamics and trends of epidemiological manifestations of TB infection in the territory of the Omsk region over a multi-year period (2009–2021).

MATERIALS AND METHODS

The study is based on the observation of the epidemic process of TB infection in the Omsk region. Retrospective epidemiological analysis of incidence of tuberculosis among the population has been carried out using data from statistical reporting forms No. 7-TB "Information about newly diagnosed patients and relapses of tuberculosis disease", No. 8 "Information about incidence of active tuberculosis", No. 33 "Information about tuberculosis patients» over the period 2009–2021. Disease incidence and disease prevalence, as well as extensive indicators characterizing the structure of incidence have been evaluated.

Trends in the development of the epidemic process were determined by straight-line equalization of the dynamic series of indicators using the least squares method and calculation of the coefficient of determination (R^2).

Bacteriological examination of patients, determination of the sensitivity spectrum of isolated *Mycobacterium tuberculosis* strains to the anti-tuberculosis drugs was carried out in accordance with the standard procedure of microbiological examination [12].

To compare demographic and clinical and epidemiological characteristics of two cohorts of patients newly diagnosed in 2009 (n = 2638) and in 2021 (n = 922), the PR prevalence ratio and its confidence intervals (CI) were calculated. Among the factors evaluated were gender, age, place of residence, clinical form of the disease, HIV status, massiveness of bacteriuria, and drug resistance pattern observed in patients discharging bacteria.

Data analysis was performed using Microsoft Office 2010 application (Microsoft Corp., USA).

RESULTS

The dynamics of TB infection prevalence in the Omsk region was characterized by a pronounced trend towards a decrease in the number of cases. The TB prevalence rate decreased by 3.7 times (from 325.6 in 2009 to 86.7 in 2021), and the patient cohort under follow-up medical care included 1,651 patients at the beginning of 2022 (Fig. 1). It should be noted that in the last two years the number of TB patients has not significantly changed, in 2020 the prevalence rate decreased by 24.3 % as compared to 2019 and amounted to 84.3 per 100 thousand population, and in 2021 it increased by 2.8 %.

The multi-year dynamics of tuberculosis incidence in population have had a similar trend, in 2021 the lowest incidence rate was observed (48.4 per 100,000 population), which is 2.7 times lower than in 2009 (2,638 cases), and 1.7 times lower than the average annual rate (83.9 cases per 100,000 population).

The mortality rate of the population caused by tuberculosis decreased 5.8 times, from 21.1 cases per 100,000 population ($n = 289$) to 3.6 ($n = 68$) cases per 100,000 population.

The incidence of bacteriologically proven tuberculosis decreased less intensively; thus, during the analysed period, the incidence of bacillary forms of tuberculosis decreased from 47.4 to 26.3 cases per 100,000 popu-

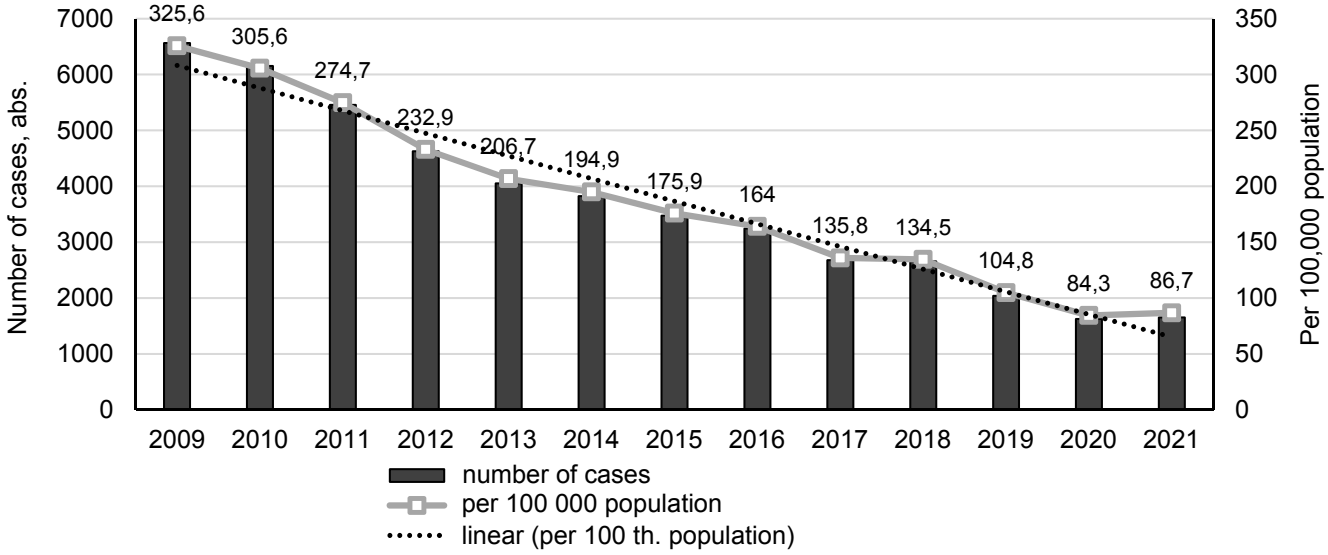

FIG. 1.
Dynamics of the spread of tuberculosis infection in the Omsk region (per 100,000 population, 2009–2021)

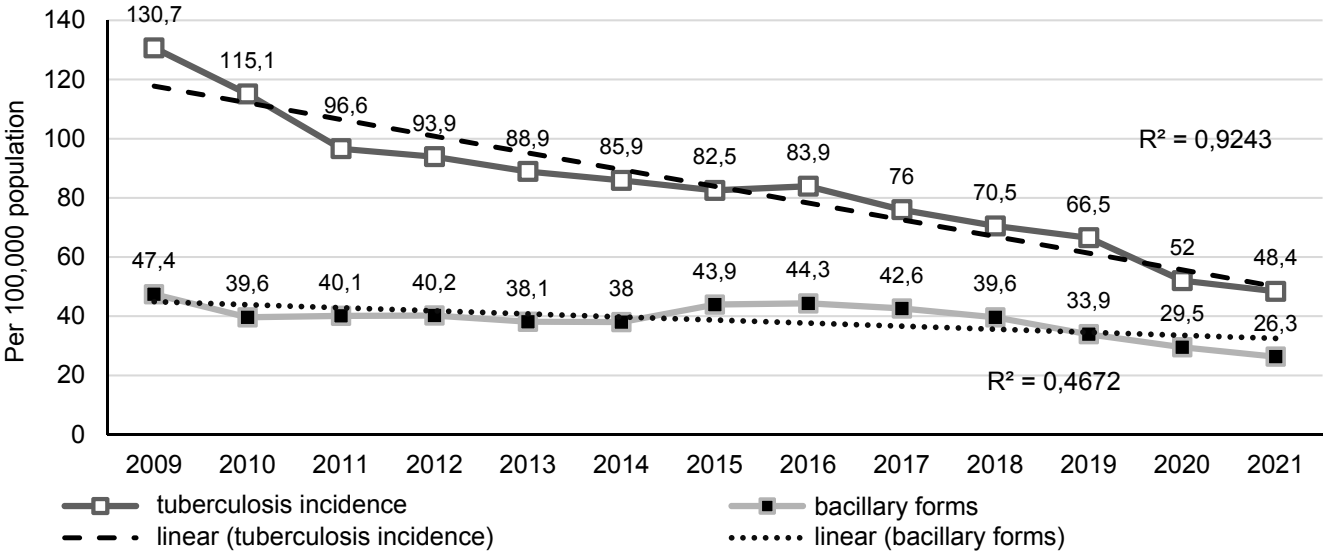

FIG. 2.
Dynamics of the incidence of tuberculosis in the population of the Omsk region (2009–2021)

lation, while the average annual rate was 38.7 cases per 100,000 population (Fig. 2).

The epidemic process of tuberculosis in the Omsk region was characterized by a number of qualitative changes. Thus, since 2009, the proportion of MDR bacterial excretion in the structure of bacteriological excretion among newly diagnosed TB cases has doubled from 13.1 % to 26.4 % (Fig. 3). Between 2016 and 2020, the proportion of MDR cases among newly diagnosed TB patients discharging bacteria averaged 30.5 %.

During the analyzed period, the average annual incidence of MDR-TB was 8.2 diagnosed in the population was 8.2 cases per 100,000 population. In the period between 2009 and 2014, the dynamics of MDR-TB incidence was stable (annual average – 7.2 cases per 100,000 population); in 2015–2016, the incidence increased to an average of 10.5 cases per 100,000 population. Incidence has been declining since 2017, with a yearly average of 8.6 cases per 100,000 population, reaching a rate of 6.5 TB cases per 100,000 population in 2021.

In the Omsk region, the prevalence of MDR-TB tended to decrease (Fig. 4). At the same time, the proportion of MDR strains of *M. tuberculosis* among patients with active tuberculosis under follow-up medical care more than tripled from 9.2 % (606/6565) to 29.8 % (478/1651), although at the end of 2021, only 66.2 % (478/721) of bacterial excretors under follow-up care were isolating MDR strains, twice as many as in 2009 (32.6 %).

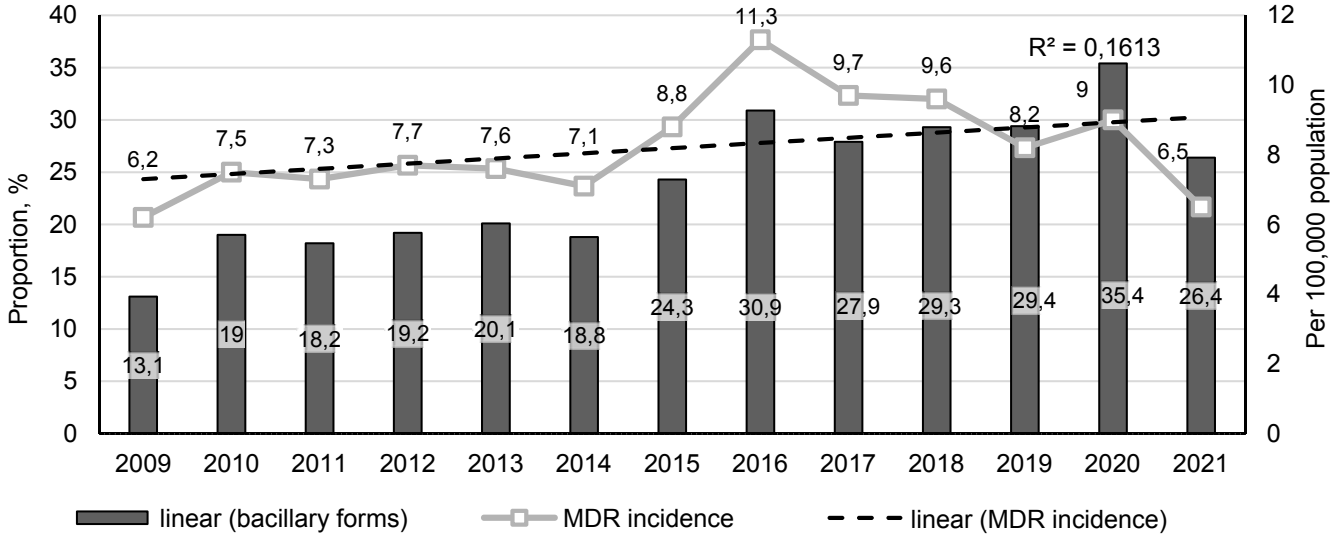

FIG. 3.

Dynamics of the incidence of multidrug-resistant tuberculosis in the population of the Omsk region (per 100,000 population)

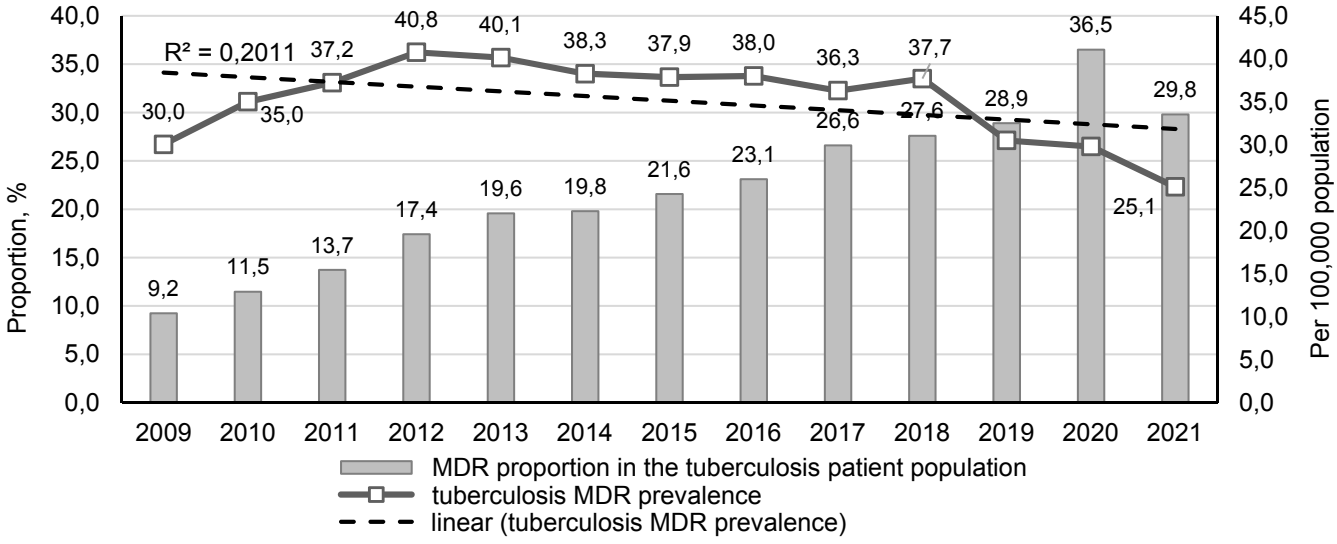

FIG. 4.

Dynamics of the prevalence of multidrug-resistant tuberculosis in the Omsk region (2009–2021)

Changes in the incidence pattern of TB infection were evaluated by comparing two patient cohorts who were first diagnosed with active TB in 2009 and 2021, i. e. at the beginning and end of the study period.

The evaluation revealed statistically significant differences in the groups of newly diagnosed patients. By the end of the study period, there was a statistically significant increase in the proportion of males among TB cases, rising from 67.1 % in 2009 to 71.9 % in 2021 (PR = 0.79; 95% CI: 0.67-0.94).

The age structure of TB patients has changed, the proportion of young population decreased: adolescents from 1.9 % to 1.0 % (PR = 0.56; 95% CI: 0.27–1.16), 18–24-year age group individuals from 28.6 % to 16.8 % (PR = 0.11; 95% CI: 0.07–0.18), 25–34-year age group from 15.6 % to 2.0 % (PR = 0.5; 95% CI: 0.41–0.61). However, there was a 2-fold increase in the proportion of the 35–44 years age group, from 17.9 % to 35.1 % (PR = 2.48; 95% CI: 2.1–2.9).

Newly diagnosed patients were represented predominantly by urban residents, with a statistically significant increase in their proportion over the period under study, from 68.5 % to 74.2 % (684/922) (PR = 0.46; 95% CI: 0.39–0.54).

Clinical forms of tuberculosis were characterized by an increase in the proportion of respiratory tuberculosis increasing from 97.6 % to 99.1 % (PR = 0.37; 95% CI: 0.17–0.77), with a decrease in the proportion of tuberculosis of extrapulmonary localizations to 0.9 % in 2021 from 2.4 % in 2009. The proportion of destructive forms of TB decreased from 42.2 % (840/1989) to 37.8 % (288/761) (PR = 1.2; 95% CI: 1.01–1.42). The proportion of fibrous cavernous tuberculosis in the structure of respiratory tuberculosis decreased by a factor of 8.6 to 0.5 % (4/761) compared to 4.3 % in 2009 (PR = 0.12; 95% CI: 0.04–0.35).

It should be noted that by the end of the follow-up period, the proportion of HIV-infected patients in the group of newly diagnosed patients significantly increased, which largely determined the clinical forms of tuberculosis and the characteristics of bacterial excretion. Among TB patients who underwent screening for human immunodeficiency virus antibodies, the proportion infected with HIV was 37.0 % (298/804) compared to 1.5 % in 2009 (34/2160) (PR = 36.8; 95% CI: 25.4–53.19). The incidence of tuberculosis combined with HIV infection has increased almost 10-fold since 2009, reaching 15.6 cases per 100,000 population in 2021 against 1.6 cases per 100,000 population.

The proportion of bacteria-excreting patients among newly diagnosed patients increased from 43.6 % to 54.5 % (PR = 0.64; 95% CI: 0.55–0.750), with bacterial excretion being diagnosed by simple bacterioscopy in 36.2 % of cases (334/922) at the commencement of treatment compared with 34.2 % in 2009 (904/2638) (PR = 1.09; 95% CI: 0.93–1.27).

The proportion of bacteriologically proven MDR *M. tuberculosis* strains doubled from 15.5 % to 30.6 % (PR = 0.42; 95% CI: 0.31–0.55).

In 2021, the pattern of drug resistance among newly diagnosed patients excreting bacteria who have been examined for drug susceptibility in 2021 is represented by 13.9% mono-resistant strains (33/237), 18.1 % poly-resistant strains (43/237), 54.8 % MDR strains (130/237), and 13.0 % XDR *M. tuberculosis* strains (31/237). The incidence of tuberculosis with XDR increased 4-fold in follow-up control for the period 2011–2021 and amounted to 1.6 cases per 100,000 population, while the average annual level was 1.1 cases per 100,000 population.

In the contingent of patients discharging bacteria examined for drug sensitivity, the proportion of bacteriologically proven strains with MDR was 15.7 % (152/966), pre-extensive drug resistance – 30.4 % (294/966), extensive drug resistance – 27.3 % (264/966).

DISCUSSION

The complex of measures to control TB infection actively implemented in our country over the past two decades has contributed to a decrease in the intensity of the epidemic process, which manifests itself in a decrease in the number of patients annually diagnosed, as well as in the patient cohort as a whole. In our study, the dynamics of population incidence of active forms of tuberculosis decreased by more than 3 times. By 2020, the target indicators of the first stage of implementation of the Strategy for TB elimination in relation to the baseline level of 2015 [2], which is the starting point for analyzing the effectiveness of the WHO global strategy implementation, were achieved in the Omsk region and reached 36.9 % (target indicator – decrease of TB incidence by 20.0 % by 2020), 85.8 % (target indicator – decrease of deaths by 35 % by 2020).

Although the worldwide incidence of tuberculosis has generally declined, the incidence of multidrug-resistant tuberculosis has increased by almost 10 % annually [3, 13].

The current trend of increasing incidence of multiple or rifampicin-resistant tuberculosis remains a hot public health problem. In 2020, the global rate of effective treatment of drug-resistant TB remained only 59 % of cases, which is a heavy economic burden on health systems, patients and their families, and reduces the effectiveness of TB control measures in different regions and countries worldwide [3, 14].

Russia has experienced a significant portion of the worldwide burden of drug-resistant tuberculosis [4, 5, 15]. Our study revealed a change in the nature of bacteriological excretion among newly diagnosed patients; despite the decrease in the number of detected cases in the structure of drug resistance, a more than 2-fold increase in the proportion of multidrug-resistant bacteriological excretion (up to 26.4 %) was observed, while the dynamics of the incidence of multidrug-resistant tuberculosis in the population remains sta-

ble with a long-term average of 8.1 cases per 100,000 population (R^2 = 0.161). In addition, at the end of the study period in the Omsk region, 66.2 % of culture-positive patients had MDR strains.

The results of the study showed that during the period of observation in the Omsk region the age group at risk has changed, the highest incidence rate was among persons between 35 and 44 years of age, the proportion of which was 35.1 %, and the incidence rate was 109.0 per 100,000 population of this age. In addition, those aged 35–44 years in the Omsk region are a group at risk of HIV infection; in 2021, the proportion of this age group in the age structure of HIV-infected people was 42.9 % [16]. The increasing burden of co-infection of tuberculosis and HIV infection is confirmed by a 10-fold increase in the incidence of comorbidity over the study period.

It should be noted that the epidemiological manifestations of TB infection were significantly influenced by the epidemic process of the new coronavirus infection COVID-19. A study of the clinical structure of newly diagnosed TB patients in the country during the COVID-19 pandemic revealed a worsening of the clinical forms of TB and an increase in their epidemic risk [17]. In our study, there was a statistically significant increase in the proportion of newly diagnosed patients discharging bacteria from 43.6 % to 54.5 % (PR = 0.64), including those detected by simple bacterioscopy to 36.2 % (PR = 1.09). At the end of the study, despite a statistically significant increase in the proportion of respiratory tuberculosis cases, no worsening of the clinical structure of the patients was observed, the proportion of destructive forms of respiratory tuberculosis and fibrous cavernous tuberculosis decreased significantly.

CONCLUSION

Despite the observed favourable trends in the development of the tuberculosis epidemic process, decrease in thetuberculosis incidence, prevalence and mortality, there is a change in the structure of bacterial excretion with the prevalence of multiple and extensive drug resistance, as well as active involvement of HIV-infected patients in the epidemic process. For further timely assessment and prognosis of the manifestations of the epidemic process of TB infection, as well as to characterize the quality and effectiveness of preventive and anti-epidemic measures under conditions of drug-resistant TB extension, it is necessary to improve the organization of the system of epidemiological surveillance and control of TB spread.

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Conflict of interest

The authors of this article declare the absence of a conflict of interest.

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