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Comparative characteristics of medical stability *m. tuberculosis* in Belgorod and Voronezh regions, Russia

Oleg A. Zemlyanski*¹, Elena B. Turina¹, Elena V. Kaliuzhnaya¹, Galina V. Efron², Luidmila O. Zemlyanskaya¹, Natalia N. Shinkarenko¹

¹Belgorod State University Russia, 308015, Belgorod, Pobeda St., 85, Russia

²TB Dispensary, Voronezh, 394000, Russia

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ABSTRACT

The purpose of the study was to evaluate and compare the incidence and dynamics of drug resistance of *M. tuberculosis* to antituberculosis drugs in the Belgorod and Voronezh regions in different categories of patients: newly diagnosed, relapse, and other cases of repeated treatment. A comparative analysis of the spectral incidence and dynamics of *M. tuberculosis* drug resistance in 2007 and 2016 in the Belgorod and Voronezh regions was carried out. The data of statistical accounting forms 07-TB and centralized bacteriological laboratories were used. When comparing the data of the two regions - the Belgorod and Voronezh regions - both general trends and significant differences in the levels and dynamics of drug resistance of *M. tuberculosis* have been identified in different categories of patients. The level of primary multiple drug resistance is higher in the Voronezh Region, its growth rates in the Belgorod Region are the same, and the growth in overall sustainability is twice higher than in the Voronezh Region. It should be noted that the proportion of mono-resistant to isoniazid strains in the Belgorod region is increasing, while in Voronezh this phenomenon does not exist. The issues of epidemiological monitoring of tuberculosis require increased attention and detailed analysis at the territorial level for the adoption of adequate and effective management decisions. The current system of routine epidemic monitoring requires improvement taking into account the Russian and international experience. Data of such monitoring can have a significant impact on management decision-making in the field of tuberculosis control. Including at the level of each region.



* Corresponding Author

Name: Oleg A. Zemlyanski
Email: zemlyansky@bsu.edu.ru

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INTRODUCTION

A crisis situation with multiple drug resistance (hereinafter referred to as MDR) of the causative agent of the disease has been identified as the second place after the problem of underdevelopment

of tuberculosis in a series of complex tasks in the fight against tuberculosis, identified in the new strategy of the World Health Organization and requiring urgent solutions (*WHO report on the global fight against tuberculosis., 2017; Vasilieva, I.A et al., 2017*).

Preservation of a high incidence of tuberculosis in the Russian Federation is due to broad dissemination of drug-resistant strains of *M. Tuberculosis* (*Tuberculosis in the Russian Federation 2013/2014/2015, 2016; Nechaeva, O.B et al., 2015; Ogarkov, O.B et al., 2014*). This is associated with inadequate treatment effectiveness and significantly longer treatment times. The spread of tuberculosis with drug resistance also indicates the low effectiveness of anti-epidemic measures, including

insufficient monitoring of the use of antituberculosis drugs (*Sterlikov, S.A., 2014*).

Monitoring the drug resistance of *M. tuberculosis* is an important part of controlling the spread of this infectious disease (*Malykhina, T.I et al., 2011; Zemlyansky, O.A et al., 2014*). However, the system of epidemiological monitoring, which is poorly developed in the Russian Federation, does not allow developing and implementing systemic epidemiological measures aimed at preventing the spread of tuberculosis infection among the population (*Amelchenko, A.A., 2017*). Currently, available statistics do not fully reflect trends in the frequency and spectrum of drug resistance of *M. tuberculosis* and do not allow comparison of these indicators at the regional level (*Popov, S.A et al. 2009*).

MATERIALS AND METHODS

A comparative analysis of the frequency spectrum and dynamics of drug resistance of *M. tuberculosis* in 2007 and 2016 in the Belgorod and Voronezh regions - the regions located in the neighbourhood, in the same climatic, geographic zone and approximately equal in economic development. The data of the organisational methods of the head antituberculous institutions (statistical accounting forms 07-TB) and centralised bacteriological laboratories were used. It should be noted that the centralised bacteriological laboratories of these regions use comparable methods for determining the drug resistance of *M.tuberculosis* regulated by the current regulatory documents, regularly and with good results participate in the Federal system for external evaluation of research quality.

Drug resistance of the causative agent of tuberculosis in patients was determined on the strains obtained at the stage of diagnosis before treatment and selected according to the principle "one patient - one strain". The methods of determination were a method of absolute concentrations on a Levenshtein-Jensen medium and proportions on a liquid medium in the BACTEC MGIT 960 system.

PURPOSE OF THE STUDY

The researchers evaluated and compared the incidence and dynamics of *M. tuberculosis* drug resistance to first and second-line antituberculosis drugs in the Belgorod and Voronezh regions in different categories of patients: newly diagnosed, relapse, and other cases of repeated treatment.

RESULTS AND DISCUSSION

Among the newly diagnosed patients, drug-resistant strains of *M. tuberculosis* are more common in the Voronezh region - 56.1% versus 46.4% in Belgorod (Figure 1).

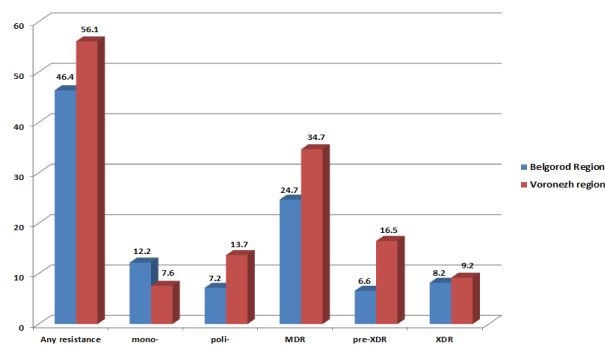


Figure 1: Comparative characteristics of drug resistance of *M. tuberculosis* in newly diagnosed patients. 2016 (%)

At the same time, strains with monoresistance to isoniazid or streptomycin are much more often found in the Belgorod Region - 12.2% versus 7.6% in the Voronezh Region. Among the drug-resistant strains prevail with MDR - 34.7% in Voronezh and 27.1% in Belgorod. Along with the multiple, there are strains with broad drug resistance (hereinafter - XDR) - 9.2% in Voronezh and 8.2% in the Belgorod region. The presence of strains with resistance preceding the broad (hereafter pre-XDR), when resistance to isoniazid and rifampicin is combined with resistance to fluoroquinolones or intravenous anti-tuberculosis drugs (kanamycin and capreomycin and amikacin), is vigilant-16.5% in Voronezh and 6.6% in the Belgorod Region.

Among relapses, on the contrary, the level of drug resistance is higher in the Belgorod Region - 83.3% versus 72.1% in the Voronezh Region (Figure 2).

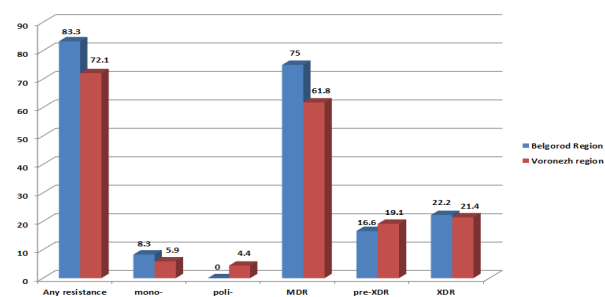


Figure 2: Comparative characteristics of drug resistance of *M.tuberculosis* in patients with relapses, 2016 (%)

The MDR level is higher - 75.0% vs 61.8% in the Voronezh region. In the Belgorod region, there are no strains with multiresistance (resistance to two or more drugs, except for the combination of isoniazid-rifampicin), the level of XDR is approximately the same - 22.2% in Belgorod and 21.4% in the Voronezh region. The pre-XDR level in the Belgorod Region is slightly lower than in the Voronezh region - 16.6% and 19.1%, respectively.

Among other cases of re-treatment, drug resistance is approximately the same in both regions (Figure 3).

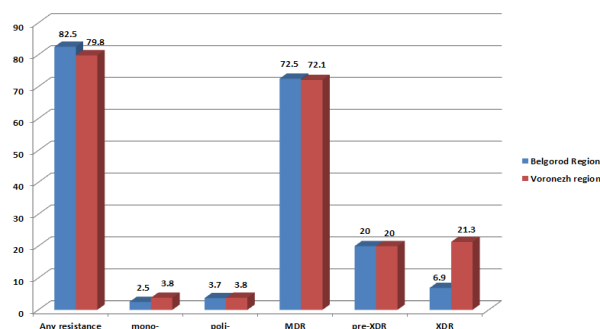


Figure 3: Comparative characteristics of drug resistance of M. tuberculosis in patients with other cases of repeated treatment 2016 (%)

However, the level of strains with XDR is much higher in the Voronezh region - 21.3%. While in Belgorod - 6.9%. Over the ten-year period from 2007 to 2016, the share of strains with any resistance increased significantly in the Belgorod Re-

the total number of tuberculosis patients there is a relative stabilization with an increase in the share indices of the stability spectra, including a large and broad range, both in the general cohort of bacterial excretors and in various groups of patients first detected and relapses.

Although at present the level of primary MDR - an important indicator that is often used to characterise the epidemiological situation in the region - is higher in the Voronezh Region, its growth rate in Belgorod is the same, and the growth in overall sustainability is twice higher than in the Voronezh Region.

It should be noted that the proportion of mono-resistant to isoniazid strains in the Belgorod region is increasing, while in Voronezh this phenomenon does not exist.

Table 1: Changes in the spectra of drug resistance in patients of different groups. 2007 and 2016

Types of resistance	Any resistance	Monoresistance	Poliresistance	MDR
Newly identified				
Belgorod Region	+ 61.6 %	+ 48.8 %	- 19.1%	growth in 2.3 times
Voronezh Region	+ 32.9 %	- 26.2 %	- 13.3%	growth in 2.2 times
Relapses				
Belgorod Region	Growth in 2.1 times	growth in 2.5 times	decrease to 0	growth in 2.2 times
Voronezh Region	+ 36.8 %	- 69.4%	- 86.6%	growth in 2.7 times
Other cases of repeated treatment				
Belgorod Region	- 4.3 %	decline in 2.0 times	+ 29.3%	- 4.7%
Voronezh Region	+ 33.4 %	- 70.1%	- 80.1%	growth in 2.6 times

gion - by 61.1%, while in the Voronezh Region - by 32.9% (Table 1).

The share of strains with any resistance increased significantly in the Belgorod region - by 61.1%, while in the Voronezh region - by 32.9%.

In both regions, the share of multidrug-resistant strains decreased by 19.1% and 13.3%, respectively. The highest growth is demonstrated by strains with MDR - 2.3 times in Belgorod and 2.2 times in the Voronezh region.

It should be noted that the share of mono-resistant strains in the Belgorod Region increased by 48.8%, while the Voronezh Oblast shows a decrease of 26.2%. This was due to an increase in mono-resistance to isoniazid in the Belgorod region.

CONCLUSIONS

When comparing the data of the Belgorod and Voronezh Regions, it was revealed that in both regions against a background of a steady decline in

Thus, when comparing the data of the two regions - the Belgorod and Voronezh regions - significant differences in drug resistance levels of M. tuberculosis were revealed in different categories of patients. This may indicate both different approaches to treatment and the shortcomings in the implementation of anti-tuberculosis activities in these regions.

In this regard, the issues of epidemiological monitoring and evaluation of the dynamics of the spread of tuberculosis, especially with drug resistance to the pathogen, require increased attention and detailed analysis at the territorial level for the adoption of adequate and effective management decisions.

The current system of routine epidemmonitoring requires improvement, taking into account the Russian and international experience in various areas (accounting and reporting, instructive, methodological, regulatory support).

It is necessary to develop a federal guide to the surveillance of tuberculosis, including drug-resistant, with molecular-genetic identification; ensuring the use of surveillance data in the practical provision of medical care to patients in medical organisations of the Russian Federation.

It is necessary to develop principles for the approach and conduct of extended monitoring of the drug resistance of *M. tuberculosis* on an ongoing basis in all regions. The data of such monitoring can have a significant impact on the adoption of management decisions in the field of tuberculosis control, including at the level of each region.

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