Ethiopian International Journal of Multidisciplinary Research

pISSN:2349-5707 Volume:12,Issue 11,November-2025 eISSN:2349-5715

DRUG RESISTANCE FEATURES IN NEWLY IDENTIFIED PATIENTS

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Abstract: This article is about drug resistance, one of the current topics in phthisiology. Currently, drug resistance remains a problem worldwide, and many countries are looking for solutions to the diagnosis, treatment, treatment effectiveness, and prevention of drug-resistant tuberculosis. In this article, we have collected and shared with you information from the literature about the types of drug resistance and their characteristics.

Key words: tuberculosis, types of drug resistance, newly patients

Relevance. According to WHO, in 2011, there were 8.7 million new cases of tuberculosis (TB), or 125 cases per 100,000 population worldwide. Of these, 59% were in Asia and 26% in Africa. In 2011, TB killed 1.4 million people, 500,000 of whom were women. There were 630,000 MDR-TB cases worldwide in 2011, with an estimated 460,000 to 790,000 cases. Among them, the number of people with pulmonary tuberculosis was 310,000 [7].

According to WHO, more than 500,000 people worldwide are infected with multidrug-resistant strains of MDR-TB. It is estimated that Mycobacterium tuberculosis infects approximately one-third of the world's population [19,20] . The annual number of new cases of tuberculosis worldwide has remained stable or is decreasing [24]. In 2007, there were 13.7 million cases of chronic tuberculosis, 9.3 million new cases, and 1.8 million deaths, mostly in developing countries [25].

According to a sample study, the prevalence of primary multidrug resistance of Mycobacterium tuberculosis in prisons reaches 37.1 % [29].

According to WHO experts, drug-resistant tuberculosis is pulmonary tuberculosis with the release of MBT resistant to one or more anti-TB drugs. According to the Central Research Institute of Tuberculosis of the Russian Academy of Medical Sciences, 50% of newly diagnosed patients who have not previously been treated with anti-TB drugs have drug-resistant MBT in their sputum, and 27.7% of them have resistance to TB. The 2 main drugs for tuberculosis are isoniazid and rifampicin.

In fibro-cavernous tuberculosis, the frequency of detection of drug-resistant MBT increases to 95.5 % [3,5].

Multidrug-resistant tuberculosis (MDR) is widespread in various countries: 0.5 -3.5% in the USA, France, England (Wales), Switzerland, Italy .

In the Dominican Republic, resistance to at least two key chemotherapy drugs, isoniazid and rifampicin, was detected in 10.2 % of cases, including 6.6% of newly diagnosed patients.

High levels of multidrug resistance are observed, especially in the Baltic countries, the CIS, Asia , and Argentina [26].

Thus, the detection rate of primary multidrug resistance (MDR) was 9.8% in 2007, and the frequency of secondary MDR was 21.4%. Clinical cure of newly diagnosed patients with destructive pulmonary tuberculosis was recorded in 33.9% of cases in 2007, but in the presence of MDR, cure was observed in only 16.2% of such patients; in patients with relapsed tuberculosis, cure was achieved in 18.3% and 10.8% of cases, respectively.

According to Danilova ID [10], those aged 18 to 34 years account for almost half (47.6%) of all newly diagnosed women and 34.2% of newly diagnosed men, meaning that more women than men are diagnosed before the age of 18.

Women of reproductive age in Uzbekistan account for 25.1 percent of the total female population. Medical examinations show that 60 percent of them suffer from anemia, and more than 40 percent suffer from various chronic diseases [13].

pISSN:2349-5707 Volume:12,Issue 11,November-2025 eISSN:2349-5715

To the development of the process and insufficiently effective treatment, concomitant diseases play an important role, i.e. they aggravate the course of tuberculosis and cause its unfavorable dynamics [9] and mortality of pulmonary tuberculosis have increased among young people aged 18 to 35. The situation is significantly complicated by the presence of not only drug-sensitive but also drug-resistant tuberculosis.

Primary and secondary drug resistance of tuberculosis bacteria is detected in newly diagnosed patients who have not previously received anti-TB drugs but are infected with resistant mycobacteria [12, 13 , 14].

Because anti-tuberculosis drugs are often used in general medicine to treat inflammatory diseases, unrecognized acquired drug resistance may arise. Therefore, when resistance is detected in a previously untreated patient, it is more accurate to speak of resistance to the original drug [14].

Thus, the phenomenon of primary drug resistance includes both primary and unrecognized acquired resistance states.

In a patient with destructive pulmonary tuberculosis, drug resistance of MBT leads to relapse of the disease, the development of chronic and incurable forms, and in some cases, death [20].

The highest proportion of MDR-TB was recorded in Baku, Azerbaijan (55.8 %). Recent data from Gujarat, India, which includes the first reliable descriptions of previously treated cases in India, put the proportion of MDR-TB in this group at 17.2 % .

Despite the implementation of large-scale comprehensive measures against tuberculosis in Uzbekistan, the epidemiological situation with tuberculosis remains acute.

Many countries, including Uzbekistan, the current epidemiological situation is characterized by a deterioration in the main indicators of tuberculosis disease (morbidity, mortality, disability) [10].

In 2009, 30% of newly diagnosed cases were patients in the acute phase of the disease.

52.9 per 100,000 population , and the intensive mortality rate in 2011 was 5.2 per 100,000 population.

The development of resistance of Mycobacterium tuberculosis (MBT) to anti-tuberculosis drugs (ATDs) is a special case of drug resistance development [22] and is observed against all currently known anti-tuberculosis drugs.

The most common clinical errors that lead to the development of drug resistance in MBT are: prescribing less than 4 anti-TB drugs during the intensive phase of chemotherapy, introducing one new drug when the previous treatment regimen was ineffective, short chemotherapy courses, and lack of control over the use of anti-TB drugs [8].

According to MD. Iseman, in 80% of cases of MDR-TB, obvious errors in previous treatment were identified: there were cases of monotherapy, drug resistance of MBT was not detected, and the intake of anti-TB drugs was not monitored.

Although chemotherapy is the mainstay of treatment for MDR pulmonary tuberculosis, the issue of determining the appropriate treatment regimen remains a complex one. In most cases, the standard treatment regimen recommended by the WHO is used, but adverse events or complications are often observed during treatment. The effectiveness of MDR tuberculosis treatment can be increased by using rapid methods for detecting drug resistance in TB, which allows for timely changes in chemotherapy regimens. The results of studies confirm that up to 70% of MDR tuberculosis can be effectively treated (Vlasova N.A., Nikishova E.I., Mironyuk O.M., Maryandyshev A.O., 2019). In primary MDR tuberculosis, the correct and controlled administration of anti-tuberculosis drugs by patients is of great importance and has a positive impact on the effectiveness of treatment.

In recent years, when developing treatment regimens for MDR tuberculosis, more attention has been paid to the use of oral drugs, including new anti-tuberculosis drugs and antibacterial drugs with anti-tuberculosis activity (Kendall EA et al., Lienhardt C. et al., 2017). According to studies conducted by local and CIS scientists, almost 90% of patients with pulmonary tuberculosis experience side effects from drugs on the background of treatment. According to various sources,

pISSN:2349-5707 Volume:12,Issue 11,November-2025 eISSN:2349-5715

up to 60-80% of patients diagnosed for the first time develop certain side effects during treatment the regimen or temporarily canceling it. Drug complications in the treatment of pulmonary tuberculosis seriously impede the formation of patient-physician cooperation in the treatment process, significantly reduce the clinical and economic effectiveness of the treatment, and increase the risk of unsuccessful treatment, and in some cases, lethal consequences (Yu.Yu. Kiseleva, N.A. Stepanova, F.K. Toshpulatova, Y.I. Feshchenko, D.A. Ivanova, S.E. Borisov et al., 2012; 2016). Rifampicin-resistant tuberculosis and MDR-TB are one of the greatest threats on a global scale (Parpieva N.N., Khamraev A., Jai Achar, James Trauber et al., 2016). Currently, MDR-TB patients are hospitalized on an indication basis; In some patient groups, the course of treatment was carried out on an outpatient basis. This made it possible to take into account the side effects of drugs and compare the results of treatment in MDR-TB patients treated in inpatient and outpatient settings (Tillyashaykhov M.N. et al., 2014; D. S. Sadirova, A. B. Trubnikov, D. Z. Mukhtarov et al., 2018).

If side effects of chemotherapy are observed in patients, it is appropriate to include measures aimed at normalizing their psychophysiological state in the main therapeutic measures, which helps in the implementation of standard chemotherapy treatment as one of the factors of effectiveness of the treatment (N.V. Zolotova, G.V. Baranova, etc.). In patients with MDR pulmonary tuberculosis, the use of regionally adapted standard and individual chemotherapy regimens in the presence of drug resistance of the tuberculosis pathogen can significantly increase the rate of effective treatment. Thus, the determination of regional drug resistance of TMB is important for the selection of optimal chemotherapy regimens.

Groups at high risk of developing MDR-TB include people who have previously been unsuccessfully treated with PTP, patients with tuberculosis with an acute progressive course of the disease, patients who have previously been in contact with patients with MDR-TB, HIV-infected patients, patients with impaired PTP absorption in the gastrointestinal tract, individuals with a high risk of developing MDR-TB (alcoholism, homeless people, unemployed people, prisoners, etc.).

Preliminary data from the DRS-Uzbekistan in-depth study of the true prevalence of drug resistance, conducted in collaboration with the international laboratory in Gauting (Germany) in 2010-2011, are as follows: among newly diagnosed patients, this figure is 23% . Among re-treated patients, it is 62%.

Thus, the study of the characteristics of the spread and course of drug-resistant pulmonary tuberculosis, as well as the search for opportunities to increase the effectiveness of its treatment, is an urgent problem of phthisiology. It has been proven that the clinical course of the disease in patients with multidrug-resistant forms of pulmonary tuberculosis in conditions of a sharply continental climate is unique.

Inadequate implementation and violation of treatment standards, harmful habits, and inadequate patient adherence to treatment have been proven to cause MDR-TB

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