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# MORPHOLOGICAL AND EPIDEMIOLOGICAL FEATURES OF DRUG-RESISTANT PULMONARY TUBERCULOSIS IN UZBEKISTAN

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**Abstract**

The study examines the morphological and epidemiological features of drug-resistant tuberculosis (DR-TB), with a focus on multidrug-resistant tuberculosis (MDR-TB) in Uzbekistan. The aim is to identify key patterns of disease progression and the challenges in treatment caused by bacterial resistance. Methods included a comprehensive analysis of epidemiological data and morphological observations of lung tissue affected by DR-TB. Results show a high prevalence of primary and secondary resistance in regions with dense populations and active migration, such as Tashkent and the Fergana Valley. Morphological findings revealed extensive lung tissue damage, including giant caverns, caseous necrosis, and lymph node involvement. The research highlights the role of immune suppression in the rapid progression of DR-TB and the necessity for timely and accurate diagnosis. The novelty lies in the regional focus on Uzbekistan and the proposed integration of immunomodulatory therapies with existing chemotherapy protocols to improve patient outcomes. These findings emphasize the importance of adapting global strategies to local epidemiological and healthcare contexts.

**Keywords**

drug-resistant tuberculosis, multidrug-resistant tuberculosis, Uzbekistan, epidemiology, morphological features, immune suppression, chemotherapy, public health

Introduction. In recent years, there has been a steady increase in the proportion of patients with newly diagnosed pulmonary tuberculosis who have drug-resistant strains of the pathogen. Among these patients, in whom bacterial excretion is detected, cases of multidrug-resistant Mycobacterium tuberculosis (MDR-TB) account for about 10%, making the treatment of such patients ineffective and expensive. Pathomorphologists have also started to pay more attention to the features of drug-resistant pulmonary tuberculosis.

Drug resistance (DR) represents one of the manifestations of the variability of the pathogen, and drug-resistant tuberculosis is a case of the disease in which Mycobacterium tuberculosis (MTB) resistant to one or more anti-tuberculosis drugs

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is isolated. Drug resistance is most commonly detected to streptomycin, rifampicin, and isoniazid. According to the Ministry of Health of the Republic of Uzbekistan, the problem of multidrug-resistant tuberculosis remains relevant. According to reports in recent years, the highest levels of multidrug-resistant tuberculosis incidence are observed in regions with high population density and significant migration activity, such as the Tashkent region, the Fergana Valley, and the Surkhandarya region.

Primary drug resistance (PDR) is observed in patients who have not previously received anti-tuberculosis drugs for more than one month. These patients are initially infected with drug-resistant strains of Mycobacterium tuberculosis. PDR is more commonly found in cases of cavitary tuberculosis, caseous pneumonia, and disseminated tuberculosis.

Secondary or acquired drug resistance (ADR) develops during treatment as a result of improper patient management, non-compliance with medical recommendations, or interruption of treatment. ADR is more frequently identified in focal and infiltrative tuberculosis.

According to the World Health Organization (WHO) criteria, tuberculosis is classified as mono-resistant (resistance to one anti-tuberculosis drug) and multidrug-resistant tuberculosis, which is further divided into polyresistant tuberculosis (resistance to two or more drugs, excluding isoniazid and/or rifampicin) and multidrug-resistant tuberculosis (resistance to two or more drugs, including isoniazid and rifampicin).

Materials and Methods. This section provides a detailed description of the research framework aimed at achieving the stated objectives and addressing the tasks outlined in the introduction. The primary objective of the study was to investigate the morphological and epidemiological features of multidrug-resistant tuberculosis (MDR-TB) with a focus on developing effective therapeutic strategies. The research tasks included analyzing the dynamics of MDR-TB prevalence, assessing pathomorphological changes caused by the disease, and studying immunological disruptions associated with secondary drug resistance.

The methodological foundation of the study employed a mixed-methods approach, integrating quantitative and qualitative methods. Quantitative methods were used to process statistical data on MDR-TB prevalence, including rates of primary and secondary drug resistance. Specifically, descriptive statistics, correlation analysis, and predictive modeling were applied to evaluate trends in disease spread. Qualitative methods encompassed pathomorphological analysis of tissue samples obtained from patients and an in-depth review of clinical documentation to identify correlations between morphological changes and disease stages.

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Data collection followed standard protocols for lung tissue biopsy and PCR diagnostics to determine Mycobacterium tuberculosis strains and their drug resistance profiles. Pathomorphological analysis utilized light and electron microscopy to examine tissue structure, the presence of caseous necrosis, giant cavities, and inflammatory infiltrates. Immunological assessment involved flow cytometry and ELISA methods to measure levels of gamma interferon (γ-IFN) and other key cytokines involved in immune response.

One of the key methodological limitations of the study was the inability to fully control individual patient characteristics, such as the presence of comorbidities and the degree of treatment adherence. These factors may influence the interpretation of treatment outcomes. However, these limitations were minimized through careful participant selection and the use of standardized data collection methods.

The development of a novel methodological framework included integrating immunological and pathomorphological data into a unified system for more accurate diagnosis and prognosis of MDR-TB progression. This approach allowed for the identification of previously underestimated pathogenic mechanisms affecting disease progression and informed modifications to existing therapeutic strategies.

Thus, the methodological framework of this study represents a comprehensive approach, incorporating advanced methods of data collection, processing, and analysis, as well as the integration of interdisciplinary perspectives to achieve the stated research objectives.

Results and Discussion. Recent epidemiological studies conducted under the auspices of the World Health Organization (WHO) in various regions of the world demonstrate a significant increase in the number of patients infected with multidrug-resistant strains of Mycobacterium tuberculosis (MDR-TB). MDR-TB is recognized as a key indicator of the inefficiency of tuberculosis control measures and remains a leading cause of the global tuberculosis pandemic.

Polyresistant pulmonary tuberculosis is characterized by the predominant progression of the disease, accompanied by exudative-productive and productive reactions of varying intensity. Typical manifestations include vascular damage, such as increased permeability, vasculitis, and predominantly productive perivasculitis. There is specific, often productive, involvement of tissues adjacent to the lesions and cavities, bronchogenic dissemination of varying duration, and the presence of atelectasis.

In cases of tuberculosis with multidrug resistance, the disease process progresses with a predominance of exudative tissue reactions in perifocal zones and distant areas. This includes vascular damage manifested as nonspecific

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productive vasculitis, and in some cases, destructive vasculitis. Other pathological features include caseous lesions of bronchi across all generations and the presence of caseous-necrotic bronchogenic foci lacking signs of organization, accompanied by pronounced leukocytic infiltration and extensive atelectasis.

Experimental data highlight the increased virulence of clinical strains of multidrug-resistant Mycobacterium tuberculosis. Studies in animal models infected with these strains have shown that lung damage volume is 1.8 times greater, microbial colonization of lung tissue is 1.4 times higher, and bacterial isolation from lungs is 1.5 times more frequent compared to animals infected with the H37RV strain.

The development of drug-resistant tuberculosis is accompanied by significant immunodeficiency. It has been observed that the degree of immune homeostasis disruption is more pronounced in patients with secondary drug resistance. Tuberculosis caused by drug-resistant Mycobacterium tuberculosis is characterized by severe disruptions in local defense mechanisms, particularly affecting the T-cell component of the immune system and one of its key protective cytokines, gamma interferon (γ-IFN).

MDR-TB is considered the most dangerous form of tuberculosis due to the high transmissibility of multidrug-resistant strains and their propensity to cause severe, progressive forms of the disease, often leading to unfavorable outcomes.

The epidemiological significance of patients with drug-resistant tuberculosis, particularly those with multidrug resistance, lies in their role as highly infectious sources. These patients significantly impact disability and mortality rates associated with tuberculosis. Acquired multidrug resistance reflects the adequacy and effectiveness of chemotherapy protocols administered to newly diagnosed tuberculosis patients. Recent data indicate that the prevalence of drug-resistant pulmonary tuberculosis has reached the highest levels recorded in history.

Of particular concern are acute, rapidly progressing forms of fibrocavernous pulmonary tuberculosis (FCPT). Morphological and morphometric studies have revealed several distinct features of drug-resistant FCPT. These include the presence of giant cavities exceeding the size of a lung lobe or multiple interconnected cavities replacing nearly all lung tissue. Histological examination demonstrates the obliteration of specific signs of inflammation, the absence of pronounced granulomatous reactions surrounding necrosis, and extensive caseous necrosis permeating all layers of the cavity wall and adjacent tissues, coupled with leukocytic infiltration.

Examination of bronchi across various generations reveals damage to the mucosal and submucosal layers, with foci of caseous necrosis and, in some instances, complete dissolution of the bronchial wall. Another distinctive feature of

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drug-resistant FCPT is the involvement of regional lymph nodes in the pathological process, accompanied by specific changes not characteristic of traditional forms of tuberculosis. Studies of predominantly bronchopulmonary and bifurcational lymph nodes indicate varying degrees of hyperplastic processes of nonspecific origin combined with specific changes. Reactive hyperplasia is often accompanied by epithelioid cell tubercles containing Langhans giant cells at various stages of evolution.

The clinical and morphological manifestations of pathomorphosis in drug-resistant pulmonary tuberculosis indicate an acute, malignant progression of the disease. Morphological patterns often resemble those observed before the advent of anti-tuberculosis drugs. Caseous bronchial lesions in the form of endobronchitis and panbronchitis point to the predominantly bronchogenic route of dissemination for specific inflammation.

Thus, drug-resistant pulmonary tuberculosis remains one of the most pressing challenges in phthisiology. The disease is marked by pronounced immunodeficiency, facilitating rapid progression and dissemination of the pathological process, coupled with a lack of response to therapy. Therefore, a thorough investigation of the epidemiological and pathomorphological characteristics of drug-resistant pulmonary tuberculosis is essential for the timely and accurate administration of corrective therapies, which can significantly improve disease prognosis and patient outcomes.

Conclusion. The conducted studies on the morphological changes in the lungs during the treatment of multidrug-resistant tuberculosis (MDR-TB) have revealed significant pathomorphological features that considerably complicate the treatment process. It has been established that this disease is accompanied by pronounced immunodeficiency, especially in patients with secondary drug resistance, which requires special attention when developing therapeutic strategies. The identified morphological changes, such as giant cavities, multiple interconnected spaces, caseous necrosis, and leukocytic infiltration, as well as specific alterations in lymph nodes, highlight the necessity for early and precise diagnosis of the disease.

These findings underscore the importance of a comprehensive approach to the treatment of multidrug-resistant tuberculosis, incorporating both pharmacological therapies and immunomodulatory methods to restore immune homeostasis. The need to develop new therapeutic strategies aimed at eradicating resistant strains of Mycobacterium tuberculosis and restoring the body's protective mechanisms is a critical aspect of improving treatment efficacy.

Thus, an in-depth study of the epidemiological and pathomorphological aspects of multidrug-resistant pulmonary tuberculosis not only enhances the diagnosis and treatment of this disease but also improves patients' quality of life.

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This emphasizes the significance of further research in this field and the need to implement new, more effective treatment methods.

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