

THE EFFECTIVENESS OF THE CLINICAL COURSE AND TREATMENT OF RESISTANT FORMS OF PULMONARY TUBERCULOSIS IN MODERN CONDITIONS

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Resume

Socio-economic changes in Uzbekistan have led to a significant deterioration in the epidemiological situation of tuberculosis, the deterioration of its characteristics and course. The article is based on the survey data of 244 patients from the southern regions of the Republic of Uzbekistan who received treatment in the centers of phthisiology and pulmonology in the period from 2016 to 2020. The age of the patients ranged from 18 to 86 years, the average age was 52.1 ± 2.9 years. Patients of the rural population were observed - in 185 (75.8%), urban population – in 56 (23.0%) and homeless people – in 3 (1.2%) cases. The analysis notes that the disease was 3.3 times more common in rural populations. Incorrect interpretation of the results of diagnostic research methods was found in non-phthisiological hospitals – in 63.5% of cases, and in polyclinics – in 29.5% and in phthisiological hospitals, this indicator was - in 4.5% of cases.

Keywords: epidemiological situation, drug-resistant pulmonary tuberculosis, diagnosis, treatment.

Резюме

Социальноэкономические изменения в Узбекистан привели к существенному ухудшению эпидемиологической ситуации по туберкулезу, утя желению его характеристики и течения. В статья основу работы положены данные обследования 244 больных из южных регионов Республики Узбекистан, которые получили лечение в центрах фтизиатрии и пульмонологии в периоде с 2016 по 2020 гг. Возраст больных варьировал от 18 до 86 лет, средний возраст при этом составил 52,1±2,9 года. Больные сельского населения наблюдался - у 185(75,8%), городского населения - у 56(23,0%) и люди БОМЖ – у 3(1,2%) случаев. При анализе отмечается, что болезнь 3,3 раза чаще встречался у сельских населений. Неправильная интерпретация методов исследования результатов диагностических встречался В профиля - у 63,5% стационарах не фтизиатрического случаев, a В



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поликлиниках – у 29,5% и в стационарах фтизиатрического профиля этот показатель составил – у 4,5% случаев.

Ключевые слова: эпидемиологической ситуации, лекарственноустойчивый туберкулез легких, диагностика, лечение.

Relevance

Acute progressive pulmonary tuberculosis (OPT) is a concept that combines various clinical forms of respiratory tuberculosis characterized by acute onset of the disease and severe progressive course with a sharply pronounced intoxication syndrome, a preponderance of exudative tissue reaction, extensive lesions and rapid formation of destruction, which are combined to varying degrees with complications (pulmonary heart failure, DVSsin drom, pulmonary hemorrhage, etc.) and concomitant pathogenic nonspecific flora. The spread of multidrug-resistant tuberculosis (MDR-TB) worldwide is a serious obstacle to the control of tuberculosis and the achievement of targets set by the World Health Assembly and included in one of the United Nations Sustainable Development Goals [3, 5,8,9].

The continued increase in the prevalence of multidrug-resistant tuberculosis (MDR) and extensively drug-resistant tuberculosis (XDR) in the era of infection with the human immunodeficiency virus (HIV) poses a serious threat to the effective fight against TB. Drug resistance in Mycobacterium tuberculosis occurs due to low-frequency spontaneous chromosomal mutations. The clinical form of drug-resistant TB occurs mainly as a result of anthropogenic selection during the treatment of the disease of these genetic rearrangements due to disorderly drug provision, doctors prescribing suboptimal treatment regimens and unsatisfactory adherence to treatment on the part of patients. According to WHO experts, drug-resistant tuberculosis is a case of pulmonary tuberculosis with the release of MBT resistant to one or more anti-tuberculosis drugs [2,5,7,29].

The program of pathogenetic therapy of OPT includes 4 stages: I – resuscitation measures (compensation of multiple organ failure, relief of life-threatening complications and treatment of concomitant diseases, when deciding on surgery for vital indications - emergency preparation); II – intensive therapy (reduction of intoxication, immunocorrection, achievement of clinical stabilization, correction of metabolic disorders preparation for surgical treatment in the absence of the effect of conservative therapy); III – supportive therapy (relief of intoxication, immunostimulation, stimulation of reparative processes, achievement of X-ray





injection, preparation for elective surgery); IV - rehabilitation (stimulation of reparative processes, preparation for elective surgery)[17,22,30].

Analysis of clinical manifestations in patients with LU MBT indicated a more severe course of the disease – with severe intoxication, febrile fever, shortness of breath at rest. Physical examination more often revealed a shortening of the percussion sound, bronchial breathing, a combination of dry and wet wheezing. Radiologically, disseminated tuberculosis, caseous pneumonia and fibrous-cavernous pulmonary tuberculosis prevailed. The process in the lungs spread to 3 lobes or more, was accompanied by the formation of caverns from 2 to 4 cm, often multiple. Bacterial excretion was more often massive and was determined already by microscopy. Polyresistance was observed in almost 1/2 of the patients in the structure of the MBT LU. At the same time, monoresistance was 37.9% and multidrug resistance was determined in 13.9% of the examined [1,5,25,37].

Currently, despite the availability of a variety of modern methods for the diagnosis of tuberculosis, there is a need to develop and implement new methods of rapid, highly sensitive and specific diagnosis [4,5,36,39].

Materials and Methods of Research

The work is based on the survey data of 244 patients from the southern regions of the Republic of Uzbekistan who received treatment in the centers of phthisiology and pulmonology of Bukhara region – 148 (60.7%), Navoi region – 30 (12.3%), Kashkadarya region - 32(13.1%) and Surkhandarya region – 34(13.9%) of cases in the period from 2016 to 2020.

Gender		Number of patients	19- 29 years	30-39 years	40-49 years	50-59 years	60-69 years	70 old and older
	Rural	118	13	16	24 9,8%	29 11,9%	22 9,0%	14
men n-	population	48,4%	5,3%	6,6%				5,7%
165	Urban	45	5	3	10	13	7	7
	population	18,4%	2,2%	1,2%	4,1%	5,3%	2,9%	2,9%
	homeless	2	-	-	-	2	-	-
	people	0,8%				0,8%		
women	Rural	67	9	11	7	10	13	17
n – 79	population	27,5%	3,7%	4,5%	2,9%	4,1%	5,3%	6,9%
	Urban	11	2	-	1	3	3	2
	population	4,5%	0,8%		0,4%	1,2%	1,2%	0,8%
	homeless	1	-	1	-	-	-	-
	people	0,4%		0,4%				
Total:		244	29	31 12,7%	42 17,2%	57	45	40
		100%	11,9%			23,4%	18,4%	16,4%

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Table 1 Distribution	of natients by g	ender place	of residence	and age
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Note: * - without a specific domicile.

The age of the patients ranged from 18 to 86 years, the average age was 52.1 ± 2.9 years. Table No. 1 shows that men were 2.2 times more than women, the number of patients aged 19-59 years - 65.2% (working age), 60-69 years - 18.4%; over 70 years - 16.4%. Patients of the rural population were observed - 185 (75.8%), urban population – in 56 (23.0%) and HOMELESS people – in 3 (1.2%) cases. The analysis notes that the disease was 3.3 times more common in rural populations.

Persistent forms of pulmonary tuberculosis develop slowly, with scant clinical signs of the disease, manifest themselves by the onset, onset and subsiding of clinical symptoms. In many cases, more than 75.0% of patients are previously treated patients, that is, those with a history of sensitive forms of tuberculosis. The clinical course is dominated by the following symptoms: cough with or without sputum, weight loss, weakness and night sweats.

Of 244 patients, 151 (61.9%) patients had the disease detected for the first time, and 93 (38.1%) had it repeatedly, i.e. they had previously received treatment. It should be noted that 21 (8.6%) patients were previously prisoners. Generalized forms of tuberculosis were found in 11 (4.5 \pm 2.5%) cases, of which the lesion of pulmonary tuberculosis with tuberculous pleurisy - in 7 (2.9 \pm 1.1%) cases, organs of the genitourinary system were determined - in 2 ($0.8 \pm 0.2\%$) and with tuberculous spondylitis - in 2 ($0.8 \pm 0.2\%$) patients. At the same time, the generalization of the tuberculosis process was observed more in the advanced stages of the disease, as well as cavernous or fibrous-cavernous pulmonary tuberculosis - in 7 (63.6%) cases. All patients underwent bacteriological examination of sputum and 100% of cases the clinical diagnosis was verified bacteriologically. In 74 (30.3±2.7%) patients, the disease developed slowly for more than 1 year, with a characteristic progression of general malaise, rare temperature rises to subfebrile, sometimes with the addition of a dry cough. The subacute course of the disease with progression during the 1st year, weight loss, subfebrile fever, dry cough and sweating in the evenings was noted in 24 $(9.4\pm1.8\%)$ patients, in 26 $(10.6\pm1.9\%)$ cases, the duration of the above symptoms is up to 6 months, it should be noted, in 120 $(47.6\pm2.4\%)$ of patients was up to 3 months - the clinical course of the disease was acute, with a rise in temperature of more than 38.0 OC, with intoxication, loss of body weight of more than 10% of the total, with a strong increase in dry or wet coughs with sputum and with deterioration in the general condition of patients. The duration of patients' complaints before the final diagnosis was from 1 month to 10 years, on average 6.3 ± 1.7 months. General condition of patients upon admission to the clinic. In patients with concomitant pathology, the clinical manifestation of the underlying disease was characterized by diversity and



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severe course. Clinical symptoms and laboratory data of the presented categories of patients are peculiar and difficult to diagnose.

When patients were admitted to clinical and laboratory studies, the following changes were observed: a decrease in hemoglobin was often observed - in 67.2% of cases; acceleration of ESR – in 55.3%; leukocytosis – in 49.6%; an increase in liver enzymes and bilirubin – in 38.1%; a violation of the filtration functions of the renal tubules – in 9.8% of patients and it should be noted, that leukocyturia – in 87.7%; erythrocyturia – in 26.6%; proteinuria – in 23.3% of cases. The clinical manifestation of generalized forms of tuberculosis had a variety of clinical signs, which were characterized by a severe general condition of patients, as well as the presence of diagnostic difficulties.

Results and Discussion

When analyzing the clinical course of resistant forms of pulmonary tuberculosis, it was noted that establishing a timely and correct diagnosis has difficulties, while errors in diagnosis are allowed. In the diagnosis of drug-resistant (LU) forms of pulmonary tuberculosis at the stages of the study, mistakes were made: in polyclinics, in hospitals of a non-phthisiological profile and in conditions of phthisiological institutions.

Table 2 Errors in the diagnosis of LU forms of pulmonary tuberculosis at the stages of the study

Medical institution	absolute number	%	P value
Polyclinic	72	29,5±2,9	p<0,01
Non-phthisiological hospitals	155	63,5±3,08	p<0,001
Phthisiological clinics	11	4,5±1,3	p<0,05

When analyzing Table No. 2, errors and shortcomings in the interpretation of the results of diagnostic methods are most often found in hospitals of a non-phthisiological profile – in 155 (63.5%) cases, and in polyclinics 2.1 times less than in hospitals of a non-phthisiological profile - in 72 (29.5%) and it should be noted that in hospitals of a phthisiological profile it is also possible to observe deficiencies or untimely detection of LU forms of pulmonary tuberculosis – in 11 (4.5%) cases.



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Table 3 Types of diagnostic research methods used in the diagnosis of resistant forms of pulmonary tuberculosis

Methods Researches	In the polyclinic n-109	In non- phthisiological hospitals n-155	In phthisiological hospitals n-244	Total n-244
Radiography	63	64	117	244
	(57,8%)	(41,3%)	(47,9%)	(100%)
MSCT of the lungs	8	11	5	26
	(7,3%)	(7,1%)	(2,1%)	(10,7%)
Bronchoscopy	-	2 (1,3%)	1 (0,4%)	3 (1,2%)
Bacteriological research	77	23	144	244
	(70,6%)	(14,8%)	(59,0%)	(100%)

Table 3 shows that in polyclinic admission of patients, lung radiography was most often performed – in 57.8% and bacteriological examination of sputum – in 70.6% of cases. It should be noted that in non–phthisiological institutions, bacteriological examination of sputum was carried out very rarely - in 14.8% of cases. In the analysis, it is noted that in relatively rare cases, MSCT examination of the chest organs was performed - in 10.7% and bronchoscopic examination – in 1.2% of cases, this is due to the high informativeness of bacteriological sputum studies, especially molecular genetic diagnostic methods.

Of the 244 patients, 109 (44.7%) patients initially applied to polyclinics in their homes; in 83 (76.1%) cases, treatment was carried out with the diagnosis: acute respiratory disease of the upper respiratory tract – in 46 (55.4%), acute bronchitis – in 18 (21.7%) and exacerbation of chronic bronchitis – in 19 (22.9%) cases. From a clinical example, one can see that treatment is carried out without examination according to the standard at the polyclinic stage, for which the prescribed therapy turns out to be ineffective. And on this example, there is a violation of the use of anti-tuberculosis drugs, in outpatient conditions of which a lot depends on the patient, the district general practitioner and the district phthisiologist.

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patient, the district general practitioner and the district phthisiologist. 155 (63.5%) patients were treated in non–phthisiological clinics, of which 149 (96.1%) cases were treated: with a diagnosis of acute pneumonia – in 74 (49.7%), acute bronchitis – in 47 (31.5%), exacerbation of chronic bronchitis - in 26 (17.5%) and exudative pleurisy - in 2 (1.3%) cases. Patients in 100% of cases received antibacterial therapy, in order to treat and relieve cough, patients were prescribed antitussive drugs (acc, acc–long, bromhexine, mukaltin, broncholitin, libexin, ambrobene, ambroxol, cough medicine, etc.), bronchodilators (euffilin), glucocorticosteroids (hydrocortisone, dexomethasone), vitamins (C, B1, B6 ...), as well as inhalation manipulations with 4% sodium bicarbonate or various medications were prescribed to patients.

In the analysis, it can be noted that in hospitals of a non-phthisiological profile, without an X-ray examination of the lung and without a bacteriological examination of the patient's sputum, inadequate treatment is carried out, which worsens the general condition of the patient and the epidemiological situation. It should be noted that out of 244 patients – in 98 (40.1%) cases, patients were self-medicating and 36 (14.8%) were treated by doctors for 1.5 to 6.2 months, aggravating the severity, the course of the disease and were admitted to more delayed stages of the disease.

In the conditions of phthisiological dispensaries, 26 (10.7%) cases had treatment deficiencies. Of these, in 16 (61.5%) cases, MBT passed from the sensitive form - Rif S to the stable form of Rif R, and in 10 (38.5%) patients, a violation of the regimen of anti-tuberculosis drugs was observed.

Thus, the analysis of the obtained results indicates that in general clinical institutions patients are examined by superficially incompetent specialists, the full scope of examination of patients is not performed, which leads to the progression of the tuberculosis process and deterioration of the general condition of patients in this category. Diagnostic errors were detected in 11 (4.5%) patients from various specialists in phthisiological clinics.

Table 4 Diagnostic errors in the treatment of resistant forms of pulmonary tuberculosis in phthisiological dispensaries n-244

Types of diagnostic errors	Abs. Number	%
Methods of radiation diagnostics	7	63,6%
Bacteriological	2	18,2%
Bacteriological + methods of radiation diagnostics	2	18,2%
Total:	11	4,5%





Table 4 shows that 4.5% of cases have mistakes. Most often, this disadvantage occurs when interpreting the conclusions of radiation research methods – in 63.6% of cases. In these 11 cases, patients were thoroughly examined bacteriologically for PCR diagnostics and bacteriological seeding methods, after which a final diagnosis with bacteriological verification was established.

From the above clinical examples, it can be seen that specialists do not always use standard methods of examination, such as bacteriological examination of sputum, radiography, lung MSCT and bronchoscopy according to strict indications.

Thus, the clinical course of LU forms of pulmonary tuberculosis is characterized by a wide variety, is difficult to diagnose and requires deep knowledge from specialists to clarify the diagnosis and conduct timely anti-tuberculosis therapy, taking into account the drug sensitivity of Mycobacterium tuberculosis.

Conclusions

1. The analysis revealed that the average age was 52.1 ± 2.9 years, the disease was more common in men by 2.2 times and in the rural population by 3.3 times.

2. The disease developed slowly for more than 1 year - in $30.3 \pm 2.7\%$, up to a year - in $9.4 \pm 1.8\%$, up to 6 months - in $10.6 \pm 1.9\%$ and up to 3 months - in $47.6 \pm 2.4\%$ of cases.

3. Incorrect interpretation of the results of diagnostic research methods was found in non-phthisiological hospitals – in 63.5% of cases, and in polyclinics - in 29.5% and in phthisiological hospitals, this indicator was – in 4.5% of cases.

4. The analysis of the obtained results indicates that patients are examined superficially in general clinical institutions, the full scope of examination of patients is not performed and inadequate treatment is carried out, which leads to the progression of the tuberculosis process and deterioration of the general condition of patients in this category.

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