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ABSTRACT

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FREQUENCY OF COMPLICATIONS AND LESIONS OF ORGANS/SYSTEMS IN PULMONARY TUBERCULOSIS AMONG HIV-PATIENTS

Objective: To study the frequency of complications and organ/system involvement in pulmonary tuberculosis in the context of HIV/AIDS infection.

Materials and Methods. We analyzed medical data from 103 patients with pulmonary tuberculosis that developed in the setting of HIV/AIDS infection. The patients were divided into groups: drug-sensitive pulmonary tuberculosis (DS-PTB) – 42 patients who excreted Mycobacterium tuberculosis (MBT) strains sensitive to anti-mycobacterial drugs (AMD); and drug-resistant pulmonary tuberculosis (DR-PTB) – 61 patients with resistant MBT strains. Data from the period 2020–2024 were analyzed.

To study the frequency of complications and organ/system involvement, the results of laboratory tests, abdominal ultrasound, computed tomography of the chest and abdominal organs, and consultations with specialized physicians were taken into account.

Microbiological detection of MBT included molecular genetic testing, microscopy and culture methods, and drug susceptibility testing of MBT strains to anti-mycobacterial drugs. HIV/AIDS infection was diagnosed using rapid tests, and viral load was determined by polymerase chain reaction. Microsoft Excel software was used for statistical analysis of the results.

Results and Discussion. In both study groups, men predominated by 1.5 times, aged over 30 to 50 years. A severe condition at admission was noted in 23.8% of patients with DS-PTB and 9.8% with DR-PTB. The average hospital stay for DS-PTB was (23.1 ± 2.1) bed-days, and for DR-PTB – (61.7 ± 4.5).

In DR-PTB/HIV, miliary tuberculosis predominated 1.7 times more often, and infiltrative pulmonary tuberculosis – 2.0 times more often. In DS-PTB/HIV, an increased frequency of disseminated pulmonary

tuberculosis was observed. Patients with DR-PTB reported pronounced intoxication and cachexia twice as often compared to those with DS-PTB.

In both groups, sepsis, pericarditis, and spontaneous pneumothorax were diagnosed with nearly equal frequency. Respiratory failure was detected 1.5 times more often in DR-PTB, while chronic obstructive bronchitis was 1.7 times more frequent in DS-PTB. In both groups, chronic hepatitis, liver cirrhosis, ascites, and toxic liver damage were noted. In DR-PTB, chronic hepatitis B, nervous system involvement, and eye disorders were observed twice as often as in DS-PTB.

Conclusions. Drug-resistant pulmonary tuberculosis in the context of HIV/AIDS infection had a significantly more severe course due to the development of multiple organ failure. These changes in the combined TB/HIV/AIDS condition contributed to disability in 24.4% (10) of patients with drug-sensitive TB/HIV and in 55.7% (34) of patients with drug-resistant TB/HIV.

Keywords: HIV/AIDS/TB co-infection, complications, organ involvement, systems.

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ЧАСТОТА УСКЛАДНЕНЬ І УРАЖЕНЬ ОРГАНІВ /СИСТЕМ ПРИ ТУБЕРКУЛЬОЗІ ЛЕГЕНЬ У ВІЛ-ПОЗИТИВНИХ

Мета роботи. Вивчити частоту ускладнень і уражень органів/систем при туберкульозі легень на тлі ВІЛ/СНІД-інфекції.

Матеріали і методи. Ми проаналізували медичні дані 103 хворих, на туберкульоз легень, який розвинувся на тлі ВІЛ/СНІД-інфекції. Хворих поділили на групи: чутливий туберкульоз легень (Ч-ТБЛ) – 42 пацієнта, які виділяли чутливі штами *Mycobacteria tuberculosis* (МБТ) до антимікобактеріальних препаратів (АМБП); і хіміорезистентний туберкульоз легень (ХР-ТБЛ) – 61 пацієнт з резистентними штами МБТ. Вивчили дані за період 2020-2024 рр.

З метою вивчення частоти ускладнень і уражень органів/систем, до уваги брали результати лабораторних досліджень, ультразвукової діагностики органів черевної порожнини та комп'ютерної томографії органів грудної клітки і черевної порожнини та висновки вузьких спеціалістів тощо.

Мікробіологічне виявлення МБТ включало: молекулярно-генетичне дослідження, методи мікроскопії та посіву, проведення тесту медикаментозної чутливості штамів МБТ до АМБП. ВІЛ/СНІД-інфекцію діагностували експрес-тестом, вірусне навантаження - використовуючи полімеразну ланцюгову реакцію. Пакет програм Excel застосували для статистичного аналізу результатів.

Результати та обговорення. В досліджуваних групах в 1,5 рази переважали чоловіки, віком понад 30 до 50 років. У важкому стані були госпіталізовані 23,8% хворих з Ч-ТБЛ і 9,8% – з ХР-ТБЛ. Середнє перебування у стаціонарі з Ч-ТБЛ склало (23,1±2,1) ліжко-днів, а ХР-ТБЛ – (61,7±4,5). При ХР-ТБЛ/ВІЛ переважав міліарний ТБ в 1,7 рази та в 2,0 рази – інфільтративний ТБЛ. При Ч-ТБЛ/ВІЛ встановлено збільшення кількості дисемінованого ТБЛ. Пацієнти в 2 рази частіше скаржились на виражену інтоксикацією, кахексією,

ніж при Ч-ТБЛ У обох групах майже з однаковою частотою діагностували сепсис, перикардит, спонтанний пневмоторакс. Респіраторну недостатність в 1,5 рази частіше виявляли при ХР-ТБЛ, а хронічний обструктивний бронхіт – у 1,7 рази при Ч-ТБЛ. В обох групах констатовано хронічний гепатит, цироз печінки, асцит і токсичне ураження печінки. При ХР-ТБЛ в 2 рази частіше спостерігали хронічний гепатит В, ураження нервової системи і органу зору, ніж при Ч-ТБЛ.

Висновки. ХР-ТБЛ на тлі ВІЛ/СНІД-інфекції перебігав значно важче внаслідок розвитку поліорганної недостатності. При цьому ці зміни на тлі поєднання ТБЛ і ВІЛ/СНІД-інфекції сприяло інвалідизації у 24,4% (10) пацієнтів з чутливим ТБЛ/ВІЛ і у 55,7% (34) - з хіміорезистентним ТБ/ВІЛ.

Ключеві слова: ко-інфекція ВІЛ/СНІД/ТБЛ, ускладнення, ураження органів, систем.

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ABBREVIATIONS: AIDS – acquired immunodeficiency syndrome, AMBDs – antimycobacterial drugs, HIV – human immunodeficiency virus, MBT – mycobacterium tuberculosis, MDR-TB – multidrug-resistant tuberculosis, XDR-TB – tuberculosis with extensive drug resistance, TB – tuberculosis, S-PTB – susceptible pulmonary tuberculosis, CR-PTB – chemoresistant pulmonary tuberculosis, WHO – World Health Organization

INTRODUCTION

In modern environment, tuberculosis (TB) is one of the most important issues in the Health system [1]. According to the World Health Organization (WHO) 10.6 million people contracted TB and 1.6 million died from it in 2021 [2, 3].

One of the main reasons for the deterioration of the epidemiological situation with TB in the World, and in particular in Ukraine, is the spread of chemoresistant TB (CR-TB) [4, 5]. As a result of the pathomorphosis of CR-TB over the past 13 years, among adult patients there is a clear trend towards an increase in primary resistance to fluoroquinolones (in particular, extensive drug resistance - XDR) from the minimum frequency in 2006 (0%) to almost 30.0% in 2019, on the background of a decrease in multidrug-resistant (MDR) TB without resistance to fluoroquinolones (from 60.0% to 40.0%) [6]. An unfavorable trend has been observed since 2017, when the number of patients with MDR-TB and XDR-TB almost equalized. At the same time, in Ukraine MDR-TB was diagnosed for the first time in 3,924 patients, of which XDR-TB – in 396 (10.1%) in 2023, and the incidence of MDR-TB was 3,645, of which XDR-TB - in 885 patients (24.3%) in 2024 [7.8].

Several main factors for risk the deterioration of the course and results of TB treatment have been identified, in particular the resistance of Mycobacteria tuberculosis (MBT); concomitant diseases – human

immunodeficiency virus (HIV), diabetes, coronavirus disease (COVID-19); war, etc. [4, 9].

Currently, TB has become the most common opportunistic disease in HIV-infection and the main cause of AIDS and death in patients with HIV [10, 11]. The researches of scientists [12] confirmed that only 10-15% of HIV-negative individuals get sick after contact with a bacterioexcreter, and 40-50% of HIV-positive individuals already get sick. It is also known that the combination of TB and HIV-infection is a risk factor for the occurrence of chemoresistant forms: only 27.3% of patients with isolated TB have resistant forms, and among patients with HIV/AIDS/TB co-infection - 60.0%.

According to the studies of Matsegora N.A. et al. [11], patients with CR-TB/HIV co-infection have been diagnosed with many forms of comorbidity, leading to multiple organ pathology, which is more pronounced in patients in a state of deep immunosuppression.

In patients with deep immunodeficiency, extrapulmonary localization of the tuberculous process, will probably be detected more often than only pulmonary localization (70.1% vs. 62.9%). Among the examined patients with HIV/AIDS/TB co-infection, 30 % had isolated pulmonary TB, 33 % had combined pulmonary/extrapulmonary [13], and the greatest specific gravity was extrapulmonary TB without pulmonary involvement [14, 15, 16].

Thus, the study of the frequency of complications and lesions of organs/systems of patients with CR-PTB/HIV co-infection is relevant for the timely diagnosis of this disease, the development of new modern methods of treatment and the improvement of the course of CR-PTB/HIV co-infection.

THE PURPOSE OF WORK: to study the frequency of complications and lesions of organs/systems in pulmonary tuberculosis on the background of HIV/AIDS-infection.

MATERIALS AND METHODS

The subjects studied were adults aged 18 years or more who contracted TB with bacteriologically confirmed results. All patients were inpatient treatment in the Anti-TB departments of the Pulmonary Health Center during 2020-2024. Retrospective analysis of medical data included patients with confirmed HIV-positive status who were diagnosed with pulmonary tuberculosis with bacterial excretion. Patients were divided into groups: susceptible pulmonary tuberculosis (S-PTB) 42 patients who isolated susceptible strains of MBT to antimycobacterial drugs (AMBDs); and chemoresistant pulmonary tuberculosis (CR-PTB) 61 patients who isolated resistant strains of MBT.

In order to study the frequency of complications and lesions of organs/systems, the results of laboratory tests, ultrasound diagnostics of abdominal organs and computer tomography of chest and abdominal organs, as well as the conclusions of narrow specialists, etc., given in the form 003 «Medical card of an inpatient patient» were taken into account.

Laboratory diagnostic methods

For the detection of MBT in sputum used microbiological research: by microscopy, seeding of material on medium Levenstein-Jensen, typing MBT on BACTEC MGIT 960, using a drug susceptibility testing of MBT to AMBDs of the I and II lines. The molecular genetic examination of sputum, in particular by the GeneXpert MTB/RIF method and linear probe analysis which included determining the susceptibility of MBT to I line (to isoniazid and rifampicin) using GenoType MTBDRplus mutation kits. Susceptibility/resistance to II line (fluoroquinolones and aminoglycosides) was determined using the GenoType MTBDRsl mutation kit [17].

HIV/AIDS infection in both groups of patients was diagnosed with an express test and the viral load was determined by polymerase chain reaction (PCR). As a screening method for the detection of HIV 1/2 in whole blood/plasma/serum, a combined test was used, which is based on an immunochromatographic analysis for the qualitative determination of immune markers/antibodies to HIV 1/2 in vitro.

Mathematical computing software, their graphical representation and analysis results in Excel with the Microsoft Office program package were used for statistical analysis of the original data. The statistical processing of the research results was carried out using the methods of parametric (variance) statistics in compliance with the conditions for evaluating the type of distribution. The results are given in the form of the average statistical value of the indicator and the error of the average $M \pm m$. The probability of the obtained results was evaluated according to the Student and Mann-Whitney criterion. The value of $p < 0.05$ was considered statistically significant. The STATISTICA 2006 software complex was used for statistical processing of the material.

RESULTS AND DISCUSSION

Our studies showed that both groups were 1.5 times predominant for male patients (69.0% and 78.7%), compared to female (31.0% and 21.3%). In the age structure up to 30 years, there were only 9.5% (4) patients with S-PTB/HIV, at the same time, with CR-PTB/HIV, there were no people under 30 years at all. Among S-PTB/HIV patients 1.3 times less likely were aged 31 to 40 years (30.9% vs. 40.0%, $p > 0.05$), 1.1 times less likely to be diagnosed between the ages of 41–50 years (42.8% vs. 47.5%, $p > 0.05$), and over 51 years – 1.5 times more likely, compared to CR-PTB/HIV. Therefore, in both groups, persons aged 31 to 50 prevailed.

In the future, we analyzed the frequency of damage to individual organs and systems depending on the sensitivity/resistance of MBT in patients with PTB/HIV (Table 1). Our studies indicate the presence of pronounced intoxication and cachexia in CR-PTB/HIV patients (54.1% vs. 28.0%, $p < 0.01$), but S-PTB/HIV patients probably complained more often about hemoptysis (16.7% vs. 8.2%, $p < 0.05$). Often, the specific process in CR-PTB on the background of HIV/AIDS was complicated by iron deficiency anemia and there were cases of coronary heart disease. Sepsis, pericarditis, chronic coronary heart disease and spontaneous pneumothorax were diagnosed with almost the same frequency in both groups.

Most often, non-specific lesions of the respiratory system were detected in the form of respiratory failure in 90.2% of CR-PTB/HIV and in 59.5% - with S-PTB/HIV, viral-bacterial pneumonia – in 19.7% and 7.1%, ($p < 0.05$), chronic obstructive bronchitis – 44.3% and 23.8%, respectively. However, chronic purulent bronchitis was observed 1.7 times more frequently in S-PTB/HIV (33.3% vs. 19.7%, $p < 0.05$).

In HIV/AIDS/TB co-infection, liver damage in both study groups was manifested as chronic hepatitis C (21.4% vs. 29.5%, $p > 0.05$), liver cirrhosis (14.3% vs.

13.1%, $p>0.05$), ascites (9.5% vs. 9.8%, $p>0.05$) and toxic liver damage (7.1% vs. 6.6%, $p>0.05$). However, chronic hepatitis B (9.8%) was observed 2 times more frequently among patients with CR-TBL/HIV, compared to S-PTB/HIV (4.7%), $p<0.05$.

We analyzed the frequency of damage to the nervous system in patients with HIV/AIDS/TB co-infection depending on the sensitivity/resistance of MBT. It has been proven that patients with CR-

PTB/HIV were more often diagnosed with damage to the nervous system, in particular, spastic paraplegia (13.1%), spastic tetralgia (9.8%) and cerebral cryptococcosis were observed in 20 (32.8%). Such changes were probably less common in patients with S-PTB/HIV.

Eye lesions diagnosed 4.1 times more frequently in patients with CR-PTB than S-PTB, in the form of astigmatism, retinal and disc lesions Table 1.

Table 1 – Frequency of complications and lesions of organs/systems in HIV/AIDS/PTB co-infection

Clinical signs of concomitant pathology	S-PTB/HIV (42 patients)		CR-PTB/HIV (61 patients)		p
	abs.n.	%	abs.n.	%	
Lesions of the respiratory system					
Respiratory failure	25	59.5	55	90.2	<0.05
Sepsis	2	4.7	4	6.5	>0.05
Pericarditis	2	4.7	3	4.9	>0.05
Pleuritis	2	4.7	5	8.2	<0.05
Hemorrhage	7	16.7	5	8.2	<0.05
Spontaneous pneumothorax	7	16.7	10	16.4	>0.05
Intoxication and cachexia	12	28	13	54.1	<0.01
Viral-bacterial pneumonia	3	7.1	10	19.7	<0.05
Chronic purulent bronchitis	14	33.3	10	19.7	<0.05
Chronic obstructive bronchitis	10	23.8	27	44.3	<0.05
Lesions of the hepatobiliary system					
Chronic hepatitis C	9	21.4	18	29.5	>0.05
Cirrhosis of the liver	6	14.3	8	13.1	>0.05
Chronic viral hepatitis B	2	4.7	6	9.8	<0.05
Toxic liver damage	3	7.1	4	6.6	>0.05
Ascites	4	9.5	6	9.8	>0.05
Lesions of the organs of vision					
Retinopathy	5	11.9	8	13.1	>0.05
Herpesvirus eye damage	1	2.4	1	1.6	>0.05
Astigmatism	1	2.4	6	9.8	<0.01
Damage to the retina of the eyes and disc	1	2.4	7	11.4	<0.01
Fungal-parasitic diseases of the nervous system					
Cerebral cryptococcosis	4	9.5	20	32.8	<0.01
Candidiasis	22	52.4	59	96.7	<0.05
Toxoplasmosis	3	7.1	18	29.5	<0.01
Lesions of the nervous system					
Spastic paraplegia	2	4.8	8	13.1	<0.05
Spastic tetraplegia	-	-	6	9.8	-
Encephalopathy	1	2.4	6	9.8	<0.05

At the same time, with HIV/TB co-infection, we diagnosed the following clinical forms of tuberculosis, which are shown in Fig. 1. In particular, CR-PTB/HIV was 1.7 times more likely diagnosed miliary tuberculosis, 2.0 times – infiltrative PTB ($p<0.05$) than

S-PTB. However, in patients with S-PTB/HIV, a tendency to increase the number of disseminated form PTB was noted. The destructive process was 2.0 times more frequent in patients with CR-PTB/HIV (59.0%) than in S-PTB/HIV (29.3%, $p<0.05$).

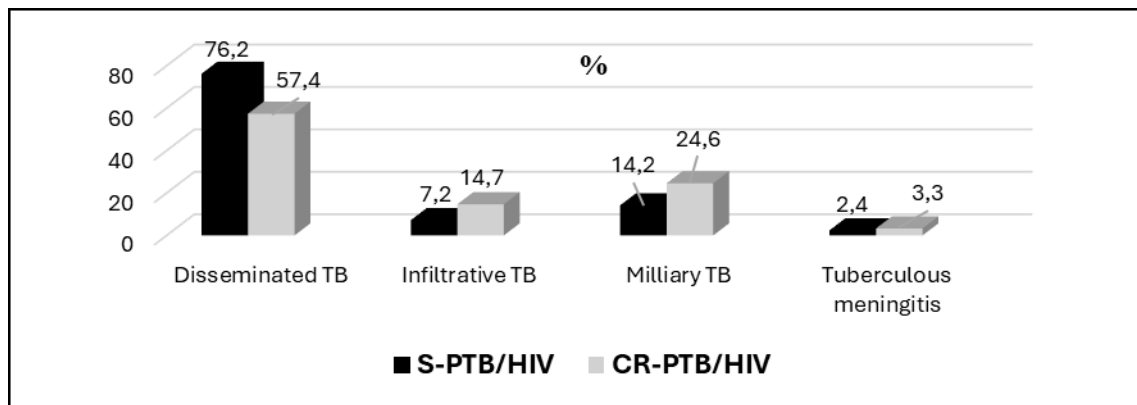


Fig. 1. Clinical forms of pulmonary tuberculosis depending on the sensitivity/resistance of MBT strains to AMBP, %

All patients received urgent inpatient treatment. At the same time, patients with S-PTB/HIV were 3.8 times more likely to be in a hospital for up to 10 days than with CR-PTB/HIV (61.9% vs. 16.4%; $p < 0.01$). The mean number of hospital bed-days in S-PTB/HIV was (23.1±2.1) and in patients with CR-PTB/HIV was (61.7±4.5). 23.8% (10) of patients with S-PTB/HIV and 9.8% (6) – CR-PTB/HIV were hospitalized in serious condition. Mortality in CR-PTB was 2 times more frequent (26.2 % vs. 11.9%; $p < 0.05$). Consequently, the majority of patients with CR-PTB/HIV (83.6%) were treated in hospital conditions probably longer than with S-PTB/HIV (38.1%), and mortality with CR-PTB/HIV was 2.2 times more frequent than with S-PTB/HIV.

Therefore, CR-PTB on the background of HIV/AIDS-infection was much more difficult than the specific process in which the patient isolated MBTs sensitive to AMBDs. The complexity of the process was due to a widespread and destructive specific process and complications that were caused by HIV/AIDS-infection. The combination of these two diseases contributed to disability in 55.7% (34) of patients with CR-PTB/HIV and 24.4% (10) - with S-PTB/HIV, in or even mortality 26.2% and 11.9%, respectively.

CONCLUSIONS

1. Men aged from 30 to 50 years predominate (69.0%) among the researched patients. 23.8% of patients with S-PTB/HIV and 9.8% of CR-PTB/HIV were hospitalized in serious condition. Average stay of patients in the hospital with S-PTB/HIV was (23.1±2.1) bed-days, and CR-PTB/HIV – (61.7±4.5).

2. Miliary TB is 1.7 times and 2.0 times – infiltrative PTB ($p < 0.05$) more frequently diagnosed in CR-PTB/HIV compared to S-PTB/HIV. However, patients

with S-PTB/HIV showed a tendency to increase the number of disseminated form PTB. The destructive process is 2.0 times more frequent in patients with CR-PTB/HIV (59.0%) than S-PTB/HIV (29.3%, $p < 0.05$).

3. Often, the specific process in patients on the background of HIV/AIDS is complicated by iron deficiency anemia (39.8±1.9)% and there were cases of coronary heart disease (9.6±0.5)%. In both groups, sepsis (4.7% and 6.5%), pericarditis (4.1% and 4.9%), respectively, are diagnosed with almost the same frequency.

4. Most often, non-specific lesions of the respiratory system were found in the form of respiratory failure in 90.2% of patients with CR-PTB/HIV, lung inflammation – in 19.7%, chronic purulent bronchitis – 44.3%. However, chronic obstructive bronchitis is 1.7 times more frequent in S-PTB/HIV (33.3% vs. 19.7%, $p < 0.05$).

5. In HIV/AIDS/PTB co-infection, liver damage manifests as chronic hepatitis C (29.5% vs. 21.4%, $p > 0.05$), liver cirrhosis (14.3% vs. 13.1%, $p > 0.05$), ascites (9.5% vs. 9.8%, $p > 0.05$), and toxic liver damage (7.1% vs. 6.6%, $p > 0.05$). However, chronic hepatitis B is observed 2 times more often (89.8%) with CR-PTB/HIV, compared to S-PTB/HIV (4.7%), $p < 0.05$.

6. The nervous system is more often affected in CR-PTB/HIV, compared to S-PTB/HIV: in particular, patients have spastic paraplegia (13.1%), spastic tetralgia (9.8%) and cerebral cryptococcosis – in 20 (32.8%). Such changes are probably less often noted with S-PTB. It should be noted that with CR-PTB/HIV, damage to the organs of vision is probably more common.

AUTHOR CONTRIBUTIONS

Sakhelashvili M.I. - Conceptualization, study design, writing of the main text, and formulation of conclusions.

Piskur Z.I. - Participation in the discussion of the obtained results, writing of the text and editing of the article text.

Sakhelashvili- Bil O.I. - Participation in the discussion of the obtained results and editing of the article text.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interest regarding the research, authorship, and publication of this article.

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Authors confirm that no artificial intelligence technologies were used during manuscript writing or editing.

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