CURRENT TUBERCULOSIS A IN HIV-INFECTED PATIENTS

Kholiev Bakhodir Oltibayevich *Bukhara State Medical Institute named after Abu Ali ibn Sina, Uzbekistan, Bukhara, A. Navoi St. 1 Phone number: +998 (65) 223-00-50 e-mail: xoliyev.baxodir@bsmi.uz*

Summary:

Tuberculosis is widespread in all regions of the world. According to WHO, in 2016, 476,774 people with tuberculosis had a positive HIV status, which accounted for 7.5% of all reported cases. In 2016, more than 374,000 people living with HIV died from tuberculosis worldwide (WHO, 2017). In recent years, the In the Russian Federation, there is a steady increase in the incidence of tuberculosis in patients with HIV infection. According to the Federal Tuberculosis Monitoring Center, the number of people living with HIV infection has doubled. The article provides an overview of the epidemic indicators of tuberculosis and HIV infection in Russia. Problems of diagnosis of tuberculosis in combination withcoinfection, as well as new laboratory and immunological methods used today in the world and domestic practice to determine tuberculosis infection.

Key words: phthisiology, tuberculosis, HIV infection, Mycobacterium tuberculosis, immunosuppression, clinical manifestations, treatment.

Currently, the problem of tuberculosis continues to pose a threat to public health around the world. According to WHO, tuberculosis remains one of the top 10 leading causes of death [28]. In 2016, 10.4 million new cases of tuberculosis were registered in the world, and 1.03 million people died from tuberculosis [28]. At the same time, the incidence of tuberculosis in the world in 2000-2016 decreased by 18%, and the mortality rate was 37% [28]. The incidence of tuberculosis in the Russian Federation in 2016 decreased by 41% compared to 2000 and amounted to 53.5 per 100 thousand population, and the death rate from tuberculosis decreased from 22.6 in 2005 to 7.8 per 100 thousand population in 2016 (a decrease of 65.5%) [10]. A major contribution to this problem is made by the spread of tuberculosis with multiple (MDR) and broad (XDR) drug-resistant Mycobactérium Mycobacterium tuberculosis (MBT) and the growing number of patients with concomitant diseases that are risk factors for the development of tuberculosis (HIV infection, diabetes mellitus, etc.) [13, 18].

In 2016, there were 490,000 new cases of MDR-related tuberculosis and an additional 110,000 rifampicin-resistant cases. With HIV infection, the function of CD4+lymphocytes, which play an important role in the fight against MBT, is disrupted. Tuberculosis can also adversely affect the course of HIV infection, since MBTs can stimulate HIV replication in people with comorbidities [21]. As can be seen from the

above data, the combination of 2 formidable infectious diseases made adjustments to the epidemiological situation of tuberculosis on the planet at the beginning of the XXI century. Currently, the features of the course and effectiveness of tuberculosis treatment in patients with HIV infection remain under the close attention of phthisiatricians around the world. A certain amount of information has been accumulated on the study of age and gender composition, social status, features of the course of the tuberculosis process and the effectiveness of its treatment in HIV-infected patients. However, the data provided is ambiguous. Available publications indicate significant differences in data on the age and sex composition of tuberculosis patients with without HIV infection. According to the majority of authors, men predominate among patients with tuberculosis combined with HIV infection (62.5 to 88.9%) [8, 12]. However, other researchers did not note significant gender differences in these groups of patients [13]. The literature data on the age of patients with tuberculosis combined with HIV infection are unidirectional: both newly diagnosed patients and previously treated patients are younger than patients without HIV infection.

The age of most patients with tuberculosis combined with HIV infection ranged from 18 to 39 years [8, 12, 24]. There is also a certain amount of information about the peculiarities of the course of tuberculosis in patients with HIV infection. The results of a number of studies indicate that in patients with tuberculosis combined with HIV infection, the specific process of extrapulmonary localization occurs 1.8 times more often than in patients without HIV infection [13]. At the same time, pleural tuberculosis, intra-thoracic lymph nodes (IHL), and upper respiratory tract tuberculosis (respiratory extrapulmonary tuberculosis) were more often observed from extrapulmonary forms; tuberculosis of extrarespiratory localization was also found [13, 27].

A.M. Panteleev etal. [11], examining 1057 newly diagnosed patients with tuberculosis and HIV It was found that the most frequent early detection of tuberculosis occurred when HPLV was affected, and it was suggested that this form should be considered as a criterion for timely detection of tuberculosis in people with HIV infection [11]. According to most authors, infiltrative and disseminated pulmonary tuberculosis predominate among the pulmonary forms of tuberculosis in HIV infection [3, 12, 20]. Analysis of the results of a number of studies has shown that the severity of clinical manifestations of tuberculosis in patients with HIV infection depends, on the one hand, on the severity of immunodeficiency, and on the other-on the time of detection of tuberculosis in relation to HIV infection [4, 6, 8].

Thus, V. N. Zimina [4], after examining 554 patients, found that the clinical and radiological manifestations of tuberculosis depend on the degree of immunosuppression. HIV infection has virtually no effect on the course of tuberculosis in patients with an initial number of CD4+lymphocytes >500 cells/mkl. When the

number of CD4+lymphocytes is 500-350 cells/mkl, the course of tuberculosis is significantly more often characterized by an acute onset and a rarer detection of destructive forms of tuberculosis. When the number of CD4+ - lymphocytes was 350-200 cells/mkl, a feature of respiratory tuberculosis was a predominant lesion of HPLC and serous membranes. For the tuberculosis process that develops in patients with CD4+ - lymphocyte infection, according to various authors, it ranged from 22.4 to 41.3% [12, 20]. At the same time, cavities with a size of 500 cells/mkl were more often observed. According to L. P. Alekseeva [1], in patients with tuberculosis combined with HIV infection, BV depended on the time of detection of tuberculosis: it was more often detected in patients with primary detection of tuberculosis than HIV infection (65.6 and 46.8%, respectively). An analysis of the literature data on the presence and spectrum of drug resistance (DR) of MBT showed that in co-infection, the level of primary DR reaches 51.3% [1,8] and does not depend on the time of detection of tuberculosis. T. Y. Salina, T. I. Morozova [12] when analyzing the DR spectrum of MBT in 129 patients with tuberculosis combined with HIV-It was found that sensitivity to anti-tuberculosis drugs (TTP) was preserved in 63.5%, monoresistance was diagnosed in 5.7%, polyresistance – in 13.5%, MDR – in 17.3% of patients. A comparative analysis showed that primary MDR of MBT was significantly more often observed in the presence of HIV coinfection [1, 4].

N. V. Belyakova [2], when examining 433 patients, found that MDR of MBT in bacterial excretors was 2.4 times more common among patients with HIV infection [2]. Tuberculosis treatment is still one of the priorities of modern phthisiology. The problem of treatment of tuberculosis combined with HIV infection has become particularly acute in recent years. The leading method in the treatment of tuberculosis is etiotropic chemotherapy PTP. However, the treatment of patients in this category should be comprehensive and include antiretroviral therapy (ART). WHO recommends highly active antiretroviral therapy (HAART) for all HIV patients positive patients with tuberculosis no later than 8 weeks after the start of antitubercular therapy [28]. According to the literature, the use of ART along with PTP increases the effectiveness of treatmentof patients in this category and reduces the mortality rate [14, 25].

T. Y. Salina, T. I. Morozova [12], after examining 129 patients, found that the frequency of effective treatment in patients receiving PTP and HAART was 45.1%, and in patients who received only PTP-35.6%.In the literature, there is evidence of a high risk of drug resistance in patients with tuberculosis in combination with HIV infection, low treatment effectiveness, frequent relapse, and high mortality after a full-fledged and comprehensive TTP [13]. According to WHO data (2015), the success rate of TB treatment in the world in patients with HIV infection was 78.0%, and in HIV-negative patients-83.0% [28]. Information in the literature regarding the effectiveness of tuberculosis treatment in patients with HIV infection varies. According to A. I.

Shchelkanova [16], the cessation of BV in patients with tuberculosis in combination with HIV infection was 42%, the rate of closure of decay cavities was 17.5% [16]; in 58% of patients, treatment was unsuccessful. According to the materials of S. Mahtaband D. Coetzee [22], success in the treatment of HIV and tuberculosis reached 66.6%; failure in the treatment of tuberculosis was noted in 28.1% of HIV -infected patients. A number of works are devoted to the comparative study of the effectiveness of treatment of patients with tuberculosis combined with and without HIV infection. Thus, according to O. A. Kuzmin [7], in the early stages of HIV infection, the frequency of stopping BV and closing the decay cavities does not significantly differ from those in patients without HIV infection. At late stages, the effectiveness of tuberculosis treatment in patients with HIV infection is significantly lower than in patients without it. [5] found that, despite the problems associated with viral liver damage and the antisocial status of patients with HIV infection, the effectiveness of tuberculosis treatment in them practically did not differ from that in HIV -negative patients.

A number of studies have shown that in coinfection, the effectiveness of treatment depended on the time of detection of tuberculosis and the degree of immunosuppression. Thus, according to the materials of L. P. Alekseeva [1], the cessation of BV in patients with HIV infection preceded the development of tuberculosis was higher than in the case of reverse order (63.7 and 50.9%, respectively). Closure of the decay cavities was 37.5 and 23.7%, respectively, and the effectiveness of treatment also depended on the immunological status: at CD4+ <100 cells/mm3, BV was stopped in 25.0% of cases, at CD4+ – 100-400 cells/mm3-in 61% , and at CD4+ - >400 cells/mm3 - in 80% of cases , N. V. Fomenkova [14] found that the effectiveness of tuberculosis treatment to stop BV in patients with HIV infection preceded the development of tuberculosis was 91.5%, with simultaneous detection of tuberculosis and HIV infection -72.0%, in patients with tuberculosis preceding HIV infection – 73.5% and 78.1% of TB patients without HIV infection. Closure of decay cavities in these groups was 57.1, 41.3, 25.7, and 66.3%, respectively. As can be seen from the above data, on average, the effectiveness of treatment to stop BV in patients with tuberculosis with and without HIV co-infection did not differ, however, the effectiveness of treatment to close the destruction cavities in patients with tuberculosis combined with HIV infection was significantly lower.

The treatment of tuberculosis patients with MDR of the causative agent in the presence of HIV coinfection is particularly difficult [25]. P. Isaakidis et al. [19] analyzed the results of a survey of 2,578 patients with MDR-tuberculosis combined with HIV infection, and noted favorable treatment outcomes in 56.9% of patients [19]. At the same time, the mortality rate was 38.0%. The effectiveness of treatment of patients in this category, despite the presence of HIV status, did not differ from that in

patients with MDR-tuberculosis without HIV infection. However, the mortality rate in this group of patients was significantly higher. Other studies also indicate a high mortality rate among TB patients тwith MDR of the pathogen in the case of combination with HIV infection [25].

Thus, the presented data confirm that tuberculosis in patients with HIV infection is an urgent problem of modern phisiology. HIV infection is not only a risk factor for the development of tuberculosis, but also a cause that aggravates the course of tuberculosis and reduces the effectiveness of treatment. Literature data on the features of the course and effectiveness of tuberculosis treatment in patients with HIV infection are contradictory. In this regard, scientific research devoted to the study of various clinical and pathophysiological aspects of the development of tuberculosis in patients with HIV infection, as well as the development of scientifically based methods of pathogenetic treatment of patients in this category, remains very popular.

Literature

1. Alekseeva L. P. Features of detection, clinical course and treatment of patients with tuberculosis and HIV infection. Abstract of the thesis. ... Candidate of Medical Sciences, Moscow, 2008; 43 p.
2. Belyakova N. V. Improvement of tuberculosis prevention in HIV-infected patients in penitentiary institutions. Abstract of the thesis. ... Candidate of Medical Sciences, Moscow, 2011; 26 p.
3. Borovitsky V. S. Roentgenological picture of pulmonary tuberculosis combined with HIV infection in patients in a medical institution of the Federal Penitentiary Service. – 2018; 1: 66–7.
4. Zimina V. N. Improving the diagnosis and effectiveness of tuberculosis treatment in patients with HIV infection with various degrees of immunosuppression. Abstract of the thesis. ... Doctor of Medical Sciences, Moscow, 2012; 45 p.
5. Ivanov A. K., Shevyreva E. V., Skrynnik N. A. et al. Treatment of patients with tuberculosis and HIV infection in a day hospital of an antitubercular dispensary. Proceedings of the X Annual All-Russian Congress on Infectious Diseases with International participation, Moscow, 2018; p. 82.
6. Oblokulov A.A., Oblokulov A.R., Ergashov M.M. Clinical and laboratory criteria for spontaneous bacterial peritonitis in liver cirrhosis of viral etiology. Central Asian journal of medical and natural sciences Volume 03, Issue 03, may-jun 2022 172-177. ISSN: 2660-4159.
7. Abdulloev Mukhriddin Ziyodulloevich. (2023). Modern Therapy of Viral Hepatitis. Texas Journal of Medical Science, 26, 66–69. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4636 9. Oblokulov R.

8. A., Abdulloev M. Z. To Study the Effectiveness of Direct-Antiviral Drug in the Treatment of Chronic Viral Hepatitis C, Your Act //Web of Scholars: Multidimensional Research Journal. – 2022. – T. 1. – №. 5. – C. 201-206.
9. Ziyodulloyevich A. M. IN CHRONIC VIRAL HEPATITIS AND CIRRHOSIS OF THE LIVER, THE STUDY OF CYTOKINE LEVELS //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2022. – T. 2. – №. 12. - pp. 784-787.
10. Ziyodulloevich A. M. EFFICIENCY OF ETIOTROPIC TREATMENT IN CHRONIC VIRAL HEPATITIS //Galaxy International Interdisciplinary Research Journal. – 2023. – T. 11. – №. 4. – C. 450-454.
11. Ziyodullayevich A. M. Studies on the Determination of Cytokines in Patients with Chronic Hepatitis C with Criglobulinemia //American Journal of Pediatric Medicine and Health Sciences (2993-2149). – 2023. – T. 1. – №. 10. – C. 487-495.
12. Salina T. Yu., Morozova T. I. Clinical manifestations and effectiveness of treatment of patients with coinfection with tuberculosis / HIV infection and hepatitis / / Tuberculosis and lung diseases. – 2017; 95 (9): 25-9. DOI: 10.21292/2075-1230- 2017-95-9-25-29.
13. Galkin V. G., Elenkina Zh. V., Epifantseva N. A. et al. TB/HIV in the Russian Federation. Epidemiology, features of clinical manifestations and treatment results. Edited by S. A. Sterlikov / Moscow: RIO TSNIIOIZ, 2017; 52 p.
14. Fomenkova N. V. Clinical and laboratory characteristics of HIV infection in combination with various forms of tuberculosis. Dis. ... candidate of Medical Sciences. St. Petersburg, 2004; 140 p.
15. Frolova O. P., Kravchenko A. B., Martynov A. A. et al. Organization of TB care for patients with HIV infection. Manual for doctors / M., Tver: OOO "Publishing House "Triada", 2007; 120 p.
16. Shchelkanova A. I. Features of the clinical course and effectiveness of tuberculosis chemotherapy in HIV-infected individuals. Abstract of the thesis.. дис ... Candidate of Medical Sciences, Moscow, 2003; 24 p.
17. Beyrer C., Wirtz A., O'Hara G. et al. The expanding epidemic of HIV-1 in the Russian Federation // PLoS Med. – 2017; 14 (11): e1002462. https://doi. org/10.1371/journal.pmed.1002462.
18. Ellis P., Martin W., Dodd P. CD4 count and tuberculosis risk in HIV-positive adults not on ART: a systematic review and meta-analysis // Peer J. – 2017; 5: e4165. DOI: 10.7717/peerj.4165. 19. Isaakidis P., Casas E., Das M. et al. Treatment outcomes for HIV and MDR-TB co-infected adults and children: systematic review and meta-analysis. // Int. J. Tuberc. Lung Dis. – 2015;
19. (8): 969–78. http://dx.doi.org/10.5588/ ijtld.15.0123.

20. Kistana J., Lahera F., Otwombea K. et al. Pulmonary TB: varying radiological presentations in individuals with HIV in Soweto, South Africa // Trans. R. Soc. Trop. Med. Hyg. – 2017; 111: 132–6. DOI: 10.1093/trstmh/trx028.
21. Lawn S., Myer L., Bekker L. et al. Tuberculosis-associated immune reconstitution disease: incidence, risk factors and impact in an antiretroviral treatment service in South Africa // AIDS. – 2007; 21: 335–41.
22. Mahtab S., Coetzee D. Influence of HIV and other risk factors on tuberculosis // S. Afr. Med. J. – 2017; 107 (5): 428–34. DOI: 10.7196/SAMJ.2017. v107i5.11271.
23. Murray J., Sonnenberg P., Shearer S. et al. Human immunodeficiency virus and the outcome of treatment for new and recurrent pulmonary tuberculosis in African patients // Am. J. Respir. Crit. Care. Med. – 1999; 159 (3): 733–40.
24. Nglazi M., Bekker L.-G., Wood R. et al. The impact of HIV status and antiretroviral treatment on TB treatment outcomes of new tuberculosis patients attending collocated TB and ART services in South Africa: a retrospective cohort study // BMC Infect. Dis. – 2015; 15: 536. DOI: 10.1186/s12879-015-1275-3.
25. Satti H., McLaughlin M., Hedt-Gauthier B. et al. Outcomes of Multidrug Resistant Tuberculosis Treatment with Early Initiation of Antiretroviral Therapy for HIV Co-Infected Patients in Lesotho // PLoS One. – 2012; 7 (10): 46943.
26. Shivacoti R., Sharma D., Mamoon G. et al. Association of HIV infection with extrapulmonary tuberculosis: a systemic review //Infection. – 2017; 1: 11–21. doi: 10.1007/s15010-016-0960-5
27. Sinshaw Y., Alemu Sh., Fekadu A., Gizachew M. Successful TB treatment outcome and its associated factors among TB/HIV co-infected patients attending Gondar University Referral Hospital, Northwest Ethiopia: an institution based crosssectional study. // BMC Infectious Diseases. – 2017; 17: e132. DOI 10.1186/ s12879-017-2238-7
28. World Health Organization, Global tuberculosis report 2017. http://www. who.int/tb/publications/global_report/en/(Accessed 2 August 2017).