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# Eight Year Evaluation of HIV/Tuberculosis co-infection in Patients Admitted to Our Hospital

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**ABSTRACT**

Human immunodeficiency virus (HIV) is a disease that causes serious mortality and morbidity worldwide. Due to the weakening of the immune system, opportunistic infections are common in HIV-positive patients. Tuberculosis, one of the most important of these infections, makes the clinical management of HIV-positive patients even more difficult. In this study, it was aimed to determine the frequency of HIV-tuberculosis coexistence.

Tuberculosis cultures of 95 HIV/AIDS patients with confirmed diagnosis between 2014-2021 at Recep Tayyip Erdoğan University Training and Research Hospital were retrospectively analyzed. The results of the patients whose anti-HIV Elisa test was reactive were confirmed at the Refik Saydam Institute of Hygiene and Public Health. The diagnosis of tuberculosis was made by detection of growth in Löwenstein-Jensen medium and Mycobacteria Polymerase Chain reaction.

We studied a total of 95 HIV positive patients consist of 87(%91.6) males and 8(%8.4) females. Positive tuberculosis culture was detected in 3 (3.1%) of these patients. One of the patients is a foreign national and two of them are Turkish citizens.

Tuberculosis is an important cause of mortality in HIV/AIDS patients. Opportunistic infections in these patients are the cause of serious mortality and morbidity; therefore, early detection and treatment of these diseases is vital. In primary care, HIV-positive patients should be screened for Tuberculosis.

**Keywords:** AIDS, opportunistic infection, HIV, tuberculosis

## Introduction

According to the UNAIDS (The Joint United Nations Program On HIV/AIDS) global 2021 report, 37.7 million people in the world are living with HIV. In 2020, 1.5 million people were infected with HIV and 680,000 AIDS-related deaths were reported (1). In Turkey, there are 29.284 HIV-positive people and 2052 AIDS cases reported between 1985 and November 2021 (2).

HIV virus is most commonly transmitted sexually and it leads up to opportunistic infections by reducing CD4 T lymphocytes (3). These infections are frequently caused by *CMV, HSV, Candida, Cryptococcus, Toxoplasma, M. tuberculosis* (3,4). Among these diseases, tuberculosis is an important cause of mortality and morbidity (5,6). Although tuberculosis is often seen due to reactivation of latent infection in HIV-infected patients, it can also be observed during primary infection. (6,7). Early diagnosis of HIV infection is important in terms of preventing the development of opportunistic infections and related mortality and morbidity (8). In this context, UNAIDS has determined its targets for 2025 as 95% of HIV-positive people to be diagnosed, initiation of antiretroviral therapy in 95% of people diagnosed and achieving viral suppression in 95% of people receiving treatment (1).

In this study, it was aimed to determine the frequency of tuberculosis developing in HIV/AIDS patients followed in our hospital for 8 years and to examine the HIV/AIDS tuberculosis coexistence.

## Materials and Methods

Tuberculosis cultures of 95 confirmed HIV/AIDS patients diagnosed between 2014-2021 in Recep Tayyip Erdogan University Training and Research Hospital were retrospectively analyzed.

**HIV Diagnosis;** The samples were first centrifuged at 4000 rpm for 20 minutes and serum was obtained. Among the evaluated samples, HIV antibody was analyzed by macro-ELISA method

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using the Architect i2000sr (Abbott, USA) from 2014 to the end of 2019, and the COBAS e601 (ROCHE, Germany) system from the beginning of 2020 to the end of 2021. Depending on the manufacturer's recommendations; samples with values below 1 s/co were considered nonreactive and samples with values above 1 s/co were considered reactive.

A new sample was requested from the patients whose anti-HIV results were reactive, and the test was repeated in both samples. Results found to be nonreactive were reported as 'Nonreactive'. Samples that resulted in both samples as reactive were sent to the National HIV-AIDS Confirmation and Viral Hepatitis Reference Laboratory for confirmation.

**Tuberculosis Diagnosis;** Culture is the gold standard method in the diagnosis of tuberculosis (6,9). Löwenstein-Jensen medium was used for tuberculosis culture. Specimens cultured in Löwenstein-Jensen medium were incubated for up to 8 weeks and they were checked twice in the first week and then at least once a week until the 8th week in terms of growth monitoring. Growth detected media were stained with the Erlich Ziehl-Neelsen (EZN) staining method for the presence of acid-fast bacilli; the samples with acid-fast bacilli were reported as "There was growth in Löwenstein Jensen medium." and the diagnosis of tuberculosis was made in this way. At the end of the 8-week incubation period, the media without growth were stained with the Erlich Ziehl-Neelsen (EZN) staining method at the end and if acid-fast bacilli were not detected, it was reported as "No growth in Löwenstein-Jensen medium". Mycobacteria Polymerase Chain Reaction (PCR) was also used (Abbott Molecular, USA). The automated isolation kit belonging to Abbott company used for DNA isolation in accordance with the company instructions.

**Statistical Analysis;** The number of samples in the data is shown as n and calculated as a percentage. SPSS (Statistical Packages of Social Sciences, SPSS for Windows, Version 21.0, Chicago, IC, USA) package program was used for statistical analysis of the data.

**Ethical Consent;** Ethics committee approval was received for this study from the Non-Interventional Ethics Committee of Recep Tayyip Erdogan University. (Approval no: 2020/244). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

## Results

We studied a total of 95 HIV positive patients consist of 87(%91.6) males and 8(%8.4) females. The average age of our patients was determined as 45.1 years and the age ranges vary between 15 and 85 years. Our patients consist of 5 (5.2%) foreign nationals and 90 (94.8%) Turkish nationals.

When we analyze the distributions by years, 10 patients in 2014, 6 in 2015, 10 in 2016, 16 in 2017, 14 in 2018, 20 in 2019, 10 in 2020 and 9 in 2021 were diagnosed with HIV/AIDS.

Tuberculosis culture positivity was detected in 3 (3.1%) of 95 HIV-positive patients we examined. All 3 of the patients are male and 1 of them is a foreign national. Their ages were 31, 37 and 43 years. Two of these patients were diagnosed with tuberculosis in 2017 and one in 2019. Details are given in Table 1.

## Discussion

HIV and related AIDS is an important cause of morbidity and mortality affecting the whole world (10). HIV is mainly sexually transmitted, other modes of transmissions include intravenous drug use, mother-to-child transmission and blood transfusion (4). Sexually active young men constitute the most common group of the disease (11). HIV/AIDS, which has started to be limited by effective policies all over the world, cannot be limited to regions such as Sub-Saharan Africa and Asia, due to reasons such as the inability to prevent mother-to-child transmission, the inability to prevent HIV-positive mothers from breastfeeding their babies and the lack of access for everyone to diagnosis and treatment equally (3,5).

HIV can cause opportunistic infections by suppressing the immune system (12). In a study, the frequency of opportunistic infections was found to be 34% (13). While there are studies reporting tuberculosis (10,11,14) most frequently among opportunistic infections, there are also studies reporting candidiasis most frequently in our country. (4,8,15). The most common cause of death in HIV-positive individuals is tuberculosis (14). According to the report of the World Health Organization, 1.5 million tuberculosis patients compared to 2010 (1). The risk of developing active tuberculosis is 26 times higher in HIV-positive people compared to HIV-negative (17).

**Table 1.** Distribution of HIV patients and TB co-infection by gender

| | HIV positive patients | HIV/Tuberculosis co-infection |
|---|---|---|
| male | 87 (91.6%) | 3 (3.1%) |
| female | 8 (8.4%) | 0 |
| total | 95 (100%) | 3 (3.1%) |

Increased susceptibility to primary infection and reactivation of latent infection paves the way for the development of tuberculosis (18,19). The difference of tuberculosis from other opportunistic infections is that it can be seen at every stage of the disease, independent of CD4 T lymphocyte count (10). Although tuberculosis usually progresses with pulmonary involvement in HIV/AIDS patients, the incidence of extrapulmonary involvement increases as the CD4 T lymphocyte count decreases (20, 21). The interaction between tuberculosis and HIV is bidirectional; tuberculosis causes the disease to progress more rapidly by accelerating the replication of HIV (11). In order to prevent the synergistic effect of HIV and tuberculosis disease; HIV/AIDS patients should receive antiretroviral therapy regardless of CD4 T lymphocyte count and patients with latent tuberculosis infection should be identified and treated prophylactically (20).

Tuberculosis treatment does not differ in HIV-positive individuals, but rifabutin is preferred over rifampicin due to interaction with antiretroviral agents (10). Increase in anti-tuberculosis drug resistance complicates the management of tuberculosis treatment in HIV-positive patients (17). While there are studies reporting an increased risk of tuberculosis with multidrug resistance in patients with HIV, there are also studies that do not detect an increased risk (22). In a study of 5200 patients in Latvia, the risk of developing multidrug-resistant tuberculosis was found to be two times higher in HIV/AIDS-infected patients (17). Multidrug-resistant tuberculosis cases in HIV/AIDS patients are thought to be due to exogenous primary infection rather than reactivation of latent infection (23).

Atypical mycobacteria can also cause infections in HIV/AIDS patients (12). Some atypical mycobacteria that are potential pathogens in humans, especially *M. avium-intracellulare*, can lead to life-threatening infections with weakening of the immune system (24). In a study conducted in Ghana, the frequency of non-tuberculosis mycobacteria in HIV/AIDS patients was found to be 8% and *M. avium complex* was the most common among them (25).

In our retrospective study with 95 patients with confirmed HIV positivity, HIV-Tuberculosis coexistence was found to be 3.1%. Considering the studies conducted in our country, the incidence of tuberculosis was reported as 11% in İzmir, 25% in Trabzon, 5.7% in Adana and 4.6% in Kayseri (15,11,5,4). Considering the studies conducted around the world, it was reported as 4.2% from Canada, 7.2% from China, 18.9% from India and 28.6% from Ethiopia (14). In many studies, tuberculosis positivity was determined based on clinical, radiological and microbiological findings. It is thought that the reason behind the lower detection in our study than in other studies was due to our microbiological test evaluation which includes only culture and mycobacteria PCR positivity in the diagnosis of tuberculosis.

Tuberculosis is an important cause of mortality in HIV/AIDS patients. The management of HIV-tuberculosis coinfection becomes even more difficult due to their synergistic effect on each other. In this respect, it is vital to know the frequency of tuberculosis in HIV/AIDS patients, to receive appropriate antiretroviral treatment, to identify latent tuberculosis patients and to initiate prophylactic treatment. In addition, tuberculosis monitoring should be done in patients diagnosed with HIV starting from primary care.

**Conflicts of interest:** The authors have no conflicts of interest to declare.

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