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## OPPORTUNISTIC INFECTIONS IN HIV POSITIVE PATIENTS – A SINGLE CENTER EXPERIENCE

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**Abstract:** (acquired immune deficiency syndrome) is a late presentation of an infection with HIV. It is characterized by a clinical picture of various opportunistic infections and a decreasing number of CD4+ T lymphocytes. Opportunistic infections are diseases caused by microorganisms, which significantly more often affect immunocompromised people. GOAL Describe the clinical and laboratory characteristics of HIV- positive individuals with one or more opportunistic infections. To examine the frequency and prevalence of the most common opportunistic infections in patients with HIV infection who are on HAART and who are older than 45 years, compared to those who are younger than 45 years. A retrospective, comparative, clinical study was conducted that included hospitalized HIV-positive patients in the period from 1/1/2018 to 31/12/2022 at the Clinic for Infectious Diseases of the Clinical Center of the University of Sarajevo, Bosnia and Herzegovina. Out of a total of 50 patients in the sample, there were 42 men (84%) and 8 women (16%). 58% of patients were under 45 years of age, and 42% were over 45 years of age. The most prevalent infection was candidiasis 32%. A significant difference in the number of people with toxoplasmosis over the age of 45 with more cases, compared to the group of patients under the age of 45, was proven. No significant difference was found in the prevalence of tuberculosis and Pneumocystis pneumoniae infection between the two age groups of patients. Continuous control examinations allow easier and faster identification of opportunistic infections, even before the infection gives changed clinical parameters.

**Keywords:** HIV, AIDS, opportunistic infections, candidiasis, toxoplasmosis

### 1. INTRODUCTION

The human immunodeficiency virus or HIV virus is increasingly present both in the world and in Bosnia and Herzegovina. There are two types of HIV virus, HIV-1 and HIV-2. The HIV-1 virus is responsible for spreading the infection around the world, and the HIV-2 virus is associated with regions of West and Central Africa. HIV belongs to the genus Lentivirus, family Retroviridae (Fanales-Belasio, E. 2010).

According to the CDC, HIV infection without treatment goes through three stages: acute infection, chronic infection and AIDS. During an acute infection with the HIV virus, a large number of CD4+ T-lymphocytes are destroyed, and after an acute attack of the virus, the number of these cells in the body gradually decreases. The CD4/CD8 ratio is used to monitor disease progression (Krkić-Dautović, S. 2011). AIDS is the late stage of infection with the HIV virus, and is characterized by the clinical picture of opportunistic infections and a drop in the number of CD4+ T lymphocytes below 200/mm<sup>3</sup>.

The most significant opportunistic infections found in HIV positive patients are oropharyngeal candidiasis, Pneumocystis pneumonia caused by Pneumocystis jirovecii, tuberculosis and toxoplasmosis. Oral candidiasis is a common occurrence in HIV-positive patients, and in some it appears as the first sign of this infection. Candida albicans is most often isolated, which causes various clinical manifestations such as oropharyngeal and vulvovaginal candidiasis, the disseminated form of infection occurs less often (Pankhurst, C. L. 2013). Pneumocystis pneumonia (PCP) is a serious infection caused by the fungus Pneumocystis jirovecii. Most people come into contact with this fungus at some point in their lives. After infection, it remains in a latent form, and with immunocompromised

patients develop a severe form of pneumonia (Limper, A. 2017). In HIV-positive patients with an optimal CD4+ cell count, Mycobacterium tuberculosis causes the pulmonary form of tuberculosis, while extrapulmonary forms are more common in persons with advanced AIDS (Bell, L. 2018). Toxoplasma gondii is a protozoan that infects humans through contaminated food by ingesting cysts. In HIV-positive patients, a cerebral abscess often occurs with multifocal localization, which is why various forms of neurological symptoms occur (Dian, S. 2023).

HIV is transmitted sexually, through the use of infected needles by intravenous drug addicts, or accidentally by medical workers due to the manipulation of infected material, and by perinatal transmission from mother to child. Cases of infection through blood transfusions or transplanted organs have been reported very rarely.

The diagnosis of HIV-1 infection is based on the detection of specific antibodies, antigens, or both, and many commercial kits are available. Serological tests are mainly used for screening. A major advance was the availability of rapid tests for HIV-1 antibodies (Simon, V. 2006).

To date, more than twenty different substances have been licensed against HIV for formal therapy of the virus worldwide, which are now divided into six categories of therapeutic mechanisms. The six forms of therapeutic mechanisms are: fusion inhibitors, non-nucleoside reverse transcriptase inhibitors, nucleoside reverse transcriptase inhibitors, chemokine receptor antagonists, protease inhibitors, integrase inhibitors. A frequent form of HAART is the combination of NNRTI/NRTI with protease inhibitors with the aim of interfering with the proliferation of the HIV virus and RT activity (Lu, D. Y. 2018).

## 2. MATERIALS AND METHODS

A retrospective, comparative, clinical study was conducted that included hospitalized HIV-positive patients in the period from January 1, 2018 to December 31, 2022. at the Clinic for Infectious Diseases of the Clinical Center of the University of Sarajevo, Bosnia and Herzegovina.

The study included 50 respondents who had to meet certain criteria: HIV positive; that they have one or more opportunistic infections; that they are on HAART treatment and that they are hospitalized. They were then divided according to age into two groups: younger than 45 years and older than 45 years. The data were collected by reviewing medical histories and entered into Microsoft Excel for tabular presentation. Statistical analysis was performed in the IBM SPSS Statistics program (version 22.0). Data were analyzed using Student T test, Man Whitney U test and Chi square test. A P value of less than 0.05 was considered statistically significant.

## 3. RESULTS

Out of a total of 50 patients who participated in this study, there were 42 men and 8 women. According to age, all patients were classified into two groups, younger (29 patients) and older (21 patients) than 45 years old (Table 1).

**Table 1: Demographic characteristics of HIV-positive patients. Data are presented as absolute numbers (and percentages)**

	Females	Males
Gender	8 (16%)	42 (84%)
Age	< 45 years	>= 45 years
	29 (58%)	21 (42%)

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The research covered the period from 2018 to 2022, and the largest number of hospitalized patients was recorded in 2018 (16 patients), and then that number began to decrease (2019/10; 2020/9; 2021/4). In 2022, 11 patients were registered, which is almost three times as many patients as the year before (Table 2).

**Table 2: Number of hospitalized patients according to the years. Data are presented as absolute numbers (and percentages)**

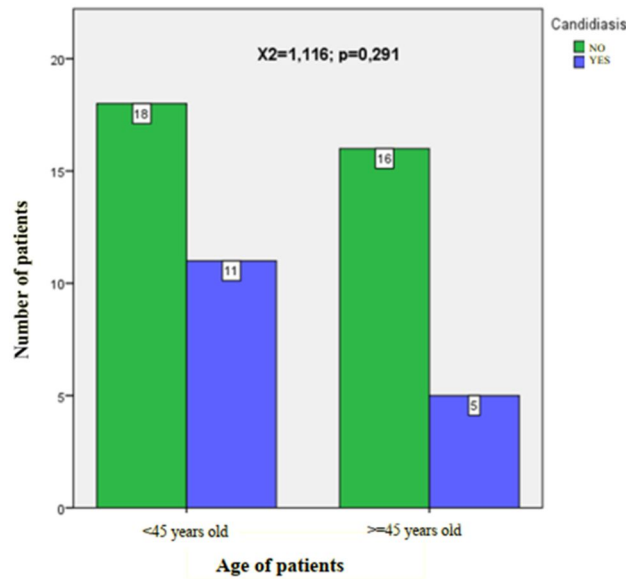
Years	2018	2019	2020	2021	2022
Number of patients	16 (32%)	10 (20%)	9 (18%)	4 (8%)	11 (22%)

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The primary causes of morbidity and mortality in persons infected with human immunodeficiency virus are opportunistic infections.

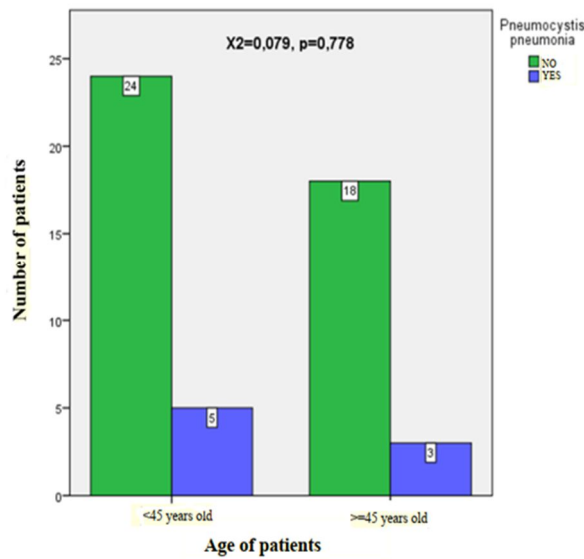
In our study, of all opportunistic infections, candidiasis was the most common in 16 patients (11 under 45 years of age, and 5 in the older group). A significantly lower number of Pneumocystis pneumonia was recorded, only in 8 patients (5 in those younger than 45, and 3 in the older group). The research results clearly show that no significant difference was found in the prevalence of candidiasis ( $\chi^2=1.116$ ;  $p=0.291$ ) and Pneumocystis pneumonia (PCP) ( $\chi^2=0.079$ ;  $p=0.778$ ) between the two age groups of patients (Figure 1 and Figure 2).

**Figure 1: Prevalence of candidiasis according to the age of the patients**



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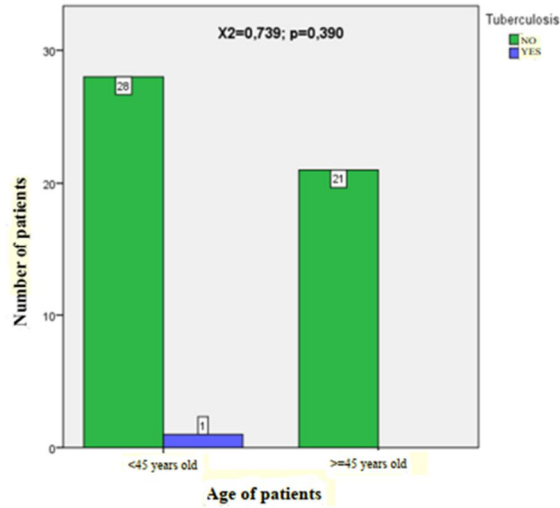
**Figure 2: Prevalence of infection with Pneumocystis pneumonia according to the age of the patients**



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Opportunistic tuberculosis infection was recorded in only one patient under the age of 45, so we can say that no significant difference in the prevalence of tuberculosis ( $\chi^2=0.739$ ;  $p=0.390$ ) was found between the two age groups of patients (Figure 3).

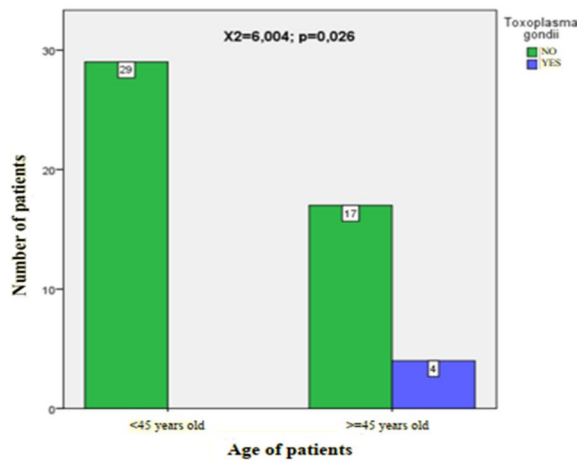
**Figure 3: Prevalence of tuberculosis according to the age of the patients**



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The obtained research results showed that *T. gondii* caused opportunistic infections only in 4 patients and only in the group over 45 years old ( $\chi^2=6.004$ ;  $p=0.026$ ), so we can safely say that there is an evident significant difference in the prevalence of toxoplasmosis between the groups patients younger than 45 years of age and the group of patients older than 15 years (Figure 4).

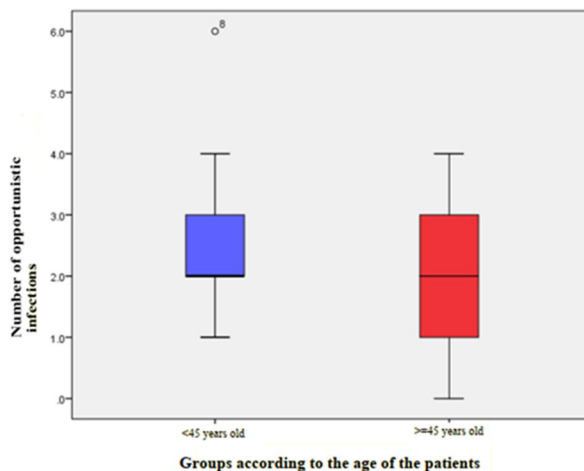
**Figure 4: Prevalence of infection with *T. gondii* according to the age of the patients**



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Based on the statistical processing of the data taken from the medical records, it can be said that no significant difference was found in the prevalence of opportunistic infections during hospitalization in patients according to age (Figure 5).

*Figure 5: Number of opportunistic infections diagnosed during hospitalization concerning age*



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#### 4. DISCUSSION

The study included 50 respondents, 84% men and 16% women. The gender structure of the population included in this study remains consistent with the data of the Institute for Public Health of the FBiH, in which we see that the newly diagnosed cases mostly represent men (ZZJZ FBiH, 2023). According to UNAIDS data, in 2018, 1,500,000 people infected with HIV lived in Eastern Europe and Central Asia, of which 520,000 were women, which is 34.6%, while 65.3% were men, and 150,000 newly diagnosed cases. The following year, 2019, there were 1,600,000 positive people, of which 550,000 were women, which is 34.3%, and 65.6% were men, and 140,000 were newly diagnosed. In 2020, the number of HIV-positive people in Eastern Europe and Central Asia was 1,700,000, women numbered 590,000 or 34.7%, and men 65.29%, while newly diagnosed patients numbered 150,000. In the fourth year of 2021, the data for this area are 1,800,000 HIV positive persons, 630,000 women or 35%, men 65% and newly diagnosed 150,000. Data for 2022 are not yet available. The total number of HIV-positive persons is growing exponentially in this area during the four presented years, and the number of infected men is continuously higher than that of women (UNAIDS, 2023).

The age structure of hospitalized patients in the five-year period shows 58% of respondents under 45 years of age, and 42% over 45 years of age. The study similar to ours has slightly different results regarding the age of the patients, In USA 2018, more than 64% of people living with HIV belonged to the 45-54 age group (28%), and people over 55 years of age accounted for 35% (Sullivan P., 2021). If we draw a parallel with this research, the total percentage of people over 45 years of age, which is 64%, is the majority, in contrast to our results, where the majority of HIV is present in people under 45.

The number of hospitalized patients showed a downward trend during the five-year period covered by the study, going from 32% in 2018, 20% in 2019, 18% in 2020, to a drop to 8% in 2021. In 2022, a slight increase in the number of hospitalized patients can be seen, which amounted to 22%. The sudden drop in the number of hospitalized patients in the given time period can be attributed to the global crisis with the COVID-19 pandemic and the mandatory isolation of the population. According to the researchers' review which included 6 different studies in the period from December 1, 2019 to October 25, 2021 in order to obtain relevant data related to HIV-positive persons who suffered from COVID-19, it turned out that a significantly larger number of persons who were HIV positive hospitalized in this period covered by the studies OR: 1.49; 95% CI 1.01– 2.21 (Danwang C., 2022). A significant difference can be seen in studies in the world where a two-year period provides data on a large number of hospitalized HIV-positive patients, in contrast to our area, where there was a tendency for the number of hospitalized patients to decrease during this time interval.

In our study, the prevalence of certain opportunistic infections among hospitalized patients was monitored. The largest number of infected patients had candidiasis, 32%, followed by PCP-Pneumocystis Pneumoniae, 16% of

respondents. A study from Nigeria, which included 17,312 respondents in a nine-year period, proved oral candidiasis as the most prevalent opportunistic infection (27.6%) (Akinyemi JO., 2017). Study from southwestern China, which included 12,612 subjects, proves in an eight-year period the highest incidence of pneumonia (39.8%), followed by tuberculosis (35.3%), and candidiasis (28.8%) (Meng S., 2023). The group of authors in a study, which includes 3,011,725 hospitalizations of HIV-positive patients in the USA in the period from 2002-2014, found a prevalence of 5% of PCP, and the percentage decreased from 6.7% in 2002 to 3.5% in 2014 (Elango K., 2022). Although PCP is in second place in terms of prevalence in our region according to the study, a high percentage of this disease is still present among the HIV positive population, compared to the rest of the world.

According to our results, a significant difference in the number of patients with toxoplasmosis older than 45 (4 patients, 8%) was demonstrated, compared to the group of subjects younger than 45 in whom this infection was not proven. The infection develops in immunocompromised patients with advanced disease, from a latent infection with toxoplasmosis, which gives us the information that there is a longer period of latency before the actual development of the manifest disease. In a study conducted in Germany, results showed out of 183 HIV-positive patients, 65 or 35.5% were IgG-seropositive for *Toxoplasma gondii*, with a seroconversion rate of 0.41 in a year. Before the development of highly active antiretroviral therapy, there was an incidence of 26-38% of activated cases of encephalitis caused by *Toxoplasma* in the USA. Based on this data, we can see how much the number of cases has decreased over the years, which can primarily be attributed to the prophylaxis that HIV-positive people use in the form of trimethoprim-sulfamethoxazole tablets (Marra CM., 2018).

In the entire examined sample, one can see a much higher number of hospitalized patients with 2 or more opportunistic infections, 74% (37 patients), compared to patients with one opportunistic infection, 26% (13 patients). However, statistical processing does not show a significant difference between the number of opportunistic infections of hospitalized patients between the two age groups, which would mean that younger and older patients more often present with more than 1 opportunistic infection.

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