

Opportunistic Infections Among Human Immunodeficiency Virus (HIV) Infected Patients in Turkey: A Systematic Review

Uğur Önal¹ , Halis Akalın¹ 

¹ Department of Infectious Diseases and Clinical Microbiology, Uludağ University School of Medicine, Bursa, Turkey

ABSTRACT

This study aimed to identify opportunistic infections among human immunodeficiency virus (HIV) infected patients in Turkey. Therefore, we conducted a systematic literature review of the studies published up to October 1, 2022, in the Pubmed, Web of Science (WoS), and ULAKBİM TR Dizin databases. We searched for medical subject headings (MeSH) terms of (HIV) OR (AIDS) OR (human immunodeficiency virus) AND (opportunistic infections) AND (Turkey). Fifty-five studies in Pubmed, 68 in WoS, and 212 in ULAKBİM TR Dizin were listed with these keywords. After removing duplicated studies, we included 22 original articles, two poster presentations, one short communication, one letter to the editor, and 17 case reports/series. Out of 1582 patients, we defined 788 patients (49.8%) as late presenters. In addition, we detected tuberculosis (286, 5.5%), candidal infections (207, 4%), and *Pneumocystis jirovecii* pneumonia (PCP) (113, 2.1%) as the most frequent opportunistic infections.

According to our analysis, late presentation is a major problem in our country, and more screening and sensitization campaigns should be carried out to ensure early diagnosis and earlier care of patients.

Keywords: HIV, AIDS, opportunistic infections, Turkey

INTRODUCTION

Patients with human immunodeficiency virus (HIV) infection or AIDS are more likely to have diseases that would not usually cause illness in a person with a healthy immune system, called opportunistic infections. Although significant efforts to improve progression along the HIV care continuum, there is still a considerable number of patients who initially present with advanced disease (1). In terms of opportunistic infections, significant differences exist in different parts of regions; for instance, tuberculosis case notification rates were 5-10 times higher in Eastern compared with Western Europe (2). Among 2953 patients with a new HIV diagnosis in our country between 2011

Corresponding Author:
Uğur Önal

E-mail:
uguronal@uludag.edu.tr

Received: January 19, 2023

Accepted: March 19, 2023

Published: June 23, 2023

Suggested citation:
Önal U, Akalın H. Opportunistic infections among human immunodeficiency virus (HIV) infected patients in Turkey: A systematic review. Infect Dis Clin Microbiol. 2023;2:82-93.

DOI: 10.36519/idcm.2023.214



Table 1. PICO framework.

Population	Intervention	Comparison	Outcome
HIV/AIDS patients	Assessment of clinical features and laboratory results	Basal CD4 ⁺ T lymphocyte count and HIV viral load	Presence of an opportunistic infection

and 2016, 29% of the cases presented with a CD4⁺ T lymphocyte count of >500 cells/mm³, whereas 46.7% presented with a count of <350 cells/mm³ (3). Similarly, among 693 patients diagnosed in 2011 and 2012, the proportion of patients presenting with advanced HIV disease was 30.6%, while 52.4% were late presenters (4).

This systematic review aimed to investigate opportunistic infections among HIV-infected patients in Turkey.

METHODOLOGY AND SEARCH STRATEGY

We searched the Pubmed, Web of Science (WoS), and ULAKBİM TR Dizin databases until October 01, 2022, for the medical subject headings (MeSH) terms of (HIV) OR (AIDS) OR (human immunodeficiency virus) AND (opportunistic infections) AND (Turkey). In addition, we reviewed the references of included articles.

Study Selection

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement in our study (5, 6). PRISMA flow diagram is presented in Figure 1. We extracted data onto a study-specific form, including the list of clinical questions under the PICO (Population-Intervention-Comparison-Outcome) framework format (Table 1). Studies were initially selected according to the title and abstract screening, and the full text of each potentially eligible study was obtained. Then we selected studies according to inclusion and exclusion criteria.

We included adult (>18-year-old) patients and the studies met all of the PICO components (Table 1). We excluded the studies which have only seroprevalence data rather than clinical features and laboratory results of the HIV/AIDS patients, the studies about HIV/AIDS patients with comorbidities or co-infections such as syphilis, hepatitis or malignancies, and the studies about opportunist-

tic infections such as pneumonia, diarrhea, wasting syndrome due to HIV, invasive cervical cancer, HIV-related encephalopathy, Kaposi sarcoma or lymphoma that were listed in Centers for Disease Control and Prevention (CDC) common opportunistic infections (7).

Synthesis of Results

All outcomes were analyzed, including the authors, study design, total number of patients, and the assessment of clinical features and laboratory results of the HIV/AIDS patients with an opportunistic infection. The results are also sorted by number of patients respectively. The reference lists of all relevant studies were also checked. Late presentation was defined as a CD4⁺ T lymphocyte count below 350

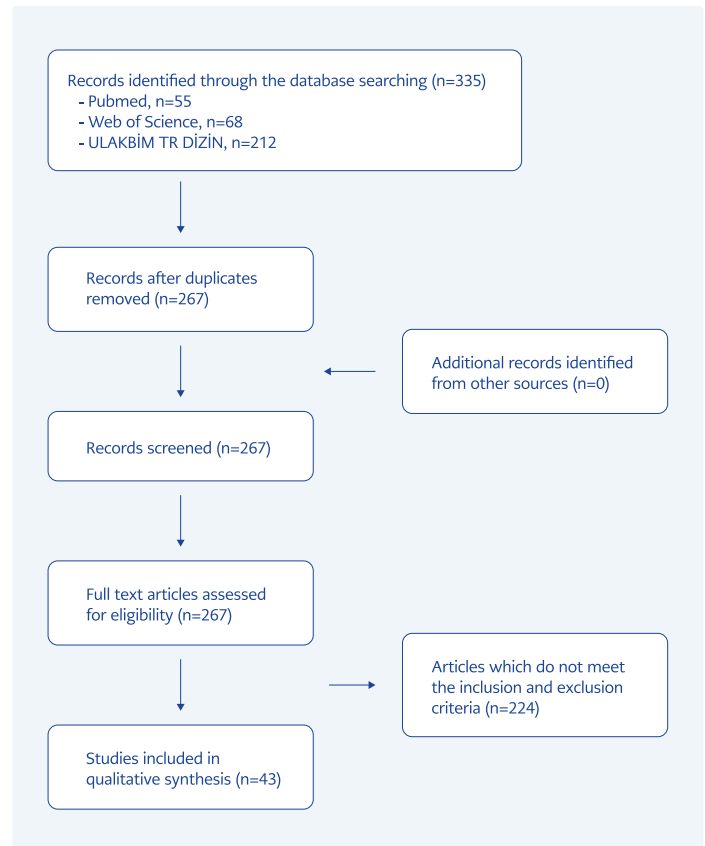
**Figure 1.** Flow diagram of study selection.

Table 2. Included studies.

Study	Years that study conducted	Study design	Number of patients with HIV/AIDS	Number of patients with late presenters among them n (%)	Number of patients with an opportunistic infection n (%) ***	Gender and age of the patients	Laboratory results of the patients with an opportunistic infection at presentation
Gümüser et al. 2018. (9)	1996-2015	Retrospective, multi-centered	1475	NA	66/1475 (4.4%) * - Tuberculosis (n=66) - CMV infection (n=3) - PCP (n=2) - Candidal infection (n=1) - Cryptococcal meningitis (n=1) - Toxoplasmosis (n=1)	Male (n=57, 86.4%) 38.7±9.2 years (mean age)	Number of patients with CD4+ T lymphocyte count >200/mm ³ at the time of tuberculosis diagnosis=20 (30.3%) Number of patients with HIV-1 RNA<100,000 (copies/ml) at the time of tuberculosis diagnosis=45 (68.2%)
Zerdali et al. 2021. (10)	2000-2016	Retrospective, single-centered	711	NA	38/711 (5.3%) * - Tuberculosis (n=38) - Candidal infection (n=28) - PCP (n=16) - CMV infection (n=6) - Cryptococcosis (n=1)	Male (n=34, 89.5%) 37.89 ± 11.45 years (mean age)	(Median) CD4+ T lymphocyte count (/mm ³)=181.5 (Median) HIV-1 RNA (copy/mL)=127,620
Şenoğlu et al. 2019. (11)	2015-2018	Retrospective, single-centered	629	239 (37.9%)	110/629 (17.4%) - Candidal infection (n=30) - Tuberculosis (n=21) - HSV infection (n=11) - PCP (n=9) - CMV infection (n=5) - Toxoplasmosis (n=3) - HPV infection (n=3) - Cryptococcal meningitis (n=2)	Male (n=43, 79.6%) 43.11 ± 9.16 years (mean age)	(Median) CD4+ T lymphocyte count (/mm ³)= 37 HIV-1 RNA viral load=NA
Kurtaran et al. 2015. (12)	1998-2015	Retrospective, single-centered	262	NA	15/262 (5.7%) * - Tuberculosis (n=15)	Male (n=13, 87%) 43 ± 10 years (mean age)	(Median) CD4+ T lymphocyte count at the time of tuberculosis diagnosis (/mm ³)= 266 HIV-1 RNA viral load=NA
Korkmaz et al. 2022. (13)	2010-2021	Retrospective, single-centered	240	116 (48.3%)	19/240 (8%) - Candidal infection (esophagitis) (n=6) - Tuberculosis (n=6) - PCP (n=3) - CMV infection (esophagitis/encephalitis/retinitis) (n=4) - PML (n=1)	NA	NA (CD4+ T lymphocyte count <200 for all of the patients with an opportunistic infection)
Yardımcı et al. 2015. (14)	2002-2012	Retrospective, single-centered	212	NA	89/212 (41.9%) - Candidal infection (oral/esophagitis) (n=19) - Tuberculosis (n=12) - Zona zoster (n=11) - PCP (n=5) - HSV infection (n=4) - Toxoplasma encephalitis (n=3) - Mycobacterium avium complex infection (n=2) - CMV infection (n=2)	Male (n=76, 85.4%) 40.8 ± 10.5 years (mean age)	(Median) CD4+ T lymphocyte count (/mm ³)=88 (Median) HIV-1 RNA (copy/ml)=545,000

Continue to Table 2

Aksu et al. 2021. (15)	1993-2015	Retrospective, single-centered	202	NA	18/202 (8.9%) - Candidal infection (oral) (n=3) - Tuberculosis (n=2) - PCP (n=2) - Cerebral toxoplasmosis (n=2) - CMV infection (n=1) - Isosporiasis (n=1) - Cryptosporidiosis (n=1)	NA	NA
Aydın-Altıntaş et al. 2010. (16)	2006-2010	Retrospective, single-centered	156	NA	10/156 (%6.4) - Tuberculosis (n=6) - PCP (n=4)	NA	NA
Ozdemir et al. 2018. (17)	2000-2015	Retrospective, single-centered	144	91 (63.1%)	23/144 (15.9%) - Tuberculosis (n=10) - HPV infection (n=8) - PCP (n=2) - Cryptococcal meningitis (n=1) - Zona zoster (n=1)	NA	NA
Karaosmanoglu et al. 2011. (18)	2006-2009	Retrospective, single-centered	136	94 (69%)	29/136 (21.3%) - Candidal infection (oral) (n=7) - PCP (n=4) - Tuberculosis (n=4) - HPV infection (n=2) - HSV infection (n=1) - Zona zoster (n=1)	NA	NA
Kaptan et al. 2011. (19)	1996-2009	Retrospective, single-centered	128	NA	43/92 (46.7%) -Candidal infection (oral/esophageal/perianal) (n=11) -Tuberculosis (n=10) -VZV infection (n=5) -CMV infection (n=3) -PCP (n=1) -Toxoplasmosis (n=1)	NA	NA
Ertunc et al. 2016. (20)	1998-2013	Retrospective, single-centered	115	NA	46/115 (40%) - Tuberculosis (n=19) - Zona zoster (n=3) - PCP (n=3) - Candidal infection (n=3) - CMV disease (n=3) - Cryptosporidium-related diarrhea (n=3) - PML (n=2) -Toxoplasmosis (n=1)	NA	NA
Uysal et al. 2017. (21)	2017 (Publication date)	Prospective randomized, cross-sectional prevalence study, single-centered	115	44 (38.2%)	24/115 (20.8%) - EBV (n=6) -Tuberculosis (n=5) - Cyclospora cayetanensis (n=3) - Cryptosporidium spp. (n=3) - Toxoplasmosis (n=2) - CMV infection (n=1)	Male (n=15, 83%) 38.3 years (mean age)	(Median) CD4+ T lymphocyte count (/mm ³) = 288 (Median) HIV-1 RNA (copy/mL)=19,119

Continue to Table 2

Celikbas et al. 2008. (22)	1993-2006	Retrospective, single-centered	97	65 (67%)	87/97 (89.6%) - Candidal infection (oral/esophagitis) (n=35) - Tuberculosis (n=11) - Cryptococcosis (n=3) - Zona zoster (n=4) - PCP (n=1) - HSV infection (n=1) - CMV infection (n=1)	NA	NA
Akin et al. 2012. (23)	1996-2012	Retrospective, single-centered	78	36 (46.2%)	23/78 (29.4%) - Candidal infection (oral) (n=11) - Tuberculosis (n=5) - Zona zoster (n=5) - Toxoplasmosis (n=3) - Cryptosporidium-related diarrhea (n=3) - CMV infection (n=2) - Salmonella bacteremia (n=2)	NA	NA
Erbay et al. 2009. (24)	2001-2008	Retrospective, single-centered	70	NA	33/70 (47.1%) - Tuberculosis (n=11) - PCP (n=8) - Candidal infection (oral) (n=7) - HSV infection (n=2) - Cryptococcal meningitis (n=2) - CMV infection (n=1) - Toxoplasmosis (n=1) - Pulmonary aspergillosis (n=1)	NA	NA
Alp et al. 2011. (25)	1992-2009	Retrospective, single-centered	68	NA	25/55 (45.5%) - Candidal infection (oral, hepatosplenic) (n=16) - PCP (n=8) - Tuberculosis (n=6) - CMV infection (n=4) - HSV infection (n=3) - HPV infection (n=2) - Zona zoster (n=2) - Cryptosporidiosis (n=1) - Isosporiasis (n=1)	NA	NA
Kurt et al. 2020. (26)	2000-2018	Retrospective, single-centered	54	NA	31/54 (57.4%) - Candidal infection (oral, esophagitis, vaginitis) (n=6) - HPV infection (n=4) - Zona zoster (n=2) - PCP (n=1)	NA	NA

Continue to Table 2

Kurtaran et al. 2006. (27)	1997-2005	Retrospective, single-centered	46	NA	20/46 (43%) - Tuberculosis (n=11) - Candidal infection (oral) (n=9) - HSV infection (n=3) - CMV infection (pneumonia/retinitis) (n=2) - Cryptosporidiosis (n=2) - Isosporiasis (n=1) - Toxoplasmosis (retinitis) (n=1) - PCP (n=1) - HPV infection (n=1) - Cryptococcal meningitis (n=1)	NA	NA
Punar et al. 2000. (28)	1991-1997	Retrospective, single-centered	44	NA	17/44 (39%) - Candidal infection (primary opportunistic infection among 17 patients)	NA	NA
Kaya et al. 2011. (29)	1999-2009	Retrospective, single-centered	36	23 (63.8%)	22/36 (61%) -Tuberculosis (n=11) - Candidal infection (oral, esophagitis) (n=5) - PCP (n=2) - Giardiasis (n=1) - Cryptosporidiosis (n=1)	NA	NA
Atalay et al. 2022. (30)	2003-2018	Retrospective, single-centered	31	15 (48.3%)	17/31 (54.7%) - Tuberculosis (n=7) - PCP (n=5) - Cerebral toxoplasmosis (n=3) - Cryptococcal meningitis (n=2)	Male (n=27, 90%) 47 years (mean age)	(Mean) CD4+ T lymphocyte count (/mm ³)=241 (Median) HIV-1 RNA (copy/mL): NA
İnci et al. 2021. (31)	2012-2019	Retrospective, single-centered	28	28 (100%)**	28/28 (100%) ** - PCP (n=28)	Male (n=18, 78.6%) 45.7 years (mean age)	(Median) CD4+ T lymphocyte count (/mm ³)=162.2 (Median) HIV-1 RNA (copy/mL): NA
Fisgin et al. 2009. (32)	2003-2008	Retrospective, single-centered	27	16 (59.2%)	6/27 (22.2%) - Tuberculosis (n=6) - PCP (n=4) - Candidal infection (oral) (n=3) - Cryptococcal meningitis (n=1)	NA	NA
Akalin et al. 2005. (33)	1997-2003	Retrospective, single-centered	21	NA	19/21 (90.4%) - Candidal infection (oral, esophagitis) (n=6) - Zona zoster (n=4) - PCP (n=1) - CMV infection (n=1) - Tuberculosis (n=1) - Toxoplasmosis (n=1) - Salmonellosis (n=1)	NA	NA

Continue to Table 2

Case reports/ series (34-51)	1998-2022 (Publication year)	-	21	21 (100%)	21/21 (100%) - Toxoplasmosis (n=6) - Tuberculosis (n=3) - Isosporiasis (n=1) - PCP (n=3) - Aspergillosis (n=3) - Salmonellosis (n=2) - HSV infection (n=1) - Mucormycosis (n=1) - Candidal infection (n=1) - CMV infection (n=2) - Cryptococcal meningitis (n=1)	Male (n=17, 81%) 38.5 years (mean age)	(Median) CD4+ T lymphocyte count (/mm ³)=49 (Median) HIV-1 RNA (copy/mL)=231,300
---------------------------------	------------------------------------	---	----	--------------	---	--	--

CMV: Cytomegalovirus, PCP: *Pneumocystis jirovecii* pneumonia, HSV: Herpes simplex virus, HPV: Human papillomavirus, PML: Progressive multifocal leukoencephalopathy, EBV: Epstein-Barr virus, NA: Not available.

* Only patients with tuberculosis coinfection were involved, ** Only patients with PCP coinfection were involved, ***some patients have more than one infection

Table 3. Most frequent opportunistic infections among HIV/AIDS patients.

Opportunistic infections	n (%)	(Median) CD4+ T lymphocyte count (/mm ³)	(Median) HIV-1 RNA (copy/mL) levels at presentation	Types of infection
Tuberculosis	286 (5.5)	181.5 [¶]	127,620 ^{¶¶}	Pulmonary (n=140) Extrapulmonary (n=54) Miliary (n=19) Unspecified (n=73)
Candidal infections	207 (4)	NA	NA	Orophageal (n=108) Esophageal (n=22) Unspecified (n=77)
PCP	113 (2.1)	162.2 ^{¶¶¶}	692,500 ^{¶¶¶}	Pneumonia (n=113)
CMV infection	41 (0.8)	NA	NA	Esophagitis (n=2) Encephalitis (n=1) Retinitis (n=2) Pneumonia (n=1) Unspecified (n=35)
Varicella-zoster virus infection	37 (0.7)	NA	NA	Herpes zoster (n=37)
Toxoplasmosis	28 (0.5)	NA	NA	Cerebral toxoplasmosis (n=27) Retinitis (n=1)
HSV	26 (0.5)	NA	NA	Unspecified (n=26)
Cryptococcus infection	15 (0.3)	NA	NA	Cryptococcal meningitis (n=14) Unspecified (n=1)

CMV: Cytomegalovirus, PCP: *Pneumocystis jirovecii* pneumonia, VZV: Varicella-zoster virus, HSV: Herpes simplex virus.

¶ Only studies with the reference number (10, 12, 34, 37, 39) were included.

¶¶ Only studies with the reference number (10, 34, 39) were included.

¶¶¶ Only studies with the reference number (31, 37, 40, 42) were included.

cells/μL or presenting with an AIDS-defining event (8). The study was designed as a systematic review, so no ethical committee permission was needed.

Clinical and Research Consequences

Fifty-five studies in Pubmed, 68 in WoS, and 212 in ULAKBİM TR Dizin were listed with these keywords.

After removing duplicated studies, we included 22 original articles, two poster presentations, one short communication, one letter to the editor, and 17 case reports/series (Table 2). A total of 5146 patients with HIV/AIDS diagnoses were investigated among 43 relevant studies. Opportunistic infections were diagnosed in 879 out of 5146 patients (17%) with



HIV/AIDS. The most frequent opportunistic infections were tuberculosis (286, 5.5%), candidal infections (207, 4%), and *Pneumocystis jirovecii* pneumonia (PCP) (113, 2.1%) (Table 3). Out of 1582 patients, we defined 788 patients (49.8%) as late presenters.

Among the studies, overall mortality rates of all patients with HIV/AIDS ranged between 0.8% to 36%. In terms of tuberculosis, the overall mortality was calculated as 18% in patients with AIDS and tuberculosis (9, 10, 12, 34, 37, 39). In addition, the median CD4⁺ T lymphocyte count was 181.5/mm³, and the median HIV-1 RNA was 127,620 copy/mL among AIDS patients with tuberculosis (Table 3). Furthermore, the overall mortality was 32.2% in patients with AIDS and PCP (32, 36, 39, 40).

Among tuberculosis patients, the clinical forms were pulmonary (140, 49%), extrapulmonary (54, 19%), miliary (19, 7%), and unspecified (73, 25%). On the other hand, among patients with candidal infections, the clinical forms were orophageal (108, 52%), esophageal (22, 11%), and unspecified (77, 37%) (Table 3).

DISCUSSION

Although the frequency of opportunistic infections is decreasing with the prophylactic and antiretroviral treatments in patients with HIV/AIDS, HIV-related opportunistic infections still remain as an important cause of mortality and morbidity, especially for low and middle-income countries (52). Due to poor immunological status, people living with HIV (PLWH) get an increasing number of severe illnesses called opportunistic infections. Furthermore, late-diagnosed individuals with HIV have higher mortality than those diagnosed earlier, resulting in significant costs to health systems. Therefore, screening for opportunistic infections such as tuberculosis and cryptococcus, the leading causes of death among PLWH, is crucial (53). We believe that our study is the first systematic review highlighting the opportunistic infections in HIV/AIDS patients from our country regarding the clinical and laboratory results of the patients.

An updated target of 95-95-95 was released by the Joint United Nations Programme on HIV and AIDS (UNAIDS) for a pathway to ending AIDS, which is

consisted of 95% of all PLWH will know their disease, 95% of all people with HIV diagnosis will receive antiretroviral therapy (ART) and 95% of all people receiving ART will have viral suppression by 2025 (54). According to UNAIDS reports, the global percentages were 84% of PLWH who knew their disease; among those, 87% were on ART, and 90% of those on ART had achieved virological suppression at the end of 2020 (55). Gokengin reviewed the targets regarding HIV infection in our country and mentioned that almost half of the patients were late presenters because of the lack of screening strategy for target populations and detection at the time of differential diagnosis (56). Between 2011 and 2016, the predicted rate of undiagnosed infection in our country was 59% and 52%, according to the HIV-TR cohort and the Ministry of Health data, respectively (57). In addition, Mete et al. also reported a cohort from İstanbul, which represents only 13% of PLWH in Turkey, and they showed that 72% and 74% of all HIV patients were diagnosed in 2016 and 2017, respectively (58).

Several important factors affect UNAIDS's targets, such as geographic differences, income inequality, and epidemiological diversities. Late presentation is still one of the major issues in Europe, Central Asia, and migrant populations. Many PLWH (especially older people, heterosexual men, people living in low HIV prevalence areas, and migrants) remain unaware of the disease, and the percentages of undiagnosed patients range from 20% in Denmark, Sweden, and Slovakia to as high as 50% in Poland and Latvia in Europe (2). Also, in the center of Europe, the percentage of late diagnoses was recorded as high as 52.8%, which varied across transmission categories and age groups (59).

Miranda et al. analyzed 907 HIV patients in Portugal, finding that 50.6% of the patients were late presenters (60). In addition, Belat et al. also found that the pooled prevalence of late presentation to HIV/AIDS care was 52.89% in Ethiopia, reviewing eight studies with 7568 participants (61). Kostaki et al. investigated the reasons for late presentation in Greece, and they demonstrated that older age, heterosexual transmission risk group, and more recent diagnosis were associated with increased risk for late presentation (62). Similar to these findings, in our country, Karaosmanoglu et al. showed that

nearly half of the patients who presented late were elderly, less educated, married, and heterosexual patients having more HIV-related diseases on admission (63).

Similarly, our study found that the percentage of late presenters was 49.8%. We believe that the major factor affecting the development of opportunistic infections with high mortality rates is late presentation in our country. Although the majority of studies included in our review were reported in the pre-pandemic period in our study, there were also reported cases that highlight the risk of misdiagnosing opportunistic infections for SARS-CoV-2 infection; difficulties in the management of opportunistic infections in a limited time to access healthcare services represent an important issue for the late presenters (64).

Szumlik et al. investigated a total number of 1313 HIV cases newly diagnosed in Poland, and they showed that PCP and esophageal candidiasis were the most common indicator diseases among AIDS cases in 2016 (65). In addition, Ali et al. found the opportunistic infection rate as 32.3% among 167 HIV patients in Qatar. They also found the most common opportunistic illness as PCP, followed by cytomegalovirus (CMV) retinitis and tuberculosis (66). Regarding opportunistic infections in small cities like Midwest Santa Catarina, Amorim et al. analyzed the records of 143 HIV/AIDS patients from Brazil, and they found that opportunistic infections were present in 38.5% of the patients (4.9% of the patients had tuberculosis) (67). On the other hand, Chepkondol et al. investigated 500 HIV-positive patients in Kenya and found the opportunistic infection rate as high as 78.8%.

Additionally, they found the most common opportunistic infection as tuberculosis with 35%, and patients with lower CD4⁺ T lymphocyte counts of 0-199 and 200-349 had two times greater odds of having tuberculosis than those with CD4⁺ T lymphocyte count of ≥ 500 (68). Among the 18 countries, including Turkey, under the program of stopping tuberculosis in the WHO European Region, the incidence of tuberculosis was estimated as 52.5 per 100,000 people (69). Wallenfels et al. investigated 88 HIV-positive patients in the Czech Republic diagnosed with tuberculosis between 2000-2020 and found that the

median CD4⁺ T lymphocyte count was 91.5 /mm³ at the time of tuberculosis diagnosis (70). Our study also found the most common opportunistic infection as tuberculosis (5.5%), and the median CD4⁺ T lymphocyte count was 181.5 /mm³.

Our study has some limitations. First of all, most of the reviewed studies were retrospective and single-center studies. Thus, none of the included studies contains specific data from big cohorts and may not reflect the real epidemiology of opportunistic infections among PLWH in Turkey. Second, the results of these studies had heterogeneities regarding the different opportunistic infections with the viral loads and CD4⁺ T lymphocyte counts. Thus, a limited number of studies were included with the descriptive data of the specified opportunistic infection. Third, even though we tried to include all of the published studies, including case reports, the patients with comorbidities or co-infections such as syphilis, hepatitis, or malignancies were excluded. In addition, although opportunistic infections were defined as infections that occur more frequently or severely in people with immunosuppression, some included studies reported only opportunistic infections, which were stated in AIDS-defining conditions in the CDC list (71). On the other hand, Croxford et al. recently published an update about late presentation, and they mentioned that patients with evidence of recent infection, a last negative HIV test within 12 months of diagnosis, or clinical evidence of acute infection, and also previously diagnosed patients should not be considered as late presentation (72). The vast majority of included studies had not excluded recent infections when calculating late presenters as a limitation of our study.

In conclusion, tuberculosis, candidal infections, and PCP are the most common opportunistic infections among HIV/AIDS patients in our country. Prevention of opportunistic infections involves a multidisciplinary approach that includes infectious disease specialists, primary care physicians, and social workers for support. In our country, late presentation of the patients is one of the major problems, and more screening and sensitization campaigns should be carried out, such as increasing the anonymous and free HIV testing services throughout the country and education on HIV/AIDS in schools.

Ethical Approval: N.A.

Informed Consent: N.A.

Peer-review: Externally peer-reviewed

Author Contributions: Concept – H.A.; Design – U.Ö., H.A.; Supervision – H.A.; Data Collection and/or Processing – U.Ö.;

Analysis and/or Interpretation – U.Ö., H.A.; Literature Review – U.Ö.; Writer – U.Ö.; Critical Reviews – H.A.

Conflict of Interest: The authors declare no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

- Summers NA, Armstrong WS. Management of Advanced HIV Disease. *Infect Dis Clin North Am.* 2019;33(3):743-67. [\[Cross-Ref\]](#)
- Mussini C, Antinori A, Bhagani S, Branco T, Brostrom M, Dedes N, et al; European Aids Clinical Society. European AIDS Clinical Society Standard of Care meeting on HIV and related coinfections: The Rome Statements. *HIV Med.* 2016;17(6):445-52. [\[CrossRef\]](#)
- Erdinc FS, Dokuzoguz B, Unal S, Komur S, Inkaya AC, Inan D, et al; Multicentric Hiv Study Group. Temporal trends in the Epidemiology of HIV in Turkey. *Curr HIV Res.* 2020;18(4):258-66. [\[CrossRef\]](#)
- Korten V, Gökengin D, Fincanci M, Yıldirmak T, Kes NU, Fişgin NT, et al. Outcomes of initial antiretroviral treatment (ART) among recently diagnosed HIV patients in HIV-TR cohort, 2011-2012. *J Int AIDS Soc.* 2014;17(4 Suppl 3):19678. [\[CrossRef\]](#)
- Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ.* 2009;339:b2700. [\[CrossRef\]](#)
- Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097. [\[CrossRef\]](#)
- AIDS and opportunistic infections. [Internet]. Atlanta: Centers for Disease Control and Prevention (CDC). [cited February 02, 2023]. Available from: <https://www.cdc.gov/hiv/basics/living-withhiv/opportunisticinfections.html>
- Antinori A, Coenen T, Costagiola D, Dedes N, Ellefson M, Gatell J, et al; European Late Presenter Consensus Working Group. Late presentation of HIV infection: a consensus definition. *HIV Med.* 2011;12(1):61-4. [\[CrossRef\]](#)
- Gümüşer F, Altınkaynak M, Yıldız-Sevgi D, Altuntaş-Aydın Ö, Mete B, Gündüz A, et al. Human immunodeficiency virus and tuberculosis coinfection: clinical features and predictors of mortality. *Turk J Med Sci.* 2018;48(3):503-8. [\[CrossRef\]](#)
- Zerdali E, Nakir İY, Sürme S, Sayılı U, Yıldırım M. Predictors for tuberculosis co-infection in people living with HIV/AIDS. *Afr Health Sci.* 2021;21(3):995-1002. [\[CrossRef\]](#)
- Şenoğlu S, Yeşilbağ Z, Karaosmanoğlu HK, Altuntaş-Aydın Ö. Epidemiological differences and risk factors for hospitalization in people living with HIV in Istanbul, Turkey. *Int J STD AIDS.* 2019;30(13):1284-9. [\[CrossRef\]](#)
- Kurtaran B, Nazik S, Aslıhan U, Inal AS, Kömür S, Kuşçu F, et al. Evaluation of Hiv infection and tuberculosis concomitance. *Mediterranean Journal of Infection Microbes and Antimicrobials.* 2015;4:4. [\[CrossRef\]](#)
- Korkmaz N, Şentürk GÇ, Şibar EG, Civelek Eser F, Duman Z. [Risk factors in individuals living with HIV presenting late diagnosis and the epidemiology of the opportunistic infections, our 10 years long experience]. *Flora.* 2022;27(2):268-75. Turkish. [\[CrossRef\]](#)
- Yardımcı AC, Fincancı M. [The relationship between the opportunistic diseases and viral load and CD4+ T cell count in patients with HIV infection]. *Klimik Derg.* 2015;28(1):28-34. Turkish. [\[CrossRef\]](#)
- Aksu M, Şaşmaz CT, Togay A, Aksu T. Evaluation of epidemiological and clinical features of 202 HIV/AIDS cases diagnosed in Mersin. *ESTUDAM Public Health Journal.* 2021;6(1):34-45. [\[CrossRef\]](#)
- Aydın-Altuntas O, Karaosmanoğlu Kumbasar H, Korkusuz R, Nazlıcan O. Clinical profile of HIV/AIDS patients admitted to a tertiary outpatient clinic in Istanbul, Turkey. *Journal of the International AIDS Society.* 2010;13(Suppl 4):P220. [\[CrossRef\]](#)
- Ozdemir B, Yetkin MA, Bastug A, But A, Aslaner H, Akinci E, et al. Evaluation of epidemiological, clinical, and laboratory features and mortality of 144 HIV/AIDS cases in Turkey. *HIV Clin Trials.* 2018;19(2):69-74. [\[CrossRef\]](#)
- Karaosmanoğlu HK, Altuntaş-Aydın O, Nazlıcan O. Profile of HIV/AIDS patients in a tertiary hospital in Istanbul, Turkey. *HIV Clin Trials.* 2011;12(2):104-8. [\[CrossRef\]](#)
- Kaptan F, Örmən B, Türker N, El S, Ural S, Vardar I, et al. [Retrospective evaluation of 128 cases infected with human immunodeficiency virus]. *Turkiye Klinikleri J Med Sci.* 2011;31(3):525-33. Turkish. [\[CrossRef\]](#)
- Ertunc B, Kaya S, Koksall I. Clinico-epidemiological analysis of HIV/AIDS patients. *Eurasian J Med.* 2016;48(3):157-61. [\[CrossRef\]](#)
- Uysal HK, Adas GT, Atalık K, Altıparmak S, Akgül O, Sarıbas S, et al. The Prevalence of *Cyclospora cayetanensis* and *Cryptosporidium* spp. in Turkish patients infected with HIV-1. *Acta Parasitol.* 2017;62(3):557-64. [\[CrossRef\]](#)
- Celikbas A, Ergonul O, Baykam N, Eren S, Esener H, Eroğlu M, et al. Epidemiologic and clinical characteristics of HIV/AIDS patients in Turkey, where the prevalence is the lowest in the region. *J Int Assoc Physicians AIDS Care (Chic).* 2008;7(1):42-5. [\[CrossRef\]](#)

- 23 Akin H, Bölük G, Akalın H, Oğuz-Ayarcı A, Kazak E, Aslan E, et al. [HIV/AIDS: Retrospective analysis of 78 cases]. *Klimik Derg.* 2012;25(3):111-6. Turkish. [\[CrossRef\]](#)
- 24 Erbay A, Kayaaslan B, Akıncı E, Öngürü P, Eren SS, Gözel G, et al. [Evaluation of epidemiological, cilinical and laboratory features of HIV/AIDS cases]. *Flora.* 2009;14(1):36-42. Turkish.
- 25 Alp E, Bozkurt I, Doğanay M. [Epidemiological and clinical characteristics of HIV/AIDS patients followed-up in Cappadocia region: 18 years experience]. *Mikrobiyol Bul.* 2011;45(1):125-36. Turkish.
- 26 Kurt EK, Kandemir B, Erayman I, Bulut R, Bitirgen M. [Evaluation of patients infected with human immunodeficiency virus followed in our clinic]. *Flora.* 2020;25(2):161-71. Turkish. [\[CrossRef\]](#)
- 27 Kurtaran B, Taşova Y, Saltoğlu N, İnal AS, Candevir A, Aksu HSZ, et al. [A retrospective assessment of individuals infected with HIV]. *Flora.* 2006;11(3):147-53. Turkish.
- 28 Punar M, Uzel S, Cemil EH, Çağatay AA, Özsüt H, Eraksoy H, et al. [HIV infection. An analysis of 44 cases]. *Klimik Derg.* 2000;13(3):94-7. Turkish.
- 29 Kaya S, Yılmaz G, Erensoy Ş, Arslan M, Köksal İ. [Retrospective analysis of 36 HIV/AIDS cases]. *Klimik Derg.* 2011;24(1):11-6. Turkish. [\[CrossRef\]](#)
- 30 Atalay S, Albayrak-Uçak H. Mortality causes of HIV-positive patients: Evaluation of 31 cases in Turkey. *J Tepecik Educ Res Hosp.* 2022;32(3):350-6. [\[CrossRef\]](#)
- 31 İnci A, Konyalı AR, San ND. [The evaluation of the factors affecting mortality in cases of HIV-infected *Pneumocystis jirovecii* pneumonia]. *Klimik Derg.* 2021;34(2):109-12. Turkish. [\[Cross-Ref\]](#)
- 32 Taşdelen-Fışgın N, Tanyel E, Sankaya-Genç H, Tülek N. [Evaluation of HIV/AIDS cases]. *Klimik Derg.* 2009;22(1):18-20. Turkish.
- 33 Akalın H, Heper Y, Yılmaz E, Kazak E, Oral B, Mistik R, et al. [Short communication: Retrospective analysis of 21 HIV/AIDS cases]. *Mikrobiyol Bul.* 2005;39(3):339-43. Turkish.
- 34 Yakar Hİ, Sargın F, Kanbay A, Ceylan E. A case of pulmonary tuberculosis in a HIV-positive patient. *Medeniyet Med J.* 2017;32(3):198-201. [\[CrossRef\]](#)
- 35 Demirel A, Ozaras R, Hakkı E, Mete B, Yemisen M, Mert A. HIV infection presented with hemiplegia: three cases of toxoplasma encephalitis. *The Medical Bulletin of Haseki.* 2013;51(2):70-6.
- 36 Uysal HK, Oner YA, Akgül Ö, Yaşar KK, Gursoy S, Çağlar S. Isospora belli associated recurrent diarrhea in a patient with AIDS. *International Journal of Infectious Diseases.* 2016;45(Suppl 1):363-4. [\[CrossRef\]](#)
- 37 Saymaz ZT, Özkara Ş. A case of suspected COVID-19 identified with AIDS, PCP and Tuberculosis. *Respiratory Case Reports.* 2022;11(2):102-6. [\[CrossRef\]](#)
- 38 Çoban E, Serindağ H, Gül ZB, Özerden M, Soysal A. Transvers myelitis due to HSV-2 Infection in an undiagnosed HIV positive patient. *Turk J Neurol.* 2021;27:91-4. [\[CrossRef\]](#)
- 39 Kostakoğlu U, Dalmanoğlu E, Yıldız İE, Özdemir-Al S, Yaşar F, Ertürk A. Fever of unknown origin: Tuberculosis and HIV coinfection. *Klimik Derg.* 2019;32(2):213-6. [\[CrossRef\]](#)
- 40 Alkan-Çeviker S, Günel Ö. [A case of AIDS diagnosed incidentally in the presence of bilateral pneumonia]. *Flora.* 2019;24(1):67-72. Turkish. [\[CrossRef\]](#)
- 41 Çakmak PG, Kutlu SS. Neurotoxoplasmosis in a patient with acquired immunodeficiency syndrome: Magnetic resonance and magnetic resonance spectroscopy findings. *İstanbul Med J.* 2019;20(2):159-62. [\[CrossRef\]](#)
- 42 Kayık SK, Acar E, Memis L. *Pneumocystis jirovecii* pneumonia in newly diagnosed HIV infection: A challenging case report. *Turk Patoloji Derg.* 2020;1(1):246-50. [\[CrossRef\]](#)
- 43 Kutlu M, Ergin C, Bir F, Hilmioglu-Polat S, Gümrall R, Necan C, et al. Pulmonary mucormycosis due to *Lichtheimia ramosa* in a patient with HIV infection. *Mycopathologia.* 2014;178(1-2):111-5. [\[CrossRef\]](#)
- 44 Demiraslan H, Alabay S, Kilic AU, Borlu M, Doganay M. Cutaneous candidiasis caused by *Candida glabrata* in a HIV/AIDS patient. *Int J STD AIDS.* 2013;24(9):753-5. [\[CrossRef\]](#)
- 45 Arikan S, Uzun O, Cetinkaya Y, Kocagöz S, Akova M, Unal S. Primary cutaneous aspergillosis in human immunodeficiency virus-infected patients: two cases and review. *Clin Infect Dis.* 1998;27(3):641-3. [\[CrossRef\]](#)
- 46 Ozdemir D, Sahin I, Sencan I. Salmonella arizonae bacteraemia in a Turkish patient with AIDS but no history of contact with reptiles. *Scand J Infect Dis.* 2006;38(3):237-8. [\[CrossRef\]](#)
- 47 Oguz-Ayarcı A, Mistik R, Akin H, Hakyemez B, Helvacı S, Akalın H, et al. Cerebral toxoplasmosis as the presenting manifestation of HIV/AIDS. *Klimik Derg.* 2011;24(1):62-4. [\[CrossRef\]](#)
- 48 İnal AS, Nazik S, Candevir A, Kurtaran B, Taşova Y, Aksu HSZ. [Toxoplasma encephalitis: an HIV/AIDS patient with cerebral mass]. *Cukurova Med J.* 2017;42(1):184-8. [\[CrossRef\]](#)
- 49 Çağatay AA, Deniz R, Gözükcük R, Özbek E, Başaran S. Acute hepatitis and pancytopenia related to non-typhoidal salmonella infection in a human immunodeficiency virus-infected patient. *Int J STD AIDS.* 2019;30(10):1034-6. [\[CrossRef\]](#)
- 50 Tanyel E, Güngör L, Sankaya H, Tülek N, Leblebicioğlu H. [Disseminated cryptococcosis in an AIDS patient]. *Turk Journal of Infection.* 2006;20(1):69-71.
- 51 Bahar AR, Bahar Y, Uysal S, Sönmezer MÇ, Gülmez D, Çelik ÖS, et al. A multidisciplinary approach to opportunistic infections in a late-presenter person living with HIV. *Mediterr J Infect Microb Antimicrob.* 2022;11:23. [\[CrossRef\]](#)
- 52 Jung IY, Rupasinghe D, Woolley I, O'Connor CC, Giles M, Azwa RI, et al; IeDEA Asia-Pacific. Trends in mortality among ART-treated HIV-infected adults in the Asia-Pacific region between 1999 and 2017: results from the TREAT Asia HIV Observational Database (TAHOD) and Australian HIV Observational Database (AHOD) of IeDEA Asia-Pacific. *J Int AIDS Soc.* 2019;22(1):e25219. [\[CrossRef\]](#)
- 53 Prabhu S, Harwell JI, Kumarasamy N. Advanced HIV: diagnosis, treatment, and prevention. *Lancet HIV.* 2019;6(8):e540-e51. [\[CrossRef\]](#)
- 54 Frescura L, Godfrey-Faussett P, Feizzadeh A A, El-Sadr W, Syarif O, Ghys PD; on and behalf of the 2025 testing treatment target Working Group. Achieving the 95 95 95 targets for all: A pathway to ending AIDS. *PLoS One.* 2022;17(8):e0272405. [\[CrossRef\]](#)

- 55 Confronting inequalities: Lessons for pandemic responses from 40 years of AIDS. *Global AIDS Update 2021*. Geneva: Joint United Nations Programme on HIV and AIDS (UNAIDS). [cited February 02, 2023]. Available from: https://www.unaids.org/sites/default/files/media_asset/2021-global-aids-update-en.pdf
- 56 Gökengin D. [HIV infection in Turkey: How close are we to the target?]. *Klimik Derg.* 2018;31(1):4-10. Turkish. [\[CrossRef\]](#)
- 57 Gökengin D, Cimen C, Cagatay A, Gencer S, Akalın H, Ceran N, et al. Abstracts of the 17th European AIDS Conference: HIV cascade of care in Türkiye: data from the HIV-TR cohort. *HIV Med.* 2019;20(S9):112-3. [\[CrossRef\]](#)
- 58 Mete B, Gunduz A, Bolukcu S, Karaosmanoglu HK, Yildiz D, Koç MM, et al. HIV care in Istanbul, Turkey: How far is it from the UNAIDS 90-90-90 targets? *Int J STD AIDS.* 2019;30(13):1298-1303. [\[CrossRef\]](#)
- 59 HIV/AIDS surveillance in Europe 2022 – 2021 data [Internet]. Copenhagen: WHO Regional Office for Europe. [cited February 02, 2023]. Available from: https://clinicalinfo.hiv.gov/sites/default/files/glossary/Glossary-English_HIVinfo.pdf
- 60 Miranda AC, Miranda M, Pingarilho M, Pimentel V, Torres J, Peres S, et al. Determinants of HIV-1 late presentation in a cohort of Portuguese HIV-1 patients. *AIDS Res Hum Retroviruses.* 2021;37(11):846-51. [\[CrossRef\]](#)
- 61 Belay GM, Endalamaw A, Ayele AD. Late presentation of HIV positive adults and its predictors to HIV/AIDS care in Ethiopia: a systematic review and meta-analysis. *BMC Infect Dis.* 2019;19(1):534. [\[CrossRef\]](#)
- 62 Kostaki EG, Limnaios S, Adamis G, Xylomenos G, Chini M, Mangafas N, et al. Estimation of the determinants for HIV late presentation using the traditional definition and molecular clock-inferred dates: Evidence that older age, heterosexual risk group and more recent diagnosis are prognostic factors. *HIV Med.* 2022;23(11):1143-52. [\[CrossRef\]](#)
- 63 Karaosmanoğlu HK, Mete B, Gündüz A, Altuntaş-Aydın Ö, Sargin F, Sevgi DY, et al. Late presentation among patients with human immunodeficiency virus infection in Turkey. *Cent Eur J Public Health.* 2019;27(3):229-34. [\[CrossRef\]](#)
- 64 Brugnaro P, Morelli E, Cattelan F, Petrucci A, Colombo F, Caputo S, et al. The serious threat of late presenters HIV-infected patients in the context of the COVID-19 pandemic. *Infez Med.* 2022;30(1):119-23. [\[CrossRef\]](#)
- 65 Szmulik K, Zakrzewska K, Niedźwiedzka-Stadnik M, Rosińska M. HIV and AIDS in Poland in 2016. *Przegl Epidemiol.* 2018;72(2):175-87.
- 66 Ali M, Razok A, Gassim M, Elmaki N, Goravey W, Alkhal A, et al. HIV and AIDS-defining opportunistic illnesses in the state of Qatar: A cohort population-based retrospective study covering 17 years (2000-2016). *Ann Med Surg (Lond).* 2022;78:103842. [\[CrossRef\]](#)
- 67 Amorim LT, Schlemper Junior BR. HIV/AIDS in small cities in Midwest Santa Catarina, south of Brazil: Clinical and epidemiological aspects, opportunistic infections. *Rev Soc Bras Med Trop.* 2019 ;52:e20180430. [\[CrossRef\]](#)
- 68 Chepkondol GK, Jolly PE, Yatich N, Mbowe O, Jaoko WG. Types and prevalence of HIV-related opportunistic infections/conditions among HIV-positive patients attending Kenyatta National Hospital in Nairobi, Kenya. *Afr Health Sci.* 2020;20(2):615-24. [\[CrossRef\]](#)
- 69 Kraef C, Bentzon A, Skrahina A, Mocroft A, Peters L, Lundgren JD, et al. Improving healthcare for patients with HIV, tuberculosis and hepatitis C in eastern Europe: a review of current challenges and important next steps. *HIV Med.* 2022;23(1):48-59. [\[CrossRef\]](#)
- 70 Wallenfels J, Malý M. Incidence of tuberculosis among HIV-positive persons in the Czech Republic between 2000 and 2020. *Epidemiol Mikrobiol Imunol.* 2022;71(2):93-101
- 71 Glossary of HIV/AIDS-related terms [Internet]. Department of Health and Human Services (HHS). [cited February 02, 2023]. Available from: https://clinicalinfo.hiv.gov/sites/default/files/glossary/Glossary-English_HIVinfo.pdf
- 72 Croxford S, Stengaard AR, Brännström J, Combs L, Dedes N, Girardi E, et al; EuroTEST HIV Late Diagnosis Definition Working Group. Late diagnosis of HIV: An updated consensus definition. *HIV Med.* 2022 Dec;23(11):1202-8. [\[CrossRef\]](#)