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Posted Date: 18 July 2025

doi: 10.20944/preprints2025071512.v1

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Article

A 30-Year Epidemiological Study of Opportunistic Fungal Infections in People Living with HIV in Greece: Associations with Demographic Characteristics and Immune Status

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Abstract

Background/Objectives: Opportunistic fungal infections are frequently observed in patients living with HIV and contribute significantly to morbidity, mortality, and hospitalization rates within this population. The aim of this study is to note the prevalence of dermatological manifestations related to fungal infections among HIV-positive patients and its correlation with demographic, other clinical characteristics and immune status of the participants. **Methods:** A retrospective review was conducted on a cohort of 2,500 patients living with HIV that have been treated at the Infectious Diseases Unit of "Andreas Syggros" Hospital for Skin and Venereal Diseases from 1988 to 2017. Data from patients diagnosed with opportunistic fungal infections were analyzed. Patients were either antiretroviral therapy (ART)-naïve or already under treatment. Recorded fungal infections were correlated with epidemiological data and CD4+ cell counts. **Results:** Opportunistic fungal infections were documented in 859 patients (34.36%), with a male predominance. Candidiasis was the most frequently reported condition, with higher prevalence among female patients. Lower CD4+ counts were significantly associated with increased risk of cryptococcal meningitis, esophageal candidiasis, Pneumocystis jirovecii pneumonia (PJP), and oral candidiasis, whereas higher CD4+ counts were observed in individuals with dermatophytosis, onychomycosis, and pityriasis/tinea versicolor. **Conclusions:** Opportunistic fungal infections remain prevalent among HIV-positive individuals, particularly in immunocompromised patients. CD4+ cell counts serve as crucial diagnostic and prognostic markers for clinical outcomes in HIV patients, underscoring their role in disease monitoring and management.

Keywords: opportunistic fungal infections; HIV; PLHIV; CD4+ cell counts; Greece

Introduction

Infection with Human Immunodeficiency Virus (HIV) is a sexually transmitted infection that compromises the immune system and increases susceptibility to life-threatening opportunistic infections, including fungal infections. HIV infection remains a global public health concern, having caused an estimated 40.4 million deaths up-to-date, affecting not only human health but economic development and social stability as well [1–5]. According to the World Health Organization (WHO), approximately 39.9 million people were living with HIV in 2023, with 1.3 million new cases recorded that year [1].

Greece has experienced a significant burden of HIV/AIDS, with 20.627 HIV cases reported to the National Public Health Organization (N.P.H.O.) by December 31, 2023, while the number of deaths among AIDS cases came up to 2.186 [6]. Of these cases, 82.1% (16.937) were males, whereas the predominant age group at the time of diagnosis was that of 30-39 years old, followed by the age group of 40-49 years old [6]. The most frequently reported mode of HIV transmission is unprotected male-to-male sexual contact (47.9% of HIV cases diagnosed in Greece by 31/12/2023) [6]. The introduction of highly active antiretroviral therapy (HAART) in 1996 has markedly improved survival rates and quality of life of people living with HIV (PLHIV), reducing AIDS-related mortality, while delaying clinical progression of the infection [7–9].

Opportunistic fungal infections are common in PLHIV, due to immunosuppression, having a significant impact on their higher morbidity and mortality and hospitalization rates [10,11]. Dermatological disorders such as skin eruptions (e.g. xerosis, acne), opportunistic fungal infections (e.g. Herpes simplex, Varicella-Zoster, Candidiasis, Dermatophytosis, Histoplasmosis, Cryptococcosis, Pneumocystis), AIDS-related malignancies (e.g. Kaposi's sarcoma) and antiretroviral therapy (ART)-associated drug eruptions are among the most common presentations of HIV/AIDS [12]. Some of them, such as oral-esophageal Candidiasis, Pneumocystis jirovecii pneumonia, may also serve as markers of the progression of the infection [12].

This study aims to assess the prevalence of dermatological manifestations of fungal infections in a large cohort of PLHIV that have received treatment in the Special Infectious Diseases Unit of “Andreas Syggros” University Hospital in Athens over a 30-year period and to correlate these infections with demographic and other clinical and immunological parameters.

Materials and Methods

Study Design and Participants/Subjects

This monocentric, retrospective, descriptive cohort study analyzed medical records of 2,500 PLHIV that received treatment in the Special Infectious Diseases Unit of “Andreas Syggros” University Hospital, a tertiary care referral center for dermatological disorders in Athens, from 1988 to 2017. This outpatient department specializes in diagnosing, monitoring and treating HIV patients. Data from individuals diagnosed with fungal infections were extracted and analyzed. Participants were either ART-naïve (initiating therapy after being diagnosed in the hospital) or already receiving treatment. Data collection was based on medical records, including demographic information (e.g. gender, age), ART history, laboratory results, and clinical outcomes. The study included patients diagnosed with a fungal infection within the first two months of HIV diagnosis.

Various clinical specimens (including oral swabs, sputum, and skin/nail) were collected according to the patient's clinical presentation. Specimens were collected under aseptic conditions and processed in the microbiology laboratory for fungal infection confirmation.

Assessment of Immune Status

CD4+ cell count was determined for each patient enrolled in our study by flow cytometry using the fluorescent activated cell sorter BD FACS Count system (Becton Dickinson) as per the manufacturer's instructions. HIV viral RNA quantification was determined by the polymerase chain reaction (PCR).

Data Analysis

Data were analyzed using SPSS software (version 28.0.1.1, IBM, Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized using means and standard deviations. Chi-square tests and t-tests were used to compare categorical and continuous variables, respectively. Statistical significance was set at $p \leq 0.05$.

Results

From 1988 to 2017, among 2,500 HIV-positive outpatients in the Special Infectious Diseases Unit of the “Andreas Syggros” University Hospital in Athens, 859 (34.36%) presented with fungal infections. Of the total of 859 patients, 744 were males and 115 females. Gender disparity was observed, participants were predominantly male (86.6%, n=744), with a median age of 34 years (range: 15-79 years). Patients aged 30-39 years accounted for the highest proportion (40.74%), followed by those aged 20-29 years (26.9%), 40-49 (18.74%), the >50 (12.92%) and finally the <20 (0.7%) age group. (Table 1). From 1988 to 1997, 503 HIV-infected patients with fungal infections were treated, while the number of the new infections diagnosed significantly decreased during 1998-2007, with 230 new cases and from 2008 to 2017 only 126 new cases were recorded (Table 1).

Table 1. Demographic characteristics of the HIV/AIDS patients.

Characteristics	Category	No. of cases
Gender	Male	744 (86.6%)
	Female	115 (13.4%)
Age	<20 y	6 (0.7%)
	20-29 y	231 (26.9%)
	30-39 y	350 (40.74%)
	40-49 y	161 (18.74%)
	>50 y	111 (12.92%)
Calendar years	1988-1997	503 (58.5%)
	1998-2007	230 (26.8%)
	2008-2017	126 (14.7%)

Clinical Characteristics

Individuals were diagnosed with HIV/AIDS through clinical symptoms or routine screening (Table 2). The most common reasons for diagnosis were the following: 11.99% (N=103) due to HIV positivity in spouses or sexual partners, 11.64% (N=100) screened at their own request, 6.05% (N=52) presented fever, 5.47% (N=47) after blood donation, 3.96% (N=34) after diagnosis with Kaposi's sarcoma (KS), 3.49% (N=30) diagnosed with PCP (Pneumocystis jirovecii pneumonia), 2.68% (N=23) lymph nodes, 2.56% (N=22) Candida, 2.56% (N=22) Syphilis and with 2.21% (N=19) genital warts.

Table 2. Reasons that lead to HIV/AIDS diagnosis.

	N	%
HIV infected sexual partners	103	11.99%
On their own initiative	100	11.64%
Fever	52	6.05%
Blood donation	47	5.47%
Kaposi's sarcoma (KS)	34	3.96%
PCP (Pneumocystis jirovecii pneumonia)	30	3.49%
Lymph nodes	23	2.68%
Candida	22	2.56%
Syphilis	22	2.56%
Genital warts	19	2.21%
VZV (Varicella Zoster Virus)	13	1.51%
Pulmonary infections	12	1.40%
Diarrhea	11	1.28%
Pre-operational check	11	1.28%
Imprisonment	11	1.28%
Pregnancy	11	1.28%
Weight loss	8	0.93%

Fatigue	8	0.93%
HSV	8	0.93%
TBC	8	0.93%
Neurological complications	6	0.70%
Check up	6	0.70%
Atypical rash	5	0.58%
Dermatological manifestations	5	0.58%
Folliculitis	5	0.58%
Psoriasis	5	0.58%
Other	99	11.52%

Furthermore, in the majority of the cases, patients were diagnosed, through a mycological study, with various fungal opportunistic infections, cutaneous as well as systemic (Table 3). The clinical evaluation of the patients showed that oral candidiasis (thrush) was the most common and recurrent fungal infection occurring in 72.6% of the cases, followed by Pneumocystis pneumonia (21.1%), Esophageal candidiasis (9.8%), Pityriasis/tinea versicolor (9.4%), Onychomycosis (due to Trichophyton rubrum) (8.7%), Plantar epidermophytosis (3.4%) and Cryptococcal meningitis (1.0%).

Table 3. Cutaneous and systemic fungal infections in PLHIV.

Types of fungal infections	Cases	%
<u>Cutaneous Fungal Infections</u>		
Oral Candidiasis (Thrush)	624	72.6%
Pityriasis/Tinea Versicolor	81	9.4%
Onychomycosis (due to Trichophyton rubrum)	75	8.7%
Plantar Epidermophytosis	35	4.1%
Tinea Capitis (due to Microsporum canis)	1	0.1%
<u>Systemic Fungal Infections</u>		
PJP	181	21.1%
Esophageal Candidiasis	84	9.8%
Cryptococcal Meningitis	9	1.0%
Pulmonary Candidiasis	1	0.1%
Candidal Meningitis	1	0.1%

Besides the fungal infections, 269 individuals (31.31%) in our cohort study also presented various comorbidities. The most prevalent comorbidities amongst the HIV patients were: Depressive disorder (3.95%), duodenal ulcer (2.56%), psychosis-schizophrenia (2.21%), drug addiction (1.98%), allergic rhinitis (1.86%) and psoriasis (1.63%) (Table 4).

Table 4. Comorbidities in PLHIV.

Comorbidities	Cases	%
Depressive disorder	34	3.95%
Duodenal ulcer	22	2.56%
Psychosis - Schizophrenia	19	2.21%
Drug addiction	17	1.98%
Allergic rhinitis	16	1.86%
Psoriasis	14	1.63%
Alcoholism	13	1.51%
Nephrolithiasis	12	1.40%

Diabetes	12	1.40%
Hypertension	10	1.16%
Asthma	10	1.16%
Other	90	10.48%

Furthermore, to explore the impact of gender on the prevalence of cutaneous and systemic fungal infections in PLHIV, chi-square test of independence was performed. The results indicate statistically significant differences between males and females in four cases. Gender differences were noted, with males exhibiting a higher prevalence of PJP ($\chi^2(1)=6.35$, $p=0.012$) and pityriasis/tinea versicolor ($\chi^2(1)=5.411$, $p=0.020$), while females had higher rates of oral candidiasis and Tinea capitis ($\chi^2(1)=10.127$, $p=0.001$ and $\chi^2(1)=6.534$, $p=0.011$, respectively) (Table 5).

Table 5. Cutaneous and systemic fungal infections in PLHIV by gender.

	Males				Females				χ^2	p
	No		Yes		No		Yes			
	N	%	N	%	N	%	N	%		
<u>Cutaneous Fungal Infections</u>										
Oral Candidiasis (Thrush)	217	29.2	527	70.8	17	14.9	97	85.1	10.127	0.001
Pityriasis/Tinea Versicolor	667	89.7	77	10.3	110	96.5	4	3.5	5.411	0.020
Onychomycosis	676	90.9	68	9.1	107	93.9	7	6.1	1.115	0.291
Plantar Epidermophytosis	711	95.6	33	4.4	112	98.2	2	1.8	1.816	0.178
Tinea Capitis	744	100	0	0	113	99.1	1	0.9	6.534	0.011
<u>Systemic Fungal Infections</u>										
PJP	576	77.5	167	22.5	101	87.8	14	12.2	6.350	0.012
Esophageal Candidiasis	668	89.8	76	10.2	106	93.0	8	7.0	1.144	0.285
Cryptococcal Meningitis	735	98.8	9	1.2	115	100	0	0	1.406	0.236
Pulmonary Candidiasis	743	99.9	1	0.1	115	100	0	0	0.155	0.694
Candidal Meningitis	742	99.9	1	0.1	115	100	0	0	0.155	0.694

Impact of HAART Therapy

Following HAART introduction in 1996, the incidence of systemic infections (PJP and cryptococcal meningitis) and mucocutaneous infections (oral and esophageal candidiasis) significantly declined (Table 6). While, onychomycosis, plantar epidermophytosis, and pityriasis/tinea versicolor showed increased prevalence post-1996 (Table 6). However, dermatophytosis, tinea capitis, cryptococcal meningitis, pulmonary candidiasis and candidal meningitis demonstrated no statistically significant differences before and after the introduction of HAART (Table 6).

Table 6. Occurrence of cutaneous and systemic fungal infections during 1988-1995 and 1996-2017.

Opportunistic fungal infections	Opportunistic fungal infections 1988-1995		Opportunistic fungal infections 1996-2017		χ^2	p
	v	%	v	%		
<u>Cutaneous fungal infections</u>						
Oral Candidiasis (thrush)	331	80.15	292	65.47	23.174	< .00001
Pityriasis/Tinea Versicolor	20	4.84	61	13.68	19.5965	< .00001
Onychomycosis	22	5.53	53	11.98	11.5678	0.000671
Dermatophytosis	26	6.30	49	10.99	1.4833	0.223263
Plantar Epidermophytosis	7	1.69	28	6.28	11.524	0.000687
Tinea Capitis	1	0.24	0	0	1.084	0.298
<u>Systemic fungal infections</u>						
PJP	131	32.11	50	11.21	54.229	< .00001
Esophageal Candidiasis	56	13.56	28	6.28	12.8859	0.000331
Cryptococcal Meningitis	6	1.45	3	0.67	1.2588	0.261876
Pulmonary Candidiasis	1	0.24	0	0	1.084	0.298
Candidal Meningitis	0	0	1	0.22	0.924	0.337

CD4+ Cell Counts and Viral Load Status in Relation to Fungal Infections

CD4+ cell counts were available for all patients, ranging from undetectable to 2345. Mean CD4+ cell counts (cells/mm3) in relation to opportunistic fungal infections, cutaneous and systemic, are summarized in Table 7. Lower CD4+ counts correlated significantly with oral candidiasis (t=4.273, p=0.000), PJP (t=4.572, p=0.000), esophageal candidiasis (t= 3.382, p=0.001), and cryptococcal meningitis (t= 4.799, p=0.001), while higher CD4+ counts were associated with dermatophytosis (t= -2.730, p=0.008), pityriasis/tinea versicolor (t= -3.252, p=0.001) and onychomycosis (t= -3.050, p=0.003) (Table 7).

Meanwhile, viral load metrics did not appear to be associated with the prevalence of fungal infections. Viral load status fluctuates significantly depending on the stage of the infection and whether or not treatment is being taken.

Table 7. CD4+ dynamics in cutaneous and systemic fungal infections in HIV/AIDS patients.

Opportunistic fungal infections	No		Yes		t	P-value
	Mean	SD	Mean	SD		
<u>Cutaneous fungal infections</u>						
Oral Candidiasis (thrush)	390.6	370.5	275.8	288.6	4.273	0.000
Pityriasis/Tinea Versicolor	296.0	314.7	415.8	321.7	-3.252	0.001
Onychomycosis	297.3	316.3	411.7	309.6	-3.050	0.003
Dermatophytosis	293.7	292.8	449.2	485.0	-2.730	0.008
Plantar Epidermophytosis	304.4	316.5	390.6	330.5	-1.381	0.177
Tinea Capitis	307.7	317.2	4.0	NA	NA	NA
<u>Systemic fungal infections</u>						
PJP	329.6	324.0	220.2	272.6	4.572	0.000
Esophageal Candidiasis	315.9	323.7	220.8	232.9	3.382	0.001
Cryptococcal Meningitis	308.9	317.8	111.9	118.7	4.799	0.001
Pulmonary Candidiasis	307.1	317.1	37.0	NA	NA	NA
Candidal Meningitis	307.1	317.1	46.0	NA	NA	NA

Note: NA denotes not available. * CDC stages of HIV infection: Stage 1 (>500 cells/μl), Stage 2 (200-499 cells/μl), Stage 3 (<200 cells/μl).

Discussion

Over the past 30 years, HIV/AIDS has remained a major public health challenge in Greece, posing significant challenges to the Greek healthcare system, leading to increased morbidity and mortality rates. Although the introduction of HAART improved considerably the life expectancy and quality of life of PLHIV, reducing AIDS-related deaths and transforming HIV into a manageable chronic condition, however, the disease remains a public health issue of utmost significance [13]. AIDS reporting system started in Greece in 1984 (Ministerial Decision A1/6122/19-9-1986) and HIV case reporting in 1998 (Ministerial Decision B1/5295/7-8-1998) [6]. For surveillance and trend analysis purposes, HIV infections before 1998 have been retrospectively reported to the Hellenic Center for Diseases Control and Prevention (HCDCP) in collaboration with the HIV/AIDS Reference Centers and the Infectious Disease Units/Outpatients Clinics for HIV (+) individuals [6].

Our findings highlight the significant burden of opportunistic fungal infections among PLHIV, emphasizing their correlation with immune status. We have shown that HIV related opportunistic fungal infections were observed in 859/2500 (34.36%) of the treated patients, a considerably higher rate than in the world's general population where it is estimated to be 20%–25% [14], with candidiasis predominating. Gender disparity and male predominance ($\chi^2(1)=460.6$, $p<0.0001$) were observed throughout the study period (1988–2017), with 744 (86.6%) affected men and 115 women (13.4%). Indeed, globally, the vast majority of new HIV cases occur in men through homosexual transmission [1]. Likewise, in the United States in 2022, 67% (21,400 of the 31,800) of all new HIV cases were among gay and bisexual men, while only 22% infections (2100 men and 4900 women) accounted among people who reported heterosexual transmission and 7% (2300 cases) occurred in individuals who inject drugs [15].

PLHIV as the disease progresses, due to their immunosuppressed state, are at a higher risk of developing both common and opportunistic fungal infections than the general population, which are manifested depending on the severity of the suppression of CD4+ counts [16]. In our study, the main clinical symptoms that lead to the diagnosis of the patients with HIV/AIDS were fever, Kaposi's sarcoma, PJP, lymph nodes, candidiasis, syphilis and genital warts. All participants were diagnosed with fungal infections the first 2 months after their HIV/AIDS diagnosis, while the most common and recurrent infections among the participants were: oral candidiasis (72.6%), PJP (21.1%), esophageal candidiasis (9.8%), pityriasis/tinea versicolor (9.4%), onychomycosis (8.7%) and plantar epidermophytosis (4.1%), which is in line with other analyses [17–19].

Male patients showed a higher prevalence of PJP and pityriasis/tinea versicolor, while female patients were more likely to present with oral candidiasis and tinea capitis. This gender disparity may be attributed to differences in immune response, exposure risks, and health-seeking behaviors. Gender-based differences in fungal infection prevalence have been observed in multiple studies. In a USA retrospective cross-sectional study of all hospital admissions with a primary discharge diagnosis of HIV between 2002 and 2014 males had a higher prevalence of PJP compared to females (70% vs. 30%, $p < 0.0001$), where the majority of the patients were Blacks, followed by Caucasians and Hispanics [20]. In another study that aimed to characterize the clinical and immunologic impact that PJP and its treatment have in patients with advanced HIV (CD4+ count ≤ 100 cells/ μ L) starting ART, scientists concluded that males were more likely to have been diagnosed with PJP than females (odds ratio [OR], 2.68; 95% CI, 1.34–5.38; $P = .004$) [21]. Moreover, researchers in an Ethiopian study assessing the prevalence and associated factors of pityriasis/tinea versicolor among patients attending Dermatovenereology clinic at the University of Gondar Comprehensive Specialized Hospital Magnitude (for any reason) concluded that the odds of experiencing pityriasis versicolor among male patients were 4.19 (AOR = 4.19, 95%CI: 1.92, 9.14) times higher than female patients [22]. However, another cross-sectional, descriptive study in South Africa, examining the prevalence and spectrum of dermatoses in a sample of 970 HIV individuals resulted that there is no significant association between skin diseases (infectious or non-infectious dermatoses) and patient demographics (gender and ethnicity) or HIV-disease characteristics (CD4+ cell count, viral load and duration of antiretroviral therapy [23].

Furthermore, our observation of increased oral candidiasis and tinea capitis prevalence among females is in accordance with Nigerian and Indian studies. Awoyeni et al (2017) [24], investigated 154 HIV patients in Nigeria and detected *Candida* species in 39.5% of the patients. The mean age of HIV individuals with candidiasis was 40.4 years with the age group of 29-39 years to be the most affected (49.2%). The prevalence of candidiasis was significantly higher in females (55, 90.2%) compared to males (6, 9.7%) ($P = 0.042$) [24]. Similarly, Lar et al (2012) [25] have also demonstrated a higher carriage rate of candidiasis in women (7.26%) than in men (2.41%). In the other hand, Suryana et al (2020) [26] in a case control study conducted at Wangaya hospital in Indonesia from March 1, 2016 and July 30, 2019, which included 448 participants (207 HIV patients and 241 controls) has shown that oral candidiasis, besides acting as an early marker for people living with HIV/AIDS, is associated with the male sex ($p=0.002$; OR=1.88; 95% CI: 1.26–2.80). In addition, Rao et al (2012) [27] also found that male HIV individuals in Southern India had a higher risk of oral lesions, especially oral candidiasis, than females (18.8% males 10.3% females, $P = 0.00$).

Infectious microbial agents (bacteria, fungi, parasites or viruses) causing opportunistic fungal infections may be asymptomatic or symptomatic in healthy individuals and usually self-limiting. However, in immunocompromised individuals and individuals with malignancy, these infections can result in a severe life-threatening disease [28]. The introduction of HAART therapy has significantly altered the epidemiology of opportunistic fungal infections in PLHIV. While systemic infections such as PJP and cryptococcal meningitis have declined [11,29], superficial infections like onychomycosis and pityriasis/tinea versicolor have shown an increase, possibly due to prolonged survival and immune reconstitution. Similar trends have also been reported in South African and Brazilian cohorts [5,23].

CD4+ count and viral load are two critical markers used in the management of HIV patients to assess the health of the immune system and the effectiveness of antiretroviral therapy. CD4+ counts provide information on the overall immune function of an individual with HIV, where lower CD4+ levels suggest increased susceptibility to opportunistic fungal infections. CD4+ count below 200 cells/mm³ is well reported in numerous studies as a significant risk factor for developing infections such as orofacial manifestations (with oral candidiasis to be the most common condition), tuberculosis, PJP and cryptococcal meningitis [30–32]. In accordance with the previous studies, we have also shown that PLHIV with lower levels of CD4+ cell counts are more likely to be diagnosed with cryptococcal meningitis ($t= 4.799$, $p=0.001$), esophageal candidiasis ($t= 3.382$, $p=0.001$), PJP ($t=4.572$, $p=0.000$) and oral candidiasis ($t=4.273$, $p=0.000$). Meanwhile, our findings suggest that increased levels of CD4+ cell counts (>400 cells/mm³) are associated with the presentation of dermatophytosis ($t= -2.730$, $p=0.008$), onychomycosis ($t= -3.050$, $p=0.003$) and Pityriasis/Tinea versicolor ($t= -3.252$, $p=0.001$). Similarly, Khat et al (2020) reported statistically significant association between elevated CD4 counts (>400 cells/mm³) and the presence of dermatophytosis and pityriasis versicolor [33].

Furthermore, VL metrics in our study did not show a strong correlation with fungal infections in our cohort, suggesting that immune suppression, rather than viral replication, plays a primary role in the development of opportunistic fungal infections. This finding is in consistence with several other researchers such as Lu et al (2012) who demonstrated low CD counts (<200 cells/mm³) and elevated HIV viral load (from 500 to 5.28×10^7 copies/mL) in 50 AIDS patients with PJP [34] and Williams et al (1999) who denoted that individuals with lower median CD4 cell counts and higher median RNA copies were associated with significantly higher risk of developing specific opportunistic fungal infections (PJP, CMV and MAC) [35].

Our study reinforces the importance of CD4+ monitoring, as lower counts were strongly associated with severe opportunistic fungal infections. Despite this, HIV viral loads did not show a clear correlation with fungal infection prevalence, suggesting that immune suppression rather than viral replication plays a crucial role in opportunistic fungal disease development. Future studies should explore targeted antifungal prophylaxis strategies and optimize ART regimens to further reduce fungal infection rates and improve patient outcomes [36–38].

Conclusions

HIV related opportunistic fungal infections were observed in 34.36% of the treated patients in our cohort, with male predominance. Candidiasis was the most commonly reported manifestation, highly prevalent in women. Immune status was closely related to several fungal infections. Cryptococcal meningitis, esophageal candidiasis, oral candidiasis and PJP predominantly occur in individuals with CD4+ counts below 200 cells/mm³, while increased CD4+ levels were found in individuals with dermatophytosis, onychomycosis and Pityriasis/Tinea versicolor. Moreover, VL metrics did not demonstrate any significant association between HIV VLs and fungal infection, but there is a strong correlation depending on the stage of the opportunistic fungal infection and drug administration.

Hence, fungal infections remain a major concern in PLHIV, particularly among those with low CD4+ counts. CD4+ cell monitoring is crucial for predicting infection risk and guiding clinical management. Given the high prevalence and clinical impact of opportunistic fungal infections, timely diagnosis and early intervention are essential in improving patient outcomes.

Additionally, further research is needed to explore innovative antifungal treatments, resistance patterns, and the potential benefits of integrating fungal infection screening into routine HIV care protocols. Enhancing awareness and education on fungal complications among healthcare providers and patients alike will play a vital role in improving long-term disease management and quality of life for PLHIV.

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

Informed Consent Statement: Patient consent was waived due to the observational nature of the study.

Authors Contributions: Douvali Theodora: Data curation, Writing-Original draft preparation; Paparizos Vasilios: Data logging, Supervision; Vasalou Varvara: Data collection, patient monitoring; Stamatis Gregoriou: patient monitoring; Chasapi Vasiliki: patient monitoring; Rigopoulos Dimitrios and Stratigos Alexandros J: Supervision; Nicolaidou Electra: Conceptualization, Methodology, Supervision.

Funding: No financial support was received for the writing, editing, approval, or publication of this manuscript.

Consent for Publication: Written patient consent was not required from the patients involved in this study due to the observational nature of the study.

Institutional Review Board Statement: Ethical review and approval were waived for this study, due to the observational nature of the study.

Data Availability Statement: Data available on request due to restrictions related to patient confidentiality, as the data include medical history information and are subject to the protection of sensitive personal data.

Abbreviations

Human Immunodeficiency Virus (HIV); World Health Organization (WHO); National Public Health Organization (N.P.H.O.); highly active antiretroviral therapy (HAART); people living with HIV (PLHIV); Pneumocystis jirovecii pneumonia (PJP).

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