

Opportunistic infections in people living with HIV/AIDS in a reference service in Southern Brazil

Infecções oportunistas em pessoas vivendo com HIV/AIDS em um serviço de referência no Sul do Brasil

Mariane D'Avila Vecchi^{1,4,*}, Marysabel Pinto Telis Silveira², Stefanie Bressan Waller³, Sônia de Avila Botton⁴, Daniela Isabel Brayer Pereira⁵

¹Ambulatório da Faculdade de Medicina, Universidade Federal de Pelotas (UFPEL), Pelotas/RS, Brasil, ²Programa de Pós-Graduação Multicêntrico em Ciências Fisiológicas, Instituto de Biologia, Departamento de Fisiologia e Farmacologia, Universidade Federal de Pelotas (UFPEL), Pelotas/RS, Brasil, ³Departamento de Veterinária Preventiva, Faculdade de Veterinária, Universidade Federal de Pelotas (UFPEL), Pelotas/RS, Brasil, ⁴Departamento de Medicina Veterinária Preventiva, Centro de Ciências Rural, Programa de Pós-Graduação em Medicina Veterinária (PPGMV) e Programa de Pós-Graduação em Ciências Farmacêuticas (PPGCF), Universidade Federal de Santa Maria (UFSM), Santa Maria/RS, Brasil, ⁵Programa de Pós-Graduação em Microbiologia e Parasitologia, Instituto de Biologia, Departamento de Microbiologia e Parasitologia, Universidade Federal de Pelotas (UFPEL), Pelotas/RS, Brasil.

ABSTRACT

Introduction: Infection by the human immunodeficiency virus (HIV) is a public health problem since the virus causes depletion of CD4 T lymphocytes with impaired immunity and may progress to acquired immunodeficiency syndrome (AIDS). **Objective:** This study aimed to verify prevailing opportunistic infections (OIs) in people living with HIV/AIDS (PLHIV/AIDS), aged 18 years or older, from 2009 to 2019 in a Specialised Assistance Service in the city of Pelotas, Rio Grande do Sul, Brazil ($n=2299$). **Methodology:** The variables analysed were opportunistic infections, gender, skin colour, age, education, marital status, heterosexual relationships, homosexual relationships, antiretroviral therapy, smokers, alcohol users, illicit drug users, AIDS diagnosis, and CD4 T cell count. **Results:** OIs were present in 30.6%, including oral candidiasis 22.26%, pulmonary tuberculosis 13.28%, herpes zoster 10.85%, pneumocystosis 10.48%, neurotoxoplasmosis 8.89%, herpes simplex 8.50%, vaginal candidiasis 5.89%, and esophageal candidiasis 4.21%. After adjusted analysis, the prevalence of OIs was 32% higher in illicit drug users and 2.3 times greater in people with AIDS; nonetheless, individuals with a current CD4 T lymphocytes count >500 cell/mm³ had a 38% lower prevalence of OIs. **Conclusions:** Therefore, the results demonstrated that OIs are more prevalent in people using illicit drugs and with AIDS, and the lower the CD4 T lymphocytes count, the higher the prevalence; however, early diagnosis, initiation of antiretroviral therapy, and continuous follow-up of people living with HIV/AIDS reduce OIs.

Keywords: HIV/AIDS; opportunistic infections; illicit drugs; CD4 T lymphocytes

RESUMO

Introdução: A infecção pelo vírus da imunodeficiência humana (HIV) é um problema de saúde pública, pois o vírus causa depleção de linfócitos T CD4+ com comprometimento da imunidade, podendo evoluir para a síndrome da imunodeficiência adquirida (AIDS). **Objetivo:** Este estudo teve como objetivo verificar as infecções oportunistas (IOs) prevalentes em pessoas vivendo com HIV/AIDS (PVHIV/AIDS), com 18 anos ou mais, no período de 2009 a 2019, em um Serviço de Assistência Especializada na cidade de Pelotas, Rio Grande do Sul, Brasil ($n=2299$). **Metodologia:** As variáveis analisadas foram infecções oportunistas, sexo, cor da pele, idade, escolaridade, estado civil, relações heterossexuais, relações homossexuais, terapia antirretroviral, tabagismo, uso de álcool, uso de drogas ilícitas, diagnóstico de AIDS e contagem de células T CD4+. **Resultados:** IOs estavam presentes em 30,6%, incluindo candidíase oral 22,26%, tuberculose pulmonar 13,28%, herpes zoster 10,85%, pneumocistose 10,48%, neurotoxoplasmose 8,89%, herpes simplex 8,50%, candidíase vaginal 5,89% e candidíase esofágica 4,21%. Após análise ajustada, a prevalência de IOs foi 32% maior em usuários de drogas ilícitas e 2,3 vezes maior em pessoas com AIDS; no entanto, indivíduos com contagem atual de linfócitos T CD4 > 500 células/mm³ apresentaram prevalência 38% menor de IOs. **Conclusões:** Portanto, os resultados demonstraram que as IOs são mais prevalentes em pessoas que usam drogas ilícitas e com AIDS, e quanto menor a contagem de linfócitos T CD4, maior a prevalência; no entanto, o diagnóstico precoce, o início da terapia antirretroviral e o acompanhamento contínuo de pessoas vivendo com HIV/AIDS reduzem as IO.

INTRODUCTION

The human immunodeficiency virus (HIV) is a challenge to health and development worldwide, causing

acquired immunodeficiency syndrome (AIDS)¹. The Joint United Nations Program on HIV/AIDS (UNAIDS) estimated that 38.4 million people live with HIV², raising concerns about these patients' medical challenges regarding health care.

When not adequately treated, HIV infection progresses to AIDS, elevating morbidity and mortality¹, and the

Correspondente/ Corresponding: Mariane D'Avila Vecchi – Endereço: Rua Almirante Guilhobel, 221, bairro Fragata, Pelotas/RS, Brasil. CEP: 96040-010. – E-mail: mariane.vecchi@ufpel.edu.br

severe systemic immunosuppression seen in people living with HIV/AIDS (PLHIV/AIDS) can lead to opportunistic infections (OIs) of fungal, bacterial, viral, and protozoal causes³.

Prophylactic treatments based on specific antimicrobials can be introduced at the diagnosis to prevent these infections, along with early initiation of ART⁴, which consists of drugs formulated to prevent HIV infection from progressing. Its regular use decreases viral replication, reconstituting the immune system by increasing the CD4+ T lymphocyte count⁵, restoring the host's defences, and reducing morbidity and mortality⁵.

The frequency and pattern of OIs vary among regions; developing countries suffer more from OIs due to resource scarcity, lack of diagnosis, low adherence to ART, drug resistance, poverty, malnutrition, and high exposure to infectious agents⁶. Studies report that these infections remain a significant cause of morbidity and mortality in PLHIV/AIDS. There are other HIV-related complications, including co-infections, comorbidities, adverse effects, drug interactions, toxicity, and drug resistance⁷. In Brazil, a study conducted in a regional reference centre in Goiás State between 2005 and 2015, with 539 PLHIV/AIDS in follow-up, revealed that pneumonia caused by *Pneumocystis jirovecii* was the most common OI, followed by neurotoxoplasmosis (*Toxoplasma gondii*), tuberculosis (*Mycobacterium* spp.), neurocryptococcosis (*Cryptococcus* spp.), oral candidiasis (*Candida* spp.), and histoplasmosis (*Histoplasma* spp.)⁸.

However, only a handful of studies have linked tuberculosis, cryptococcosis, and histoplasmosis, including those associated with COVID-19, as important infections in PLHIV/AIDS in Rio Grande/RS, and Chagas disease and toxoplasmosis in PLHIV/AIDS in Pelotas/RS⁹⁻¹⁴. Although these studies analysed specific infections, there is a gap in the literature regarding the scope of the infections involving different PLHIV/AIDS, which can assist in clinical diagnosis. Therefore, we sought to identify the most prevalent OIs in individuals with HIV/AIDS in Pelotas/RS and establish a correlation with the sociodemographic, behavioural, and clinical profiles during 11 years of study.

MATERIAL AND METHODS

Retrospective study of data from medical records

A retrospective descriptive study was conducted using medical records from the Specialised Assistance Service of the Outpatient Clinic of the Federal University Hospital of Pelotas (Pelotas, RS, Brazil). Hence, 2,758 medical records of patients living with HIV/AIDS, aged 18 years or older, whose first consultation occurred from 2009 to 2019, were analysed. This study was approved by the Ethics Committee of the Federal University of Pelotas for research with human beings (CEEa no. 34942720.7.0000.5317) and conducted with complete confidentiality.

Variables analysed

From the medical records, data on the following variables were collected: sociodemographic characteristics, gender (male/female), skin color (white, black, brown/yellow), age (continuous, later categorised as 18–30, 31–40, 41–50, 51–60, and 61 or older), and education in years of study (continuous, further categorised as 0–4, 5–8, 9–11, and 12 or more). Regarding the behavior, we analysed marital status (lives alone or with others), heterosexual (yes or no) and homosexual (yes or no) relationships, use of ART (yes or no), smoking (yes or no), alcohol use (yes or no), and illicit drug use (yes or no). For clinical characteristics, we collected: the presence of OIs (yes or no), AIDS diagnosis (yes or no), the value of the first CD4 T lymphocyte count (continuous, subsequently categorised into <200, 200–300, 301–500, >500 cell/mm³), current CD4 T lymphocyte count (continuous, later categorised into <200, 200–300, 301–500, >500 cell/mm³), and lowest CD4 T lymphocyte count (continuous, further categorised into <200, 200–300, 301–500, >500/cell/mm³).

Statistical analysis

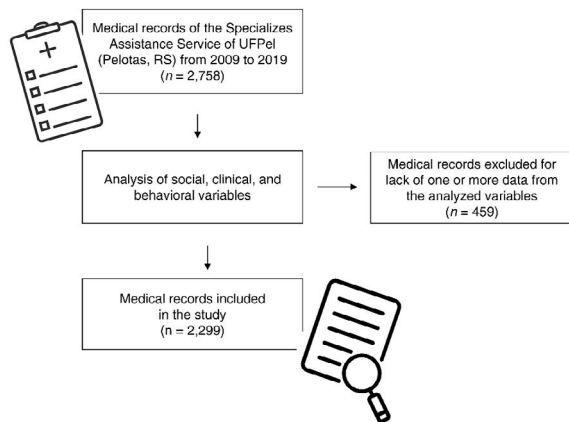
The data collected was transcribed to an Excel spreadsheet, 20% was checked, quality control was performed, and the information was transferred to a database using the Stata 17 statistical package (StataCorp LP, College Station, United States). Initially, descriptive sample analysis was carried out among the various categories of the variables studied, with their respective 95% confidence intervals, and stratified for opportunistic infections. Pearson's chi-square test was used to verify statistical differences between variables. Pearson's exact test was adopted when necessary, and the linear trend test for ordinal categorical variables was applied to consider significant values of $p < 0.05$. The crude and adjusted analyses were conducted through Poisson Regression with robust variance at three levels to verify the association between the outcome and the independent variables. The first included sociodemographic variables (gender, skin color, age, and education), the second used behavioral variables (marital status, homosexuality/heterosexuality, smoking, and use of ART, alcohol, and illicit drugs), and the third adopted clinical variables (OIs, AIDS diagnosis, value of the first current, and lower CD4 T lymphocyte count).

RESULTS

Records analysed

Of the 2,758 consultations performed during the study period, 2,299 (83.3%) were included in the study. In contrast, the others ($n = 459$) were excluded because they did not present all the variables (Figure 1).

Figure 1 - Flowchart schematising the clinical records of PLHIV/AIDS in Pelotas, RS, Brazil, and assisted at the Specialised Assistance Service of the Federal University of Pelotas (UFPEl) from 2009 to 2019.



Most of the PLHIV/AIDS were male, white, adults, educated, smokers, and drinkers

The sociodemographic, behavioural, and clinical characteristics of the PLHIV/AIDS assisted in the Specialised Assistance Service, and those who presented OIs, are listed in Table 1. After analysing 2,299 medical records of PLHIV/AIDS, we found that 860 (38.2%) were diagnosed with AIDS and 2,069 (94.9%) were taking ART; besides, most patients were male (1,334, 58%), white (1,335, 68.7%), between 31 and 50 years old (1,227, 53.4%), 12 years of education or more (1,428, 62.1%), living with someone (1,224, 69.8%), smokers (1,157, 64%), and alcohol users (850, 54.9%).

Table 1 – Sociodemographic, behavioural, and clinical variables of PLHIV/AIDS in Pelotas, RS, Brazil, and assisted at the Specialised Assistance Service of the Federal University of Pelotas (UFPEl) from 2009 to 2019.

Variables analyzed	Total sample: n (%)	Presence of IOs [#] n (%)	p-value
Gender (n = 2299)*			
Male	1334 (58.0)	411 (31.6)	0.204
Female	965 (42.0)	276 (29.1)	
Skin color (n = 1943)*			
White	1335 (68.7)	402 (30.8)	0.722
Black	411 (21.2)	130 (32.4)	
Brown/yellow	197 (10.1)	57 (29.4)	
Age (n = 2299)**			
18–30	450 (19.6)	95 (21.9)	<0.001
31–40	672 (29.2)	201 (30.5)	
41–50	555 (24.1)	182 (33.5)	
51–60	377 (16.4)	128 (34.5)	
61 or more	245 (10.7)	81 (33.8)	
Education in years of study (n = 2299)**			
0–4	200 (8.7)	69 (35.4)	0.004
5–8	417 (18.1)	119 (29.8)	
9–11	254 (11.1)	64 (25.6)	
12 or more	1428 (62.1)	435 (30.2)	

Marital status (n = 1734)*			
Living alone	530 (30.2)	157 (30.6)	0.675
Living with someone	1224 (69.8)	356 (29.6)	
Heterosexual relationships (n = 1762)*			
No	181 (10.3)	42 (23.9)	0.063
Yes	1.581 (89.7)	475 (30.6)	
Homosexual relationships (n = 1097)*			
No	739 (67.4)	218 (30.3)	0.012
Yes	358 (32.6)	81 (23.0)	
Use of ART (n = 2181)			
No	112 (5.1)	16 (14.3)	<0.001
Yes	2069 (94.9)	644 (31.5)	
Smoker (n = 1808)*			
No	651 (36.0)	171 (26.8)	0.011
Yes	1157 (64.0)	372 (32.6)	
Alcohol use (n = 1548)*			
No	698 (45.1)	226 (32.8)	0.227
Yes	850 (54.9)	248 (29.9)	
Illicit drug use (n = 1474)			
No	879 (59.6)	239 (27.7)	0.012
Yes	595 (40.4)	198 (33.9)	
AIDS diagnosis (n = 2249)			
No	1389 (61.8)	227 (16.7)	<0.001
Yes	860 (38.2)	453 (53.1)	
First CD4 count (cell/mm³) (n = 2210)**			
<200	629 (28.5)	195 (31.5)	0.911
200–300	419 (19.0)	124 (30.7)	
301–500	428 (19.4)	125 (29.7)	
>500	734 (33.2)	215 (29.9)	
Current CD4 count (cell/mm³) (n = 2189)**			
<200	461 (21.1)	240 (52.6)	<0.001
200–300	451 (20.6)	147 (33.0)	
301–500	452 (20.7)	106 (23.9)	
>500	825 (37.7)	170 (20.9)	
Lower CD4 count (cell/mm³) (n = 2229)**			
<200	808 (36.3)	251 (31.9)	0.103
200–300	542 (24.3)	158 (29.5)	
301–500	399 (18.0)	135 (34.3)	
>500	480 (22.0)	126 (27.0)	

OIs, opportunistic infections; *Pearson's chi-square test; **Linear trend test; some variables did not close in the full sample due to missing data.

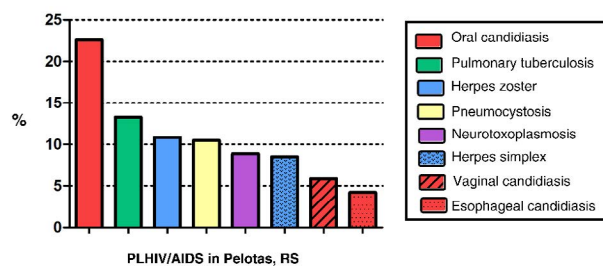
Prevalence of OIs in PLHIV/AIDS

Considering the PLHIV/AIDS who presented OIs (Table 1), there was a higher prevalence of OIs as age increased in those who were not homosexuals, smokers, illicit drug users, and diagnosed with AIDS. We also observed that as education and CD4 T lymphocyte count decreased, there was an increase in the OIs. The results revealed that 30.6% (687/2,247) of the people presented OIs.

Candidiasis was the primary opportunistic infection among PLHIV/AIDS

The most frequent were oral candidiasis 22.26% (238/1,069), pulmonary tuberculosis 13.28% (142/1,069), herpes zoster 10.85% (116/1,069), pneumocystosis 10.48% (112, 1,069), neurotoxoplasmosis 8.89% (95/1,069), herpes simplex 8.50% (91/1,069), vaginal candidiasis 5.89% (63/1,069), and esophageal candidiasis 4.21% (45/1,069) (data not shown in Table 1). They also had miliary tuberculosis, tuberculous meningitis, cryptococcal meningitis, histoplasmosis, oesophageal cytomegalovirus, and other infections (Figure 2). Generally, we observed that candidiasis was the main OI (32.37%, 346/1,069), affecting the oral, esophageal, and vaginal cavities, and 10.4% (238/2,299) had two or more concomitant OIs.

Figure 2 - Prevalence (%) of opportunistic infections in PLHIV/AIDS in Pelotas, RS, Brazil, and assisted at the Specialised Assistance Service of the Federal University of Pelotas (UFPe) from 2009 to 2019.



The presence of AIDS and illicit drug use favoured the emergence of OIs

Table 2 shows the crude and adjusted analysis between the variables under study and the presence of OI. In the crude analysis, there was a higher prevalence of OIs as age increased ($p < 0.001$); the same was observed with people who were not homosexual ($p = 0.014$), used ART ($p = 0.001$), smoked ($p = 0.013$), used illicit drugs ($p = 0.012$), and was diagnosed with AIDS ($p < 0.001$). Additionally, those with current CD4 T lymphocyte counts $>500 \text{ cell/mm}^3$ ($p < 0.001$) had a lower prevalence of OIs than those with $<200 \text{ cell/mm}^3$. After adjusting the data for age, homosexual relations, use of ART or illicit drugs, smoking, AIDS diagnosis, and current CD4 T lymphocyte count, the variables illicit drug use ($p = 0.041$), AIDS diagnosis ($p < 0.001$), and current CD4 T lymphocyte count ($p = 0.012$) remained statistically significant. Prevailing OIs were 32% higher in illicit drug users and 2.3 times higher in people with AIDS; however, those who had a current CD4 T lymphocytes count $>500 \text{ cell/mm}^3$ had 38% less prevalence of OIs than individuals with current CD4 T lymphocytes count $<500 \text{ cell/mm}^3$.

Table 2 – Crude and Adjusted Analysis of the characteristics of PLHIV/AIDS with opportunistic infections, treated at a Specialised Assistance Service of Pelotas, RS, Brazil, from 2009 to 2019.

Variables	Crude analysis*		Adjusted analysis**	
	PR (95%CI)	p-value	PR (95%CI)	p-value
Gender				
Male	1		1	
Female	0.92 (0.81–1.05)		1.06 (0.81–1.37)	
Skin color				
White	1			
Black	1.05 (0.89–1.24)	0.980		
Brown/yellow	0.96 (0.76–1.21)			
Age				
18–30	1		1	
31–40	1.39 (1.12–1.72)	<0.001	1.24 (0.83–1.83)	0.258
41–50	1.52 (1.23–1.89)		1.11 (0.74–1.66)	
51–60	1.57 (1.25–1.97)		1.28 (0.85–1.93)	
61 or more	1.54 (1.20–2.00)		1.29 (0.80–2.08)	
Education (years)				0.971
0–4	1		1	
5–8	0.84 (0.66–1.07)	0.663	0.66 (0.44–0.99)	
9–11	0.72 (0.54–0.96)		1.05 (0.68–1.63)	
12 or more	0.87 (0.71–1.07)		0.83 (0.60–1.14)	
Marital status				
Living alone	1	0.674		
Living with someone	0.97 (0.83–1.13)			
Heterosexual relationships				
No	1	0.075		
Yes	1.28 (0.98–1.69)			
Homosexual relationships				
No	1	0.014	1	0.879
Yes	0.76 (0.61–0.95)		0.96 (0.72–1.27)	
Use of ART				
No	1	0.001	1	0.470
Yes	2.20 (1.39–3.48)		1.22 (0.61–2.44)	
Smoker				
No	1	0.013	1	0.249
Yes	1.21 (1.04–1.42)		1.17 (0.90–1.53)	
Alcohol use				
No	1	0.227		
Yes	0.91 (0.79–1.06)			
Illicit drug use				
No	1	0.012	1	0.041
Yes	1.22 (1.05–1.43)		1.32 (1.01–1.73)	
AIDS diagnosis				
No	1	<0.001	1	<0.001
Yes	3.19 (2.79–3.65)		2.30 (1.64–3.21)	
First CD4 count (cell/mm³)				
<200	1			
200–350	0.97 (0.81–1.17)	0.506		
351–500	0.94 (0.78–1.14)			
>500	0.95 (0.81–1.12)			
Current CD4 count (cell/mm³)				
<200	1		1	
200–350	0.63 (0.53–0.73)	<0.001	0.87 (0.64–1.17)	0.012
351–500	0.45 (0.38–0.55)		0.68 (0.45–1.02)	
>500	0.40 (0.34–0.47)		0.62 (0.42–0.92)	
Lower CD4 count (cell/mm³)				
<200	1			
200–350	0.92 (0.78–1.09)	0.228		
351–500	1.07 (0.90–1.27)			
>500	0.85 (0.71–1.01)			

*PR, Poisson regression; **Poisson regression adjusted for age, homosexual relations, ART, smoking, illegal drug use, AIDS diagnosis, and current CD4 count.

DISCUSSION

This study evaluated the prevailing OIs in PLHIV/AIDS patients assisted in a reference service in southern Brazil. Sociodemographic, behavioral, and clinical variables were related to the prevalence found, and 30.6% of people had a documented diagnosis of OI, which can be compared with a retrospective follow-up study conducted in a specialised hospital in Dessie (Ethiopia), with 354 PLHIV/AIDS from 2015 to 2020, when there was 32.2% prevalence of OIs¹⁵. Similarly, a 17-year retrospective population-based cohort study conducted in Qatar found that, out of 167 PLHIV/AIDS, 32.3% had OIs, and one of the significant risk factors was low CD4 count¹⁶. However, in Aracaju/SE (Brazil), the prevalence of OIs was lower (19.3%)¹⁷, thereby diverging from our study, probably due to the lack of diagnosis and records in specialised services.

Illicit drug users had a 32% higher occurrence of OIs than those who did not use drugs. These findings are aligned with a longitudinal analysis conducted in St. Petersburg between 2012 and 2015 with 165 PLHIV¹⁸, evidencing a higher vulnerability of illicit drug users to OIs.

Studies conducted in different regions in Brazil showed that OIs strongly correlate with CD4 count. In Joaçaba/SC, a quantitative, exploratory, cross-sectional cohort conducted with 143 PLHIV/AIDS in a public health service unit from 2014 to 2015 found that the incidence of OIs was significantly higher in people with low CD4 count¹⁹. In a Medical Speciality Centre in Aracaju/SE, a documental, retrospective, and transversal study from the medical records of PLHIV/AIDS evidenced a significant relationship between the decrease in CD4 count and the increase in the frequency of OIs¹⁷. These results corroborate those of the present study: the lower the CD4 T lymphocyte count, the higher the prevalence of OIs, while people with CD4 T lymphocyte counts >500 cell/mm³ had fewer cases of OIs.

The most common OI identified in this study was oral candidiasis, which is aligned with what Brito et al.¹⁷ observed in northeastern Brazil. Similarly, studies in India with HIV-infected individuals showed a significant association between oral candidiasis and low CD4 T lymphocyte counts (less than 200 cell/mm³)^{20,21}. Oral lesions represent important clinical markers of ART failure. They may be present from acute infection to advanced stages of HIV infection, and professionals must be alerted as oral lesions may suggest HIV infection or indicate a worsening in PLHIV/AIDS health status²². In the present study, oral candidiasis represented a prevalence of 22.26%, and analogous results were observed in research conducted in the Specialised Care Service of Cacoal/RO, where oral candidiasis was 21.8%²³; another study in Bahia revealed that the most prevalent OI was oral/oesophageal candidiasis (21%)²⁴.

Fungal infections are persistent in this population, contributing to increased OIs. In addition to candidiasis, we identified infections with the fungus *P. jirovecii*, which is responsible for causing pneumocystosis, an

opportunistic pneumonia considered an AIDS-defining disease. Although it has been decreasing among HIV individuals due to ART and prevention, this pneumonia remains a frequent OI among PLHIV/AIDS worldwide²⁵. Population-based longitudinal research combined with a retrospective multicenter study in Germany found that 17.1% of people with HIV had pneumocystosis²⁵, differing from the 10.48% identified in this study. Articles from different regions of Brazil have also found variations in the prevalence of pneumocystosis^{24,26-29}, which may be due to the retrospective nature of the data studied, geographical differences, time of diagnosis, and management of patients in each specialised service³⁰. Although cryptococcosis and histoplasmosis were observed less frequently, they are relevant as they cause severe fungal infections in PLHIV/AIDS. In other studies, in Rio Grande/RS, these diseases were found with higher frequency^{11,12}.

OIs increase morbidity and mortality, reducing the life expectancy of PLHIV/AIDS^{30,31}. An adequate and specific treatment identifying the pathogens is necessary to improve diagnosis and therapy, decreasing mortality rates³². Therefore, prevention and timely intervention in OIs increases life expectancy and helps prevent the transmission of infections between individuals³³. Studies in Brazil are needed to evaluate the burden of OIs to improve the planning of the organisation of health services in HIV/AIDS³¹.

The prevalence and lack of data reinforce the importance of research in this region. The reference service of this paper assists 21 cities in Brazil. The article's main author works where the research was carried out, having easy access to the medical records, which facilitated clarifying doubts, both with the patients and the physicians of the service, and all data collected went through quality control. Additionally, this study encourages referral services to improve strategies for preventing, diagnosing, and treating OIs in this population; however, interpreting the present results must consider some limitations, such as using secondary data from medical records prone to underreporting and incomplete data.

CONCLUSIONS

The findings revealed that the prevalence of OIs in PLHIV/AIDS treated at a Specialised Assistance Service of the Outpatient Clinic of the Federal University Hospital of Pelotas was 30.6%. The prevalence of IOs is higher as the value of CD4 T lymphocytes decreases, in individuals with AIDS and illicit drug users. Candidiasis was the most frequent infection identified. The OIs among PLHIV/AIDS remain a public health concern as they decrease the quality and survival of people. Early care seeking, initiation of ART, and continuous follow-up of PLHIV/AIDS are essential to reduce OIs, significantly improving the quality of life of the PLHIV/AIDS.

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