



## Opportunistic infections in individuals living with HIV/AIDS: what is the situation found in a specialized care service located in Northeastern Brazil?

Infecções oportunistas em pessoas vivendo com HIV/AIDS: qual a situação encontrada em um serviço de atendimento especializado situado no nordeste Brasileiro?

Infecciones oportunistas en individuos que viven con VIH/SIDA: ¿cuál es la situación encontrada en un servicio de atención especializada ubicado en el noreste de Brasil?

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### ABSTRACT

**Introduction:** Opportunistic infections are not uncommon in individuals living with the Human Immunodeficiency Virus (HIV), being one of the main causes of morbidity and mortality associated with Acquired Immunodeficiency Syndrome (AIDS). **Aim:** to conduct a survey on the prevalence of opportunistic infections in individuals living with HIV/AIDS assisted by a Specialized Care Service (SCS). **Design:** For this purpose, an epidemiological, analytical, and retrospective study was conducted, in which data collection was performed from patient records. The association of variables such as sex, age, education, income, treatment, viral load, CD4+ T lymphocytes, and opportunistic infection was verified through Fisher's exact test to identify possible factors associated with infections. **Results:** From 2014 to 2020, 214 cases were reported, of which 65 had some opportunistic infection, the most frequent being: oral candidiasis (58.46%); cytomegalovirus (16.92%); pulmonary tuberculosis (12.31%); and herpes zoster (10.77%). A higher frequency was observed in males (73.85%); age between 20 and 59 years (44.61%); income below one minimum wage (50%); and incomplete elementary education (37.04%). There was no statistical significance ( $p < 0.05$ ) among the associated variables in the study. **Implications:** It can be concluded that oral candidiasis remains one of the main coinfections in individuals living with HIV/AIDS. Additionally, these results may contribute to the development of prevention strategies, reducing the number of cases of opportunistic infections, and improving the survival of individuals living with HIV/AIDS.

### DESCRIPTORS

Candidiasis; Immunosuppression Therapy; Anti-Retroviral Agents.

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## INTRODUCTION

The infectious disease Acquired Immunodeficiency Syndrome (AIDS) is caused by the Human Immunodeficiency Virus (HIV), which was first identified in the 1980s, initiating a serious national and global public health problem, affecting various age groups to this day and requiring strategies for control and prevention.<sup>1-2</sup>

HIV is a spherical particle, measuring 100 to 120 nm in diameter, belonging to the Lentivirus genus and Retroviridae family, targeting CD4+ T cells.<sup>3</sup> Monitoring and follow-up of People Living with HIV/AIDS (PLWHA) occur through CD4+ T lymphocyte quantification tests and viral load, showing effectiveness in determining the disease progression level and assessing the risks of opportunistic infections to which the individual is exposed.<sup>4</sup>

In Brazil, AIDS was first reported in 1982 when cases of the disease were diagnosed in the states of Rio de Janeiro and São Paulo. To combat the epidemic, measures of epidemiological surveillance, educational interventions, health information, and voluntary testing were established through the creation of the National STD/AIDS Control Program, becoming an international reference in the fight against the AIDS epidemic in the early years of the disease.<sup>5</sup>

Since its discovery, HIV has been a significant public health problem, as the disease it often causes still lacks a cure, requiring continuous prevention and treatment measures. Through research and health management, several advances have been significant for the detection, treatment, and prevention of infection by this virus. Since the implementation of Antiretroviral Therapy (ART), AIDS-related deaths have decreased by 23% worldwide, resulting in reduced virus transmission and occurrences of opportunistic infections. However, there is still a portion of PLWHA who receive a late diagnosis, do not adhere to ART, or do not accept the diagnosis, contributing to the emergence of these infections. All

these factors lead to a decrease in CD4+ T cell counts and an increase in blood viral load, weakening the individual's immune system and making them more susceptible to infections.<sup>6-9</sup>

It is estimated that there are 38 million people living with the virus worldwide, with over 33 million deaths recorded by the end of 2019. In Brazil, from the beginning of the pandemic until 2022, 1,088,536 cases of AIDS were registered. In 2021, 40.8 thousand cases of HIV and another 35.2 thousand cases of AIDS were reported in Brazil. In the state of Rio Grande do Norte, there has been an increase in AIDS cases from 1980 to 2020, with a total of 9,175 cases reported in the Notifiable Diseases Information System (SINAN), declared in the Mortality Information System (SIM), and registered in the Drug Logistics Control System (SISCEL/SICLOM), making it the sixth state in the Northeast to have a higher total of cases in this period. Additionally, there has been an increase in the mortality rate from 2009 to 2019 in Rio Grande do Norte.<sup>10-12</sup>

Infections caused by immunosuppression resulting from AIDS are termed opportunistic. These can be fungal, viral, bacterial, and parasitic. Patients become susceptible to these infections when the count of CD4+ T cells is  $< 200$  cells/mm<sup>3</sup>, a factor that triggers an "AIDS worsening alert." The emergence of these diseases is the most frequent cause of death in PLWHA, with tuberculosis being prominent among them.<sup>2,9</sup>

In light of the above, this study aimed to verify the prevalence of opportunistic infections in PLWHA and assess the association of study variables conducted in the Specialized Care Service (SCS) in a municipality in the state of Rio Grande do Norte.

## METHOD

The study occurred in the municipality of Caicó, situated in the microregion of Western Seridó, 273 km from the capital of the state of Rio Grande do Norte. It was an epidemiological cross-sectional

study, where data collection involved reviewing archived medical records of patients seen at the SAE from 2014 to 2020. The information was reported following the STROBE recommendations - Strengthening the Reporting of Observational Studies in Epidemiology.

All PLWHA assisted by the service and diagnosed with opportunistic infections during the follow-up period were included in the study population. Medical records with illegible data and records of deceased patients were excluded from the research.

Data were collected by investigating patient records linked to the SAE with a diagnosis of at least one opportunistic infection. This involved conducting a data review using the following independent study variables: gender (male and female), age (<20 years, 20-39 years, 40-59 years, and over 60 years), education (elementary, high school, and higher education, complete and incomplete), income (<1 minimum wage, 1 to 2 minimum wages, 3 to 4 minimum wages or higher), treatment (lamivudine/tenofovir/dolutegravir or other), viral load (between 100,000 and 1 million, between 10,000 and 99,999, between 50 and 9,999, and <50 copies), CD4+ T lymphocytes (<200, 300-350, and >350); and the dependent variable: diagnosed opportunistic infection.

Statistical analysis of the data was conducted in two stages. Firstly, a descriptive analysis was performed, presenting absolute frequencies (n), relative frequencies (%), and the 95% confidence interval of the opportunistic infections variable for

the respective study. Subsequently, the association was assessed using Fisher's exact test with the assistance of Epi Info 7.2.3.0 software to identify potential factors associated with these infections among PLWHA linked to the SAE. Statistical significance was considered when the p-value was <5%. The analyzed data were presented in tables.

## RESULTS

A total of 214 reported cases of HIV/AIDS were identified in the specialized care service located in the municipality of Caicó, Rio Grande do Norte, Brazil, from 2014 to 2020. Among them, 65 patients were found to have at least one opportunistic infection.

Upon examining the frequency of variables regarding the epidemiological profile of these patients, a predominance of males (73.85%) was noted, with the age group of 20 to 39 years being the most common (44.61%). Furthermore, 37.04% had incomplete elementary education, and 50% of the studied individuals had an income below one minimum wage (see Table 1).

Regarding age analysis, the most frequent age group was 20 to 39 years, representing 44.61% of the sample. Regarding education, the majority of individuals had incomplete elementary education (37.04%), followed by complete high school education (22.22%).

In this study, it was observed that 50% of the individuals had an income below one minimum wage, indicating a higher number of people infected with HIV with low socioeconomic status.

**Table 1.** Socioeconomic profile of people living with HIV/AIDS, with opportunistic infections, attended at the Specialized Care Service (SAE) in Caicó, Rio Grande do Norte, from 2014 to 2020

Variables	N= 65	(%)
<b>Sex</b>		
Male	48	73.85
Female	17	26.15
<b>Age (years)</b>		
< 20	1	1.54
20-39	29	44.61
40-59	27	41.54

Above 60	8	12.31
<b>Education</b>	<b>n=54</b>	
Incomplete elementary education	20	37.04
Complete elementary education	1	1.85
Incomplete high school education	10	18.52
Complete high school education	12	22.22
Incomplete higher education	5	9.26
Complete higher education	6	11.11
<b>Income</b>	<b>n=42</b>	
< 1 minimum wage	21	50.0
1 to 2 minimum wages	20	47.62
3 to 4 minimum wages	1	2.38

Source: Own authorship, 2022.

The most frequent opportunistic infections in PLWHA attended at the specialized care service were oral candidiasis (58.46%), followed by cytomegalovirus (16.92%), pulmonary tuberculosis (8%), and herpes zoster (10.77%) (Table 2). Following oral candidiasis, cytomegalovirus IgM reactive (acute phase) stands as the second most common infection among patients attended at the SAE (16.92%).

Furthermore, among the most frequent opportunistic diseases analyzed in this study, pulmonary tuberculosis was observed with a frequency of 12.31%.

In line with the results of Martins<sup>23</sup> and Chaves et al.<sup>29</sup>, herpes zoster infection in this study occupied the fourth position among the infections most affecting PLWHA (Table 2).

**Table 2.** Absolute frequency, relative frequency, and 95% confidence interval for opportunistic infections among people living with HIV/AIDS

Opportunistic Infection	N	%	IC 95%
Oral Candidiasis	38	58.46	45.56-70.56
Cytomegalovirus	11	16.92	8.76-28.27
Pulmonary Tuberculosis	8	12.31	5.47-22.82
Herpes Zoster	7	10.77	4.44-20.94
Toxoplasmosis	2	3.08	0.37-10.68
Cryptococcosis	1	1.54	0.04-8.28
Histoplasmosis	1	1.54	0.04-8.28
Neurotoxoplasmosis	1	1.54	0.04-8.28
Neurotuberculosis	1	1.54	0.04-8.28
Pneumocystosis	1	1.54	0.04-8.28
Tinea Capitis	1	1.54	0.04-8.28
Tinea Corporis	1	1.54	0.04-8.28
Tinea Cruris	1	1.54	0.04-8.28
Ocular Toxoplasmosis	1	1.54	0.04-8.28

Source: Own authorship, 2022.

In this study, we did not find a statistically significant association between the most frequent opportunistic infections and low CD4+ T lymphocyte counts, high viral load, and other study variables such

as age, sex, and income, except for the variable infection period (2018-2020) and oral candidiasis ( $p < 0.05$ ) (Table 3). In summary, the prevalence of opportunistic infections did not vary concerning the investigated factors.

**Table 3.** Association of independent variables with the four most prevalent opportunistic infections among people living with HIV/AIDS in the period 2014-2020

	Oral Candidiasis		Cytomegalovirus		Pulmonary Tuberculosis		Herpes Zoster	
	n (%)	p	n (%)	p	n (%)	p	n (%)	p
<b>Age</b>		0.40		0.11		0.18		0.30
< 20 years	0 (0.0)		1 (9.1)		0 (0.0)		0 (0.0)	
20-39 years	15 (39.5)		6 (54.6)		3 (37.5)		5 (71.4)	
40-59 years	19 (50)		4 (36.4)		2 (25.0)		1 (14.3)	
60 years or more	4 (10.5)		0 (0)		3 (37.5)		1 (14.3)	
<b>Sex</b>		0.57		0.26		1.00		0.08
Female	12 (31.6)		1 (9.1)		2 (25.0)		4 (57.1)	
Male	26 (68.4)		10 (90.9)		6 (75.0)		3 (42.9)	
<b>Income</b>		0.73		0.56		0.41		1.00
< 1 minimum wage	13 (54.2)		3 (14.3)		1 (25.0)		3 (60.0)	
1 to 2 minimum wages	10 (41.7)		5 (62.5)		3 (75.0)		2 (40.0)	
3 to 4 minimum wages	1 (4.2)		0 (0)		0 (0.0)		0 (0.0)	
<b>Infection Period</b>		0.03		0.15		0.71		1.00
2014-2017	8 (21.1)		6 (54.6)		3 (37.5)		2 (28.6)	
2018-2020	30 (78.9)		5 (45.4)		5 (62.5)		5 (71.4)	
<b>Treatment</b>		1.00		1.00				0.67
Lamivudine/tenofovir/dolutegavir	26 (68.4)		8 (72.7)		5 (62.5)		4 (57.1)	
Other	12 (31.6)		3 (27.3)		3 (37.5)	0.71	3 (42.9)	
<b>CD4+ T Cell Count</b>		0.83		0.73		0.07		1.00
<200 cells/mm <sup>3</sup>	10 (26.3)		2 (18.2)		5 (62.5)		2 (27.6)	
200-350 cells/mm <sup>3</sup>	7 (18.4)		2 (18.2)		0 (0.0)		1 (14.3)	
>350 cells/mm <sup>3</sup>	21 (55.3)		7 (63.6)		3 (37.5)		4 (10.1)	
<b>Viral Load</b>		0.85		0.59		0.95		0.72
Between 100.000 and 1 million copies	9 (23.7)		4 (36.4)		2 (25.0)		3 (42.9)	
Between 10.000 and 99.999 copies	8 (21.1)		0 (0.0)		2 (25.0)		1 (14.3)	
Between 50 and 9.999 copies	4 (10.5)		0 (0.0)		1 (12.5)		0 (0.0)	
< 50 copies (undetectable)	17 (44.7)		3 (21.3)		3 (37.5)		3 (42.9)	

The test employed was the Fisher exact test.

Source: Own authorship, 2022.

## DISCUSSION

Studies conducted at a specialized reference unit for infectious and parasitic diseases in Belém and at healthcare service institutions in Colombia showed a predominance of males among HIV/AIDS cases, accounting for approximately 70%, corroborating the current study findings.<sup>9,13</sup> Several factors may be related to the prevalence of cases in men, including programmatic, social, and behavioral vulnerabilities. Men have less access to testing, treatment, and care due to low utilization of healthcare services. Factors such as lack of knowledge about disease prevention, inconsistent condom use, variability in sexual

partners, as well as illicit drug and alcohol use, influence the dominance of HIV infection in men.<sup>14-15</sup>

The present research found information that agrees with studies conducted in the state of Mato Grosso do Sul, where the prevalent age group, with the highest number of HIV/AIDS cases, also ranged from 20 to 39 years (51.2%).<sup>16</sup> Similarly, data from the epidemiological bulletin provided by the Ministry of Health indicates that the highest concentration of AIDS cases in Brazil during the period from 2009 to 2019 was observed among individuals aged 25 to 39, in both sexes.<sup>11</sup> Several factors make this population, comprising young adults, more susceptible to the

virus, such as early initiation of sexual activity, sporadic condom use, and lack of information about sexually transmitted infections.<sup>17</sup>

Regarding education, previous studies conducted in specialized service units in the municipalities of Quixadá/CE and Içara/SC also found a higher frequency of patients with incomplete elementary education, at 40% and 49.3%, respectively.<sup>18-19</sup> However, according to the epidemiological bulletin released by the Ministry of Health (2020), out of a total of 342,459 reported cases of HIV infection in the SINAN from 2007 to June 2020, the majority of people had completed high school, accounting for 21.1% of the total, followed by incomplete elementary education (11.9%). Low educational levels reflect misinformation about HIV transmission and diagnosis, as well as treatment adherence due to comprehension difficulty and accessibility to healthcare services.<sup>20</sup>

In the study by Motta et al., as in the present study, more people diagnosed with HIV/AIDS were observed to have an income below one minimum wage.<sup>21</sup> With existing inequalities, the pauperization of AIDS has been considered due to the lack of access to essential services, social, cultural, and economic exclusion of people with lower education and income levels, highlighting the need for centralized health actions aimed at this population segment.<sup>22</sup>

The prevalent infection in this study was oral candidiasis, consistent with the findings of a study conducted at a healthcare service in Palmas/TO, as well as at the care unit in Ribeirão Preto - SP, where this fungal infection predominated.<sup>23-24</sup> It is estimated that over 90% of AIDS patients present one or more oral manifestations during the course of the disease. Colonization by *Candida* spp. is present in almost the entire population, mainly in the oral cavity; however, for this microorganism to manifest, the host's immune system must be weakened. Thus, the highest number of candidiasis cases occurs in HIV-positive patients. The initial signs of HIV infection are usually oral

manifestations. These lesions can be indicative of disease progression towards AIDS, usually associated with decreased CD4+ T cell count and increased viral load.<sup>25</sup>

A study conducted at a reference center for the diagnosis of infectious diseases in Cascavel, PR, detected 414 (63.98%) people living with HIV (PLHIV) with antibodies (IgM and/or IgG) against cytomegalovirus (CMV),<sup>26</sup> validating the results of the present study, as the frequency of CMV infection is high among individuals living with viral infection.

It is evident that tuberculosis remains a concern among PLHIV. Similarly, a survey conducted in Ribeirão Preto - SP, where 10.2% of the 498 medical records had records of tuberculosis,<sup>24</sup> as well as in the research conducted at a healthcare unit in São José do Rio Preto/SP, where 23.2% of the subjects had tuberculosis-HIV coinfection, can be cited. There is an increase in the incidence of tuberculosis-HIV coinfection in Brazil,<sup>27</sup> mainly in the North and Northeast regions. In Rio Grande do Norte, there was a predominance of 71.62% of tuberculosis cases in PLHIV in recent years, with clinical presentation in the pulmonary form of the disease, confirming that tuberculosis is often associated with HIV infection, with the pulmonary form being the most recurrent. When there is this association, the patient's prognosis becomes poor due to the high lethality caused by *Mycobacterium tuberculosis*.<sup>23,28</sup>

In the study results, there was no statistically significant association regarding the most frequent opportunistic infections with low CD4+ T lymphocyte counts, high viral load, and other study variables, except for the infection period variable (2018-2020) and oral candidiasis ( $p < 0.05$ ). This outcome was similar to investigations<sup>29</sup> in a sample of 55 PLHIV with at least one opportunistic infection at the Pedro Kourí Institute of Tropical Medicine in Cuba, with no statistically significant association with low CD4+ T lymphocyte counts and high viral load, as well as the current study. This lack of statistical significance in

the current work may be explained by the sample size or by the categorical manner in which the variables were collected, as low CD4+ T cell counts and increased viral load are associated with an increased risk of opportunistic diseases indicative of AIDS.

Studies with this purpose are of great importance for public health, as they allow healthcare professionals to access the epidemiology of opportunistic infections that AIDS can cause. Thus, knowledge of these factors can help in detecting patients at risk of opportunistic diseases, for example, those with CD4+ T lymphocyte counts < 200 cells/mm<sup>3</sup> and viral load > 50 copies, directing efforts towards better management of these patients in the development of adherence, prevention, and early diagnosis strategies for this population.

### Limitations

Sole reliance on patient records as a data source, preventing a deeper analysis of the research problem. Lack of conversation and interaction with patients to gather more socioeconomic data, such as sexual orientation and mode of virus transmission. Therefore, a more comprehensive study in this research line is recommended, with interviews with SAE users, mainly focused on medication adherence

and the use of computerized means such as the T CD4+ and Viral Load Laboratory Exam Control System for more reliable data and more comprehensive studies.

### CONCLUSION

Based on the findings presented, we can conclude that the incidence of HIV/AIDS cases, accompanied by opportunistic infections, was higher among male patients, aged between 20 and 59 years, with low income and limited education levels. Notably, oral candidiasis was the most prevalent opportunistic infection, affecting 58.46% of PLHIV in the study cohort. Despite rigorous statistical analyses, we did not identify significant associations between the studied dichotomous variables—age, sex, income, treatment, viral load, CD4+ T lymphocyte count—except for a notable correlation between the infection period (2018 to 2020) and oral candidiasis. However, a subset of patients with infections exhibited low CD4+ T lymphocyte counts and high viral loads, indicative of advanced disease progression. Looking ahead, we aspire to extend this study prospectively, aiming for a larger sample size of SAE users, thereby mitigating the limitation of the assessed cases and delving deeper into variables such as sexuality.

### RESUMO

**Introdução:** Infecções oportunistas não são incomuns em pessoas que vivem com o Vírus da Imunodeficiência Humana (HIV), sendo uma das principais causas de morbimortalidade associadas à Síndrome de Imunodeficiência Adquirida (AIDS). **Objetivo:** Realizar um levantamento sobre a prevalência de infecções oportunistas em pessoas vivendo com VIH/SIDA assistidas por um Serviço de Atendimento Especializado (SAE). **Delineamento:** Para tanto, realizou-se um estudo epidemiológico, analítico e retrospectivo, no qual a coleta de dados foi realizada a partir dos prontuários dos pacientes. Sendo verificada a associação de variáveis: sexo, idade, escolaridade, renda, tratamento, carga viral, linfócitos T CD4+ e infecção oportunista por meio do teste Exato de Fisher para a identificação de possíveis fatores associados às infecções. **Resultados:** No período de 2014 a 2020 foram notificados 214 casos, destes 65 possuíam alguma infecção oportunista, sendo as mais frequentes: candidíase oral (58,46%); citomegalovírus (16,92%); tuberculose pulmonar (12,31%) e herpes zoster (10,77%). Observou-se maior frequência de pessoas do sexo masculino (73,85%); idade entre 20 a 59 anos (44,61%); renda inferior a um salário mínimo (50%) e escolaridade fundamental incompleto (37,04%). Não houve significância estatística ( $p < 0,05$ ) entre as variáveis associadas no estudo. **Implicações:** Pode-se concluir que a candidíase oral continua sendo uma das principais coinfeções em pessoas vivendo com VIH/SIDA. Além disso, estes resultados poderão colaborar para o desenvolvimento de estratégias de prevenção, reduzindo o número de casos de infecções oportunistas, contribuindo para a melhoria da sobrevida das pessoas convivendo com HIV/AIDS.

### DESCRITORES

Candidíase; Terapia de Imunossupressão; Antirretrovirais.

### RESUMEN

**Introducción:** Las infecciones oportunistas no son poco comunes en individuos que viven con el Virus de Inmunodeficiencia Humana (VIH), siendo una de las principales causas de morbilidad y mortalidad asociadas con el Síndrome de Inmunodeficiencia Adquirida (SIDA). **Objetivo:** realizar una encuesta sobre la prevalencia de infecciones oportunistas en individuos que viven con VIH/SIDA asistidos por un Servicio de Atención Especializada (SAE). **Delineación:** Para este fin, se realizó un estudio

epidemiológico, analítico y retrospectivo, en el cual la recopilación de datos se realizó a partir de registros de pacientes. La asociación de variables como sexo, edad, educación, ingresos, tratamiento, carga viral, linfocitos T CD4+ e infección oportunista se verificó a través de la prueba exacta de Fisher para identificar posibles factores asociados con infecciones. **Resultados:** De 2014 a 2020, se informaron 214 casos, de los cuales 65 tenían alguna infección oportunista, siendo las más frecuentes: candidiasis oral (58.46%); citomegalovirus (16.92%); tuberculosis pulmonar (12.31%); y herpes zóster (10.77%). Se observó una mayor frecuencia en hombres (73.85%); edad entre 20 y 59 años (44.61%); ingresos por debajo de un salario mínimo (50%); y educación primaria incompleta (37.04%). No hubo significancia estadística ( $p < 0.05$ ) entre las variables asociadas en el estudio. **Implicaciones:** Se puede concluir que la candidiasis oral sigue siendo una de las principales coinfecciones en individuos que viven con VIH/SIDA. Además, estos resultados pueden contribuir al desarrollo de estrategias de prevención, reduciendo el número de casos de infecciones oportunistas y mejorando la supervivencia de individuos que viven con VIH/SIDA.

#### DESCRIPTORES

Candidiasis; Terapia de Inmunosupresión; Antirretrovirales.

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## COLLABORATIONS

ABOR: contributed to the study conception, data collection, data interpretation, manuscript drafting, data analysis, methodology, and results statistics. ESC: contributed to the study conception and design, evaluation of stages, manuscript drafting and critical content review, data analysis, methodology, and results statistics. SMG: contributed to the study conception and design, evaluation of stages, data analysis, methodology, and results statistics. **All authors agree and are responsible for the content of this version of the manuscript to be published.**

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**AVAILABILITY OF DATA**

The original data are found in the medical records archived in the specialized care service where the study was conducted.

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Not applicable.

**CONFLICTS OF INTEREST**

There are no conflicts of interest to declare.