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Original research

Predictors of mortality among individuals with advanced HIV disease in a contemporary Brazilian cohort

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ABSTRACT

Objective. To identify clinical characteristics and risk factors associated with mortality, with a focus on opportunistic infections (OIs), in patients with advanced HIV in Brazil.

Methods. A prospective cohort study was conducted in five Brazilian tertiary hospitals, including 419 adults with advanced HIV. Baseline demographic and clinical data were collected during hospital admission, and participants were screened for tuberculosis, cryptococcosis, and histoplasmosis using rapid diagnostic tests. Participants were followed for 90 days to assess mortality, with causes of death classified using the Coding of Death in HIV (CoDe) protocol. Statistical analysis identified the variables associated with mortality.

Results. The median CD4 count was 66 cells/mm^3, and the median HIV viral load was 104 887 copies/mL. After 90 days, 18.1% of participants had died. ART-naive status, mental confusion, anemia, and elevated creatinine levels were strongly associated with mortality. OIs were diagnosed in 45.6% of participants, with severe histoplasmosis and cryptococcal meningitis significantly increasing the risk of mortality. Social determinants, such as sex, race, gender, and education level, did not have a significant impact on mortality, but socioeconomic factors influenced health care access.

Conclusion. Early HIV diagnosis and continuous ART are essential to reduce mortality. Public health strategies should prioritize improving HIV testing, treatment adherence, and addressing social disparities to mitigate health care inequalities.

Keywords HIV; AIDS-related opportunistic infections; point-of-care testing; mortality; risk factors.

Although HIV-associated morbidity and mortality have decreased over the past years due to the implementation and improvement of antiretroviral therapy (ART), persistently high mortality rates continue to pose a major a major public health challenge worldwide (1). In 2023, over 630 000 HIV/AIDS-related deaths were reported globally (2). In Brazil, the standardized mortality rate in 2022 was 4.1 per 100 000 population. However, in the state of Rio Grande do Sul, the standardized mortality rate rose to 7.3 per 100 000 population, and in the city of Porto Alegre, it reached 23.8 per 100 000 population, the highest among Brazilian capitals (3). Delays in HIV diagnosis; limited access to health care services, including ART; and nonadherence to treatment are common factors driving these high mortality rates, which are compounded by social disparities (4). Furthermore, advanced HIV disease is associated with increased health care costs (5).

Currently, a substantial number of patients are still being diagnosed with HIV at advanced stages, heightening the risk of mortality and the opportunistic infections (OIs) associated with AIDS (6). Additionally, many patients return to the health care

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system after discontinuing ART, often at similarly advanced stages (7). While OIs remain the leading cause of death in people living with HIV/AIDS, mortality is also influenced by a range of complex social determinants that heighten the risk of OIs (8). Individuals with low socioeconomic status and other vulnerabilities face a higher likelihood of developing HIV-related OIs and encounter significant barriers to assessing health care, contributing to greater morbidity and mortality (9).

To address these challenges, the World Health Organization (WHO) recommends a comprehensive package of tests for the rapid diagnosis of tuberculosis, cryptococcosis, and histoplasmosis (10), along with preventive measures, such as the latent tuberculosis infection treatment co-trimoxazole prophylaxis, and the use of preemptive therapy for those with positive *Cryptococcus* antigen who show no neurological involvement. This study is derived from an original cohort conducted in Brazil, aimed at assessing the feasibility of utilizing rapid diagnostic tests for histoplasmosis, cryptococcosis, and tuberculosis, as well as to determine the prevalence of these OIs (11). This paper describes the clinical characteristics and risk factors associated with overall mortality and OI-related mortality in this cohort.

METHODS

This prospective cohort study was conducted across five tertiary hospitals in Brazil: four in Porto Alegre (Hospital Nossa Senhora da Conceição, Hospital de Clínicas de Porto Alegre, Hospital Vila Nova, and Santa Casa de Porto Alegre) and one in Goiânia (Hospital Estadual de Doenças Tropicais Dr Anuar Auad). Participants were recruited between January and December 2023 if they met the following criteria: (1) adults with HIV infection; (2) diagnosed with advanced HIV, defined as a CD4 count of <200 cells/mm^3 up to 3 months before inclusion, or any symptom suggesting advanced HIV disease and systemic infection, such as fever, cough, expectoration, weight loss, night sweats, altered mental status, headache, focal neurological signs, lymphadenopathies, or extensive mucosal or skin lesions, independently of CD4 count, in the past 14 days; and (3) not using effective ART, including initiation or reintroduction of therapy in less than 3 months, treatment abandonment for more than 3 months, or virological failure (11).

Participants voluntarily consented to participate in the study, and all provided signed informed consent forms. The study protocol was approved by the Pan American Health Organization Research and Ethics Committee (PAHOERC) under registry number PAHOERC.0347.01, as well as by the ethics committees of all participating institutions. No identifiable personal information was collected in the database. Data were compiled by trained professionals and securely stored in a protected database.

Procedures and Definitions

Demographic data, including age, gender, sexual orientation, ethnicity, education, family income, and occupation, were collected, as well as clinical data, such as comorbidities, diagnoses of OIs prior to study entry, signs and symptoms within the past 14 days, and use of alcohol and illicit drugs. The most recent CD4 and viral load counts (up to 3 months before inclusion) were documented. Previous antiretroviral exposure was determined using the unified database of HIV patients within the Brazilian public health care system, Sistema Único de Saúde (SUS). Patients were classified as having discontinued treatment if they reported at the time of enrollment that they were no longer using antiretroviral medications. The duration of ART interruption was self-reported.

After enrollment, patients were screened for tuberculosis (TB), cryptococcosis, and histoplasmosis using a package of lateral flow tests: urine TB-LAM (Alere Determine TB LAM Ag; Abbott, Palatine, IL, USA), serum cryptococcal antigen (CrAg lateral flow assay; IMMY, Norman, OK, USA), and urine *Histoplasma* antigen (MiraVista lateral flow assay, Indianapolis, IN, USA). Additional diagnostic tests, such as rapid molecular tests, culture samples, and further examinations, were performed at the physician's discretion. Disseminated TB was defined as the presence of a positive culture or rapid molecular test in any extrapulmonary sample or a positive TB-LAM test without confirmed pulmonary TB.

Patients were followed up at 30 and 90 days after enrollment either through in-person visits or follow-up phone calls. *Loss to follow-up* was defined as the absence of information regarding a patient's status (alive or dead) 90 days after recruitment. Missing data refer to information that was not properly recorded at the time of enrollment. Causes of death were classified according to the Coding of Death in HIV (CoDe) protocol (12) and grouped into the following categories: AIDS-related deaths, possibly AIDS-related, not AIDS-related, and unknown.

Statistical Analysis

Baseline characteristics and outcomes of participants were presented as the median (interquartile range, IQR) or mean (standard deviation, SD) for continuous variables, and as counts and percentages for categorical variables. The primary outcome was time to death, with follow-up extending up to 90 days after enrollment. A multivariate regression model was built using variables with statistical significance (p values of <0.20 from the univariate model in an enter select method) and potential clinical relevance. Variables that maintained a p value of <0.05 in the final model were considered statistically significant. Survival analyses were performed using Kaplan-Meier curves with factors associated with 90-day mortality evaluated using Cox proportional hazard regression models for univariate and adjusted analyses. All statistical analyses were conducted using R version 4.3.1 software (R Foundation for Statistical Computing). For Kaplan-Meier survival curves and mortality rate estimation, the date of study entry and the time until the outcome of death were used.

RESULTS

A total of 419 participants were included in the study. The baseline characteristics of the cohort who were screened for opportunistic infections using point-of-care tests are presented in Table 1. Most patients had previous exposure to ART (68%), and 171 (58.2%) had abandoned treatment. The mean time from HIV diagnosis to study inclusion was 6 years (range, 0–35 years). A CD4 cell count of <200 cells/mm^3 was observed in 95% of participants, with a median count of 66 cells/mm^3. The median HIV viral load was 104,887 copies (5.02 log10).

TABLE 1. Baseline characteristics of this cohort study involving people living with HIV/AIDS in Brazil who were screened for opportunistic infections using point-of-care tests

	Total (*n* = 419)	Alive at day 90 (*n* = 306)	Dead at day 90 (*n* = 76)	Lost of follow-up (*n* = 37)	Missing data
Age (years)					0 (0.0%)
Mean (+ standard deviation)	44.7 (+12.6)	41.4 (+10.9)	45.4 (+12.3)	42.8 (+11.1)	
18–24	17 (4.1%)	12 (3.9%)	2 (2.6%)	3 (8.1%)	
25–49	289 (69.0%)	221 (72.2%)	43 (56.6%)	25 (67.6%)	
50+	113 (26.9%)	73 (23.9%)	31 (40.8%)	9 (24.3%)	
Skin color					4 (0.9%)
Black-brown	264 (63.6%)	192 (62.9%)	46 (62.2%)	26 (72.2%)	
White	151 (36.4%)	113 (37.1%)	28 (37.8%)	10 (27.8%)	
Income (US dollars)					132 (31.5%)
Median (Q1; Q3)	229.4 (229.4; 382.4)	252.3 (232.9; 394.9)	232.9 (135.8; 291.1)	232.9 (116.4; 465.8)	
Gender identification					0 (0.0%)
Cisgender man	230 (54.9%)	160 (52.3%)	52 (68.4%)	18 (48.7%)	
Cisgender woman	183 (43.7%)	140 (45.7%)	24 (31.6%)	19 (51.3%)	
Transgender woman	6 (1.4%)	6/6 (2.0%)	0 (0.0%)	0 (0.0%)	
Gender at birth					0 (0.0%)
Male	233 (55.6%)	163 (53.3%)	51 (67.1%)	19 (51.3%)	
Female	186 (44.4%)	143 (46.7%)	25 (32.9%)	18 (48.7%)	
Sexual orientation					34 (8.11%)
Heterosexual	317 (82.3%)	235 (82.5%)	51 (77.3%)	31 (91.2%)	
Homosexual	42 (10.9%)	29 (10.2%)	11 (16.7%)	2 (5.9%)	
Bisexual	19 (4.9%)	16 (5.6%)	12 (3.0%)	1 (2.9%)	
Other	7 (1.8%)	5 (1.7%)	2 (3.0%)	0 (0.0%)	
Education					0 (0.0%)
Incomplete elementary school	190 (45.3%)	141 (46.1%)	34 (44.7%)	15 (40.5%)	
Complete elementary school	108 (19.1%)	82 (26.8%)	17 (22.4%)	9 (24.3%)	
Complete middle school	96 (19.1%)	68 (22.2%)	21 (27.6%)	7 (18.9%)	
Graduation	25 (6.0%)	15 (4.9%)	4 (5.3%)	6 (16.2%)	
Comorbidities (e.g., diabetes, obesity)	280 (66.8%)	202 (66.0%)	53 (69.7%)	25 (67.6%)	0 (0.0%)
At least one of the OI screened	191 (45.6%)	143 (46.7%)	36 (47.4%)	12 (32.4%)	0 (0.0%)
Tuberculosis (TB)	143 (34.1%)	109 (35.6%)	23 (30.3%)	11 (29.7%)	0 (0.0%)
Histoplasmosis (Histo)	41 (9.8%)	30 (9.8%)	10 (13.2%)	1 (2.7%)	0 (0.0%)
Cryptococosis (Crypto)	52 (12.4%)	36 (11.8%)	16 (21.1%)	0 (0.0%)	0 (0.0%)
Multiple infections					
TB + Crypto	22 (5.3%)	18 (5.9%)	4 (5.3%)	0 (0.0%)	0 (0.0%)
TB + Histo	19 (4.5%)	11 (3.6%)	8 (10.5%)	0 (0.0%)	0 (0.0%)
Histo + Crypto	11 (2.6%)	8 (2.6%)	3 (3.9%)	0 (0.0%)	0 (0.0%)
Histo + TB + Crypto	7 (1.7%)	5 (1.6%)	2 (2.6%)	0 (0.0%)	0 (0.0%)
Psychiatric disorders	65 (23.5%)	53 (26.5%)	4 (7.6%)	8 (33.3%)	142 (33.9%)
Alcohol abuse	95 (34.3%)	66 (33.2%)	20 (37.7%)	9 (36.0%)	142 (33.9%)
Use of illicit drugs	128 (46.6%)	100 (50.5%)	16 (30.2%)	12 (50.0%)	144 (34.4%)
ART-naive	133 (31.8%)	89 (29.2%)	37 (48.7%)	7 (18.9%)	1 (0.2%)

ART: antirretroviral therapy; OI: opportunistic infection; Q1: first quartile; Q3: third quartile.
Source: Table prepared by the authors based on the study results.

Additionally, 221 (53%) participants had experienced at least one AIDS-defining condition prior to inclusion: 118 (28%) had TB, 83 (20%) had toxoplasmosis, 14 (3%) had cryptococcosis, 9 (2%) had histoplasmosis, 4 (1%) had lymphoma, and 1 (0.2%) had Kaposi sarcoma. During the study period, at least one OI was diagnosed in 191 (46%) patients, including TB (34%), cryptococcosis (12%), and histoplasmosis (10%). Among these, 157 (83%) had a positive point-of-care test: 106/131 (81%) had a positive TBLAM, 47/50 (94%) had a positive cryptococcal antigen, and 40/41 (99%) had a positive *Histoplasma* antigen.

A total of 76 (18%) participants died during the study. After 30 days of follow-up, 51 (12%) patients had died, and by 90 days, an additional 25 patients (6%) had died. Thirty-seven (9%) participants were lost to follow-up by the end of the study. Among these deaths, 66 (87%) were due to AIDS-related causes, 1 (1%) to possibly AIDS-related causes, 3 (4%)

to non-AIDS-related causes, and 6 (8%) to unknown causes. The factors associated with 90-day mortality, based on Cox multiple regression with univariate and adjusted analyses, are presented in Table 2. Interaction terms were assessed using binomial logistic regression for altered mental status, focal deficits, and headache; however, the interaction coefficients among these covariates were not statistically significant. Similarly, interaction terms were evaluated using binomial logistic regression for hemoglobin and ferritin, but the interaction coefficient between these covariates was also not statistically significant.

Male gender at birth and heterosexual orientation constituted the majority of the study participants. Neither gender, race, education level nor sexual orientation were associated with mortality.

TABLE 2. Cox proportional hazards model for factors associated with 90-day follow-up mortality

	Survival	Death	Crude HR (CI 95%)	*p* value	Adjusted HR (CI 95%)	*p* value
Skin color						
Black-brown	192/264 (72.7%)	46/264 7.4%)	1	0.684		
White	113/151 (74.8%)	28/151 (18.5%)	1.11 [0.67; 1.84]			
Gender identification						
Cisgender man	160/230 (69.6%)	52/230 (22.6%)	1.66 [1.01; 2.73]	0.047		
Cisgender woman	140/183 (76.5%)	24/183 (13.1%)	1			
Transgender woman	6/6 (100%)	0/6 (0.0%)	NA	0.995		
Gender at birth						
Male	163/233 (69.9%)	51/233 (21.9%)	1.56 [0.95; 2.0]	0.076		
Female	143/186 (76.9%)	25/186 13.4%)	1			
Sexual orientation						
Heterosexual	235/317 (74.1%)	51/317 (16.1%)	1			
Homosexual	29/42 (69.0%)	11/42 (26.2%)	1.72 [0.87; 3.40]	0.121		
Bisexual	16/19 (84.2%)	2/19 (10.5%)	0.65 [0.16; 2.66]	0.546		
Other	5/7 (71.4%)	2/7 (28.6%)	2.14 [0.52; 8.83]	0.291		
Education						
Incomplete elementary school	141/190 (74.2%)	34/190 (17.9%)	1			
Complete elementary school	82/108 (75.9%)	17/108 (15.7%)	0.82 [0.44; 1.52]	0.523		
Complete middle school	68/96 (70.8%)	21/96 (21.9%)	1.29 [0.73; 2.29]	0.343		
Graduation	15/25 (60.0%)	4/25 (16.0%)	1.24 [0.44; 3.52]	0.683		
Comorbidities						
No	104/139 (74.8%)	23/139 (16.6%)	1	0.684		
Yes	202/280 (72.1%)	53/280 (18.9%)	1.11 [0.67; 1.84]			
ART-naive						
No	216/285 (75.8%)	39/285 (13.7%)	1	0.002	1	0.010
Yes	89/133 (66.9%)	37/133 (27.8%)	2.10 [1.31; 3.38]		1.91 [1.17; 3.14]	
Previous OIs						
No	134/198 (67.7%)	43/198 (21.7%)	1	0.008		
Yes	172/221 (77.8%)	33/221 (14.9%)	0.52 [0.32; 0.84]			
Previous histoplasmosis						
No	297/410 (72.4%)	76/410 (18.5%)	1	0.995		
Yes	9/9 (100%)	0/9 (0.0%)	NA			
Previous cryptococcosis						
No	295/405 (72.8%)	73/405 (18.0%)	1	0.813		
Yes	11/14 (78.6%)	3/14 (21.4%)	0.84 [0.21; 4.44]			
Previous tuberculosis						
No	214/301 (71.1%)	60/301 (19.9%)	1	0.113		
Yes	92/118 (77.9%)	16/118 (13.6%)	0.62 [0.34; 1.12]			
Fever						
No	152/211 (72.0%)	42/211 (19.9%)	1	0.309		
Yes	153/207 (73.9%)	34/207 (16.4%)	0.78 [0.49; 1.26]			
Cough						
No	165/226 (73.0%)	43/226 (19.0%)	1	0.902		
Yes	140/192 (72.9%)	33/192 (17.2%)	0.97 [0.60; 1.56]			

(Continued)

TABLE 2. (Cont.)

	Survival	Death	Crude HR (CI 95%)	*p* value	Adjusted HR (CI 95%)	*p* value
Weight loss >10%						
No	140/181 (77.4%)	23/181 (12.7%)	1	0.041		
Yes	165/237 (69.6%)	53/237 (22.4%)	1.69 [1.02; 2.81]			
Night sweats						
No	219/306 (71.6%)	56/306 (18.3%)	1	0.964		
Yes	86/112 (76.8%)	20/112 (17.9%)	1.01 [0.60; 1.72]			
Mental confusion						
No	230/302 (76.2%)	44/302 (14.6%)	1	0.019	1	0.002
Yes	75/116 (64.7%)	32/116 (27.6%)	1.78 [1.10; 2.90]		2.33 [1.38; 3.93]	
Headache						
No	203/292 (69.5%)	60/292 (20.5%)	1	0.025		
Yes	102/126 (80.9%)	16/126 (12.7%)	0.50 [0.27; 0.92]			
Focal neurological signs						
No	268/359 (74.6%)	59/359 (16.4%)	1	0.018		
Yes	37/59 (62.7%)	17/59 (28.8%)	1.97 [1.12; 3.45]			
Gastrointestinal symptoms						
No	186/253 (73.5%)	41/253 (16.2%)	1	0.300		
Yes	119/165 (72.1%)	35/165 (21.2%)	0.78 [0.49; 1.25]			
Hemoglobin						
≥10.4	172/212 (81.1%)	22/212 (10.4%)	1	<0.001	1	< 0.001
<10.4	133/206 (64.6%)	54/206 (26.2%)	2.66 [1.57; 4.37]		3.89 [2.11; 7.16]	
Platelets	225 000 (143 000; 301 000)	186 500 (109 750; 72 500)	1 [1; 1]	0.731		
White blood cells	5 559 (3 555; 7 480)	5 740 (3 662; 7 745)	1.06 [1.01; 1.12]	0.033		
Ferritin	449.7 (218; 787)	578.4 (322.9; 980.6)	1.01 [1.01; 1.02]	0.017		
AST	30.5 (20; 53)	35.5 (25; 64.5)	1.00 [0.99; 1.01]	0.225		
ALT	26 (15; 45.5)	25.5 (17; 42.5)	0.99 [0.99; 1.00]	0.618		
Lactate dehydrogenase						
≤500	213/296 (71.9%)	52/296 (17.6%)	1	0.137		
>500	47/67 (70.1%)	18/67 (26.9%)	1.54 [0.87; 2.72]			
Creatinine						
≤2.4	283/378 (74.9%)	61/283 (16.1%)	1	<0.001	1	0.101
>2.4	7/23 (30.4%)	14/23 (60.9%)	5.60 [3.10; 10.11]		1.52 [0.92; 2.50]	
Opportunistic diseases						
No	163/228 (71.5%)	40/228 (17.5%)	1	0.681		
Yes	143/191 (74.9%)	36/191 (18.8%)	1.10 [0.69; 1.78]			
CNS cryptococcosis						
No	294/399 (73.7%)	68/399 (17.0%)	1	0.018		
Yes	12/20 (60.0%)	8/20 (40.0%)	1.99 [1.13; 3.55]			
Severe histoplasmosis						
No	288/392 (73.5%)	67/392 (17.1%)	1	0.015		
Yes	17/26 (65.4%)	9/26 (34.6%)	2.40 [1.19; 4.83]			

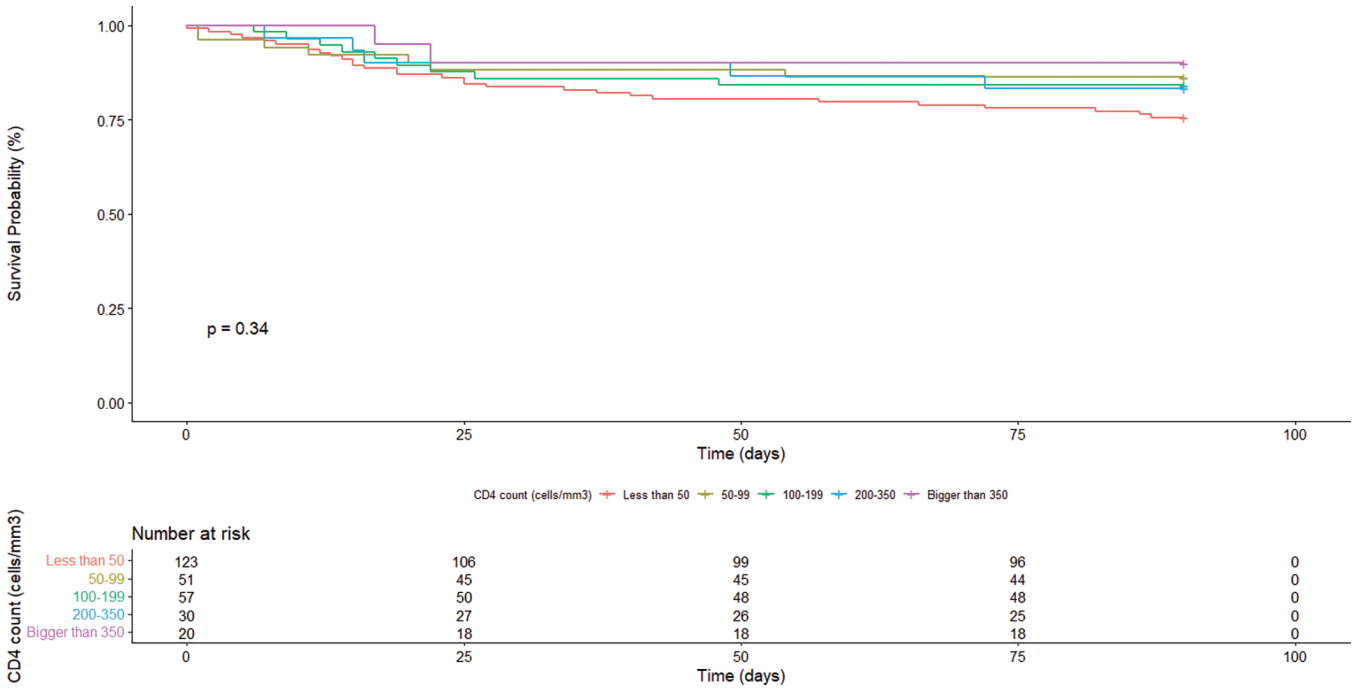
ALT: alanine aminotransferase; ART: antiretroviral therapy; AST: aspartate aminotransferase; CI: confidence interval; CNS: central nervous system; HR: hazard rate; NA: not applicable; OI: opportunistic infection.
Source: Table prepared by the authors based on the study results.

Although sexual orientation was significantly associated in the univariate analysis, it did not remain significant in the final Cox regression model. Variables such as income, psychiatric disorders, excessive alcohol consumption, and illicit drug use were excluded from the final analyses due to high levels of missing data.

ART-naive status was strongly associated with mortality and remained in the final Cox regression model (adjusted hazard rate 1.91 [95% confidence interval 1.17–3.14]; $p = 0.010$). A previous diagnosis of OI was not associated with mortality. Among the symptoms reported at study recruitment, weight loss >10%, focal deficits, and altered mental status were associated with mortality in univariate analysis, but only altered mental status remained in the final model (adjusted hazard rate 2.33 [95% confidence interval 1.38–3.93]; $p = 0.002$).

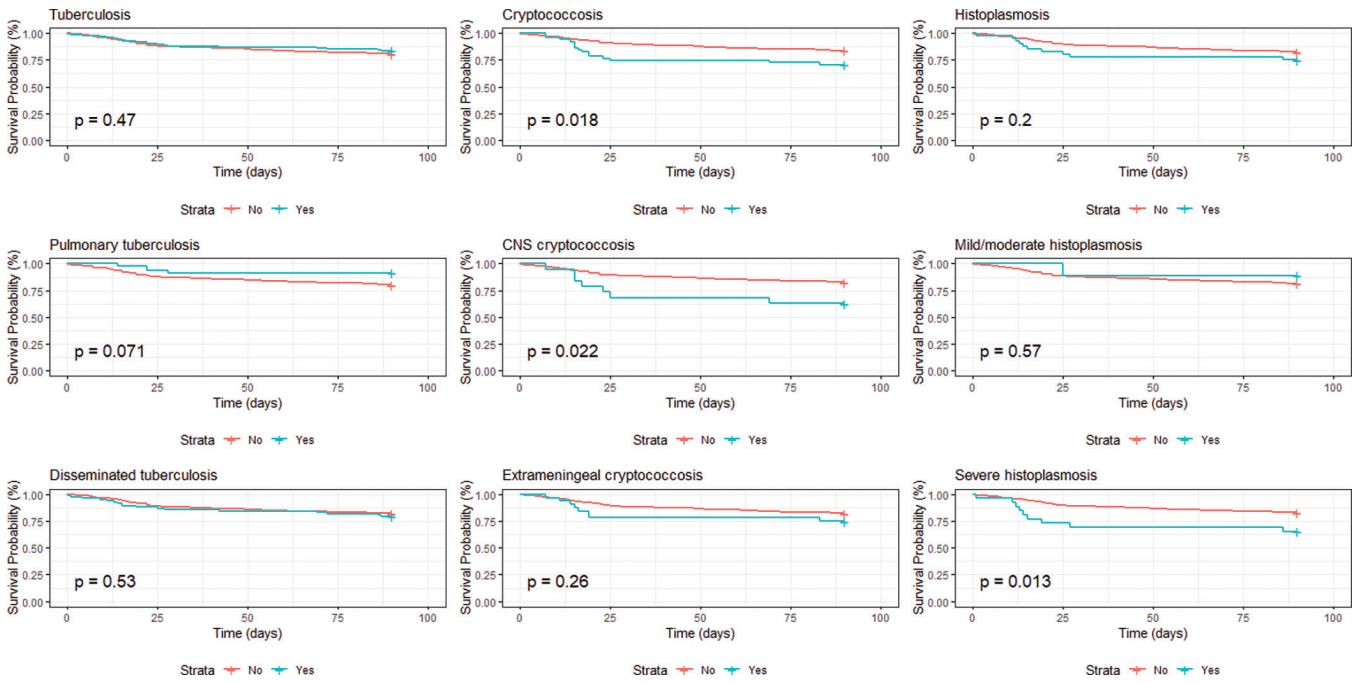
Participants with a CD4 count of <50 cells/mm^3 showed a higher probability of death throughout the study, although this was not statistically significant ($p = 0.34$) (Figure 1).

FIGURE 1. Probability of survival according to CD4 intervals



Source: Original figure created for this article.

FIGURE 2. Probability of survival according to each opportunistic infection



Source: Original figure created for this article.

Regarding laboratory tests, the median hemoglobin level among surviving patients was 10.4 g/dL, and lower values were strongly associated with mortality ($p < 0.001$). Similarly, creatinine levels more than twice the upper limit of normal were also strongly associated with mortality in the final model.

A diagnosis of TB, whether pulmonary or extrapulmonary, during the study had no significant impact on patient mortality. However, patients diagnosed with severe histoplasmosis and cryptococcal meningitis had significantly higher mortality rates over the course of the study with $p = 0.0063$ and $p = 0.012$, respectively (Figure 2).

DISCUSSION

This study included 419 individuals with HIV who were not on effective ART, screened for the three most common OIs, and followed up at 30 and 90 days in tertiary hospitals in Brazil. During the follow-up period, 76 participants died. The factor most strongly associated with mortality was being ART-naive, and other indicators of severe illness, such as anemia, elevated creatinine levels (more than twice the upper limit of normal), and altered mental status, also contributed to the higher mortality risk. Many social determinants, including sex, race, gender, sexual orientation, and education level, were not directly associated with mortality in this study. However, a high proportion of missing data on certain demographic variables, combined with the predominance of self-reported brown/black ethnicity and low education levels in the sample, made it difficult to fully assess the impact of these factors on mortality.

Despite the gradual decline in HIV/AIDS-related mortality in Brazil, the epidemic is currently concentrated in vulnerable populations (8). In Porto Alegre, 26% of the population self-identify as brown and black (13); however, in this study, these ethnicities accounted for 64% of patients admitted for HIV/AIDS-associated conditions. Additionally, low education levels impact health care access, underscoring the need for public policies that more effectively target vulnerable populations (14). While the study did not demonstrate a direct association between low educational levels and mortality, the high proportion of participants with limited education suggests the broader impact of socioeconomic factors on health outcomes.

A significant proportion of patients in this study (32%) were recently diagnosed, and the majority (95%) had a CD4 count of <200 cells/mm^3, indicating that both naive and re-engaged patients were entering the health care system at an advanced stage of disease. This delay hinders the individual and community benefits of the "test and treat" strategy (15). ART-naive status was strongly associated with mortality, a finding consistent with another study showing that patients unaware of their HIV status had an increased risk of death compared to those already diagnosed (16). These results highlight the need to improve public health actions to expand early HIV diagnosis, particularly among vulnerable populations.

Among participants who had already received ART in the past (68%), 59% had abandoned treatment, with a mean time of abandonment of 8 months. Another 9.6% were irregular users with unsuppressed viral loads. These findings underscore the importance of implementing systemic outreach strategies, as recommended by the WHO (17, 18), to re-engage individuals who have disengaged from care.

Nearly half of the participants (46%) had at least one of the screened OIs. While TB and histoplasmosis were not significantly associated with worse survival outcomes in the multivariate analysis, cryptococcosis and altered mental status were strongly associated with mortality. Meningeal cryptococcosis is a leading cause of death in patients with OIs involving the central nervous system (19). This is in accordance with our findings, considering that meningeal cryptococcosis led to death in 40% of patients in this study who had an OI, the lowest survival rate during follow-up. A similar scenario is observed on the African continent, where high HIV infection rates, late access to health care, low retention rates, and OIs such as TB and cryptococcal meningitis are strongly associated with mortality (20).

This study has several limitations, including missing data due to incomplete case report forms. The findings of this study may not be representative of the broader Brazilian population, as four of the five participating hospitals were located in Porto Alegre and one in Goiânia, limiting the generalizability of the results to other regions or populations. Additionally, 9% (37/419) of participants were lost to follow-up by 90 days. Many of these patients faced significant social vulnerabilities, such as alcohol and illicit drug abuse, and a large proportion was homeless; however, due to missing data, it was not possible to assess the correlation between these factors and ART nonadherence or mortality. As a result, the overall mortality rate in our study may be underestimated. Previous research has demonstrated that adjusting mortality estimates to account for those lost to follow-up can provide a more accurate assessment of the outcomes of care programs for people living with HIV/AIDS (21).

Despite these limitations, the study provides a comprehensive assessment of HIV care in Brazilian hospitals. The findings offer valuable insights into the risk factors associated with mortality. To reduce mortality among people living with HIV/AIDS, it is crucial to incorporate new diagnostic tools for detecting OIs and to enhance initiatives aimed at screening and early diagnosis of HIV infections, particularly among vulnerable populations, facing barriers to greater health care access. Investment in social programs aimed at reducing inequalities and empowering individuals to manage their health are also essential for improving retention in care and treatment adherence.

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Factores predictivos de la mortalidad en personas con infección avanzada por el VIH en una cohorte brasileña contemporánea

RESUMEN

Objetivo. Determinar las características clínicas y los factores de riesgo asociados a la mortalidad, en especial por lo que respecta a las infecciones oportunistas, en pacientes con infección avanzada por el virus de la inmunodeficiencia humana (VIH) en Brasil.

Método. Se realizó un estudio prospectivo de cohorte en cinco hospitales terciarios brasileños, con la inclusión de 419 personas adultas con infección avanzada por el VIH. Se recopilaron los datos demográficos y clínicos iniciales durante el ingreso hospitalario, y se realizó un tamizaje para la detección de tuberculosis, criptococosis e histoplasmosis en todos los participantes mediante pruebas de diagnóstico rápido. Se llevó a cabo un seguimiento durante 90 días para evaluar la mortalidad; se clasificaron las causas de muerte mediante el protocolo de codificación de causas de muerte en la infección por el VIH (CoDe). El análisis estadístico determinó las variables asociadas a la mortalidad.

Resultados. La mediana del recuento de linfocitos CD4 fue de 66 linfocitos/mm^3 y la mediana de la carga viral del VIH fue de 104 887 copias/ml. Después de 90 días, el 18,1% de los participantes había fallecido. Se observó una asociación intensa de los siguientes factores con la mortalidad: el hecho de no haber recibido ningún tratamiento antirretroviral anteriormente, la confusión mental, la anemia y los niveles elevados de creatinina. En el 45,6% de los participantes se diagnosticaron infecciones oportunistas, y la meningitis criptocócica y la histoplasmosis grave se asociaron a un aumento significativo de la mortalidad. Los determinantes sociales, como el sexo, la etnia, el género y el nivel de estudios, no tuvieron un impacto significativo en la mortalidad, pero los factores socioeconómicos influyeron en el acceso a la atención de salud.

Conclusiones. El diagnóstico temprano de la infección por el VIH y el tratamiento antirretroviral continuado son esenciales para reducir la mortalidad. Las estrategias de salud pública deben priorizar la mejora de las pruebas de detección del VIH, la adhesión al tratamiento y el abordaje de las desigualdades sociales para mitigar las inequidades en la atención de salud.

Palabras clave VIH; infecciones oportunistas relacionadas con el SIDA; pruebas en el punto de atención; mortalidad; factores de riesgo.

Preditores de mortalidade em indivíduos com doença avançada pelo HIV em uma coorte contemporânea brasileira

RESUMO

Objetivo. Identificar as características clínicas e os fatores de risco associados à mortalidade, com ênfase nas infecções oportunistas, em pacientes com doença avançada pelo HIV no Brasil.

Métodos. Um estudo de coorte prospectivo foi realizado em cinco hospitais terciários brasileiros, incluindo 419 adultos com doença avançada pelo HIV. Os dados demográficos e clínicos para a linha de base foram coletados durante a internação hospitalar dos participantes, que foram rastreados para tuberculose, criptococose e histoplasmose por meio de testes de diagnóstico rápido. Os participantes foram acompanhados por 90 dias para avaliar a mortalidade, e as causas de morte foram classificadas segundo o protocolo *Coding Causes of Death in HIV* (CoDe). A análise estatística identificou as variáveis associadas à mortalidade.

Resultados. A mediana da contagem de linfócitos T CD4+ foi de 66 células/mm^3, e a mediana da carga viral de HIV foi de 104 887 cópias/mL. Após 90 dias, 18,1% dos participantes tinham falecido. Ser virgem de terapia antirretroviral (TARV) ou ter confusão mental, anemia ou níveis elevados de creatinina foram fatores fortemente associados à mortalidade. Foram diagnosticadas infecções oportunistas em 45,6% dos participantes, e quadros graves de histoplasmose e meningite criptocócica aumentaram significativamente o risco de morte. Determinantes sociais, como sexo, raça, gênero e escolaridade, não tiveram um impacto significativo na mortalidade, mas fatores socioeconômicos tiveram influência sobre o acesso à atenção à saúde.

Conclusão. O diagnóstico precoce do HIV e a TARV ininterrupta são essenciais para reduzir a mortalidade. As estratégias de saúde pública devem priorizar o aprimoramento da testagem de HIV, a adesão ao tratamento e a abordagem das disparidades sociais de modo a mitigar as desigualdades na atenção à saúde.

Palavras-chave HIV; infecções oportunistas relacionadas com a AIDS; testes imediatos; mortalidade; fatores de risco.