10.18606/2318-1419/amazonia.sci.health.v13n1p111-125

ARTIGO ORIGINAL

<< Recebido em: 01/05/2025 Aceito em: 15/08/2025 >>

REVISTA AMAZÔNIA Science & Health ISSN: 2318-1419

One in Four Hospitalized HIV Patients Dies in the Brazilian Amazon: A Five-Year Analysis of Letality and its Associated Factors

Letalidade Hospitalar entre pacientes infectados pelo HIV na Amazônia Brasileira: um estudo retrospectivo de cinco anos

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ABSTRACT

Objective: To analyze the clinical and epidemiological risk factors associated with Hospital Case Fatality Rate (HCFR) among HIV/AIDS patients hospitalized at João de Barros Barreto University Hospital (HUJBB) between 2018 and 2022 in the city of Belém, Pará. **Methods:** The study analyzed medical records of patients hospitalized with a principal diagnosis of HIV (ICD-10 B24). The HCFR was calculated, and associations between patient characteristics and outcomes were assessed using Pearson's chi-square test. **Results:** Among 569 cases analyzed, the overall HCFR was 28.12% (95% CI: 24.47%–31.96%). Most patients were male (63.09%) between 31 and 50 years of age. Among the 330 with recorded anamnesis, “Irregular use” or “discontinuation of Antiretroviral Treatment (ART)” was reported in 31.52% of admissions. CD4+ lymphocyte counts ≤200 cells/mm³ were significantly associated with higher fatality rate (OR = 7.25; 95% CI: 1.52–34.54; p = 0.006). Symptoms during admission most strongly associated with death were dyspnea (41.9%), cough (32.7%), and fever (27.3%). The main causes of death were HIV-related complications (B24), sepsis, and respiratory failure. **Conclusions:** The 28.12% HCFR, with fatality strongly associated with CD4+ counts ≤200 cells/mm³ (OR=7.25, p=0.006) and prevalent irregular ART use (31.52%), underscores the critical need for enhanced ART adherence, early diagnosis, and robust outpatient follow-up to mitigate HIV-related hospital fatalities in the Brazilian Amazon

Keywords: Antiretroviral Therapy, Highly Active. Fatal Outcome. AIDS-Related Opportunistic Infections. CD4 Lymphocyte Count. Medication Adherence

RESUMO

Objetivo: Analisar os fatores de risco clínicos e epidemiológicos relacionados à Taxa de Letalidade Hospitalar (TLH) de pacientes com HIV/AIDS internados no Hospital Universitário João de Barros Barreto (HUJBB), no período de 2018 a 2022, na cidade de Belém, Pará. **Métodos:** O estudo analisou prontuários de pacientes internados com diagnóstico principal de HIV (CID-10 B24). A TLH foi calculada, e associações entre características dos pacientes e desfechos foram analisadas por meio do teste qui-quadrado de Pearson. **Resultados:** Entre 569 casos analisados, a TLH geral foi de 28,12% (IC 95%: 24,47%–31,96%). A maioria dos pacientes era do sexo masculino (63,09%), com idade entre 31 e 50 anos. Entre os 330 com anamnese registrada, o “Uso irregular” ou “abandono da TARV” foi relatado em 31,52% das internações. Contagens de linfócitos CD4+ ≤200 células/mm³ estiveram significativamente associadas à maior letalidade (OR = 7,25; IC 95%: 1,52–34,54; *p* = 0,006). Os sintomas durante a admissão mais associados ao óbito foram dispneia (41,9%), tosse (32,7%) e febre (27,3%). As principais causas de morte foram complicações relacionadas ao HIV, sepse e insuficiência respiratória. **Conclusões:** A TLH de 28,12%, com letalidade fortemente associada a contagens de CD4+ ≤200 células/mm³ (OR=7,25, p=0,006) e o uso irregular da TARV (31,52%), evidenciam que a adesão à TARV, o diagnóstico precoce e o acompanhamento ambulatorial contínuo são essenciais para reduzir a letalidade hospitalar por HIV/AIDS na Amazônia Brasileira.

Palavras-chave: Terapia Antirretroviral de Alta Atividade. Evolução Fatal. Infecções Oportunistas Relacionadas com a AIDS. Contagem de Linfócito CD4. Adesão à Medicação.

1. INTRODUCTION

The Human Immunodeficiency Virus (HIV) poses a significant global and national public health challenge. In 2023, an estimated 39.9 million people worldwide were living with HIV (PLHIV). In Brazil, 541,759 cases were reported between June 2007 and June 2024. The North region accounted for 10.4% of these diagnoses[1]. Despite significant national efforts to control the epidemic, marked regional disparities persist, particularly in the Brazilian Amazon region, underscoring the complex and evolving nature of the fight against HIV/AIDS.

HIV belongs to the *Retroviridae* family, genus *Lentivirus*, and primarily targets the human immune system by infecting CD4+ T lymphocytes and other cells, mediated by viral glycoproteins interacting with cellular receptors like CD4 and CCR5. This progressive depletion of immune cells leads through distinct stages of infection, culminating in Acquired Immunodeficiency Syndrome (AIDS). AIDS is marked by profound immunodeficiency and severe susceptibility to opportunistic infections and life-threatening complications affecting multiple organ systems[2–4].

Faced with a growing epidemic and high mortality in the 1980s, Brazil implemented a comprehensive and groundbreaking response. A cornerstone of this strategy was the establishment of universal and free access to Antiretroviral Therapy (ART) through the Unified Health System (SUS), solidified by Law 9.313/96. This policy dramatically improved outcomes for people living with HIV, positioning Brazil as a global model for equitable access to treatment and care[2,3,5].

Despite these national successes, however, significant challenges and disparities persist, particularly in the Brazilian Amazon. The North region continues to exhibit high rates of HIV/AIDS detection[1], and concerningly, has shown a rising trend in hospitalizations for HIV/AIDS cases, contrasting with national decreases[6]. This regional burden is compounded by structural barriers to accessing consistent care, such as geographical distances in vast territories and insufficient infrastructure, contributing to delayed diagnosis, presentation at advanced stages, and challenges with ART adherence[7]. These factors collectively impact patient outcomes and contribute to severe disease requiring hospitalization.

Located within this challenging regional context, the João de Barros Barreto University Hospital (HUJBB) in Belém serves as a key reference center for infectious diseases, managing a significant number of people living with HIV. However, like many facilities in the region, it faces substantial pressures, including demand exceeding capacity

and difficulties in providing timely access to patients from remote areas who often present with advanced disease[4,8]. Understanding the factors associated with severe outcomes in this high-burden hospital setting is crucial. Therefore, this study aims to analyze clinical and epidemiological factors associated with case fatality among individuals hospitalized with HIV/AIDS at HUJBB between 2018 and 2022, providing critical insight into the drivers of severe disease in this vulnerable population within the Brazilian Amazon.

2. METHODS

This observational study, primarily descriptive in nature, aimed to analyze the hospital case fatality rate among patients hospitalized with HIV (ICD-10 B24) as the principal diagnosis at the João de Barros Barreto University Hospital (HUJBB), located in the Amazon region of Brazil, in the municipality of Belém, state of Pará. Data collection was conducted through a retrospective chart review of patients hospitalized between January 2018 and December 2022.

Inclusion criteria were charts of patients hospitalized with HIV (ICD-10 B24) as the principal diagnosis during the study period. Exclusions were repeated chart entries, patients transferred to other facilities, charts lacking documented discharge/admission records, patients who left against medical advice, hospitalizations discontinued due to non-adherence to hospital protocols, and voluntary discontinuation of treatment.

Data were collected independently by two researchers and compared after collection to ensure consistency and accuracy. Discrepancies were resolved by a third researcher. Data were classified into three groups: a) identification (chart number, name initials, date of birth, mother's name initials, date of hospitalization, outcome); b) hospital admission (time since diagnosis, symptoms, illicit substance use, alcohol use, tobacco use, treatment history from admission text); c) death (principal, secondary, direct, contributing, underlying causes from clinical summary).

According to the Ministry of Health criteria, individuals are considered to have experienced abandonment of treatment for HIV if they: I) did not pick up antiretroviral medications within three months after the scheduled date; or II) did not return for medical appointments within six months[9]. Due to the urgent nature of the hospital service and the inherent limitations imposed on the admission consultation, for the purposes of this study, patients were considered to meet the criteria for HIV treatment abandonment if they: met the Ministry of Health criteria, confirmed by the description of dates in the admission text; or

were actively described in the admission text as having abandoned treatment by the admitting physician. Irregular ARV use was defined as consistently erratic use reported, differing from prescription.

Data were compiled into an Excel 2010 spreadsheet. Statistical calculations used Minitab version 22.2. Hospital case fatality rate was calculated by dividing deaths by total hospitalizations with ICD-10 B24. Due to sample size variability, the 95% confidence interval was calculated using the adjusted Blaker's exact method[10].

To analyze death distribution and case fatality rate associations, Pearson's chi-square test was used ($p < 0.05$ considered significant). For significant associations, the Phi (Φ) effect size was calculated[11]. Recommended requirements and interpretations from the scientific community[11] and the statistical software itself[12] were adopted. For variables with an expected count less than 5, the chi-square test was not calculated.

All ethical and legal aspects recommended by Resolution No. 510/16 of the National Health Council were respected. This study adheres to all guidelines of the Declaration of Helsinki and the data confidentiality procedures previously described in the project submitted to the Research Ethics Committee (CEP). Prior to the start of data collection, approval was obtained from the Research Ethics Committee under the following Certificate of Presentation of Ethical Appreciation (CAAE): 76440023.5.0000.5174.

3. FINDINGS

Between 2018 and 2022, 605 patients were hospitalized with HIV (ICD-10 B24) as the principal diagnosis. Of these, 10 had no discharge or admission record available in the electronic record, 2 voluntarily discontinued treatment, 1 left against medical advice, 11 whose hospitalization was discontinued due to non-adherence with hospital regulations or treatment protocols, and 12 were transferred to another hospital. These records were excluded from this study. After excluding these cases, 569 records remained for analysis. Among these, 330 (58%) had an admission record in the electronic record, and 561 (98.59%) had a discharge or death summary

There was a higher predominance of males (359; 63.09%) compared to females (199; 34.97%) among hospitalized patients. Common age groups were 21-30 (126; 22.14%), 31-40 (191; 33.57%), and 41-50 years (130; 22.85%). No significant difference was found in the distribution of deaths between sexes [$X^2(2) = 0.01$; $p = 0.921$] or between age groups ≥ 21 years [$X^2(4) = 2.882$; $p = 0.588$]. The Pearson's chi-square test could not be calculated

for the age group below 21 years due to the low sample size (n = 22). The hospital case fatality rate for HIV hospitalizations between 2018 and 2022 was 28.12% (95% CI: 24.47%-31.96%). The fatality rate stratified by sex and age is described in Table 1.

Table 1. Hospital Case Fatality Rate for Patients Hospitalized with HIV at the João de Barros Barreto University Hospital (2018-2022), Stratified by Recorded Sex and Age Group.

Variables	Outcome		p-value*	Hospital Case Fatality Rate	
	Death	Discharge		Rate	95% CI† (lower - upper)
Admission Record Status			-		
Not available in electronic record	73	171		29.92%	(24.29%-36.01%)
Available in electronic record	92	238		27.88%	(23.16%-32.98%)
Discharge/Death Summary Status			-		
Not available in electronic record	3	5		37.50%	(11.11%-71.08%)
Available in electronic record	157	404		27.99%	(24.38%-31.88%)
Sex	-	-	**0.921**	-	-
Male	99	260		27.58%	(23.05%-32.40%)
Female	57	142		28.64%	(22.48%-35.36%)
Sex Not Recorded	4	7		36.36%	(13.51%-66.71%)
Age Group (≤20 years)			-		
< 10 years	0	13		0.00%	(0.00%-22.51%)
10 - 15 years	0	3		0.00%	(0.00%-63.16%)
16 - 20 years	3	3		50.00%	(15.32%-84.68%)
Age Group (>20 years)			**0.588**		
21 - 30 years old	35	91		27.78%	(20.43%-36.41%)
31 - 40 years old	53	138		27.75%	(21.59%-34.48%)
41 - 50 years old	42	88		32.31%	(24.43%-40.76%)
51 - 60 years old	15	52		22.39%	(13.78%-34.11%)
> 60 years old	9	14		39.13%	(20.71%-61.34%)
Age Not Recorded	3	7		30.00%	(8.73%-61.94%)
Total	**160**	**409**		**28.12%**	**(24.47%-31.96%)**

95% CI - 95% confidence interval
* Pearson's Chi-square test for association.
† Calculated using the adjusted Blaker's exact method

Approximately 90% of the admissions recorded in the electronic record refer to the years 2020 to 2022. From these admissions, the characteristics history and symptoms presented by patients on the first day of hospitalization were extracted. Of the 330 patients with a recorded admission, 98 (29.70%) had received an HIV diagnosis more than 1 year before hospitalization, 96 (29.09%) were diagnosed within the 3 months preceding hospitalization, and 15 (4.55%) were diagnosed between 3 months and 1 year. Only 22 (6.67%) patients did not report a confirmed HIV serological diagnosis upon hospitalization.

In addition, 66 (20.00%) patients had a history of previous ARV non-adherence, with 35 of these related to the last prescribed treatment, and 38 (11.52%) patients reported irregular ARV use. In 84 (25.45%) admissions, there was no mention of ARV medication, and in 40 (12.12%), there was no information on the regularity of ARV use. Only 68 (20.61%) patients reported regular medication use.

Table 2. Hospital case fatality rate among individuals hospitalized with HIV at João de Barros Barreto University Hospital between 2018 and 2022, stratified by time since diagnosis and ART history (n = 330).

Variables	Deaths	Discharges	Total	(%)	p-value*	Hospital Case Fatality Rate	
						Rate	95% CI† (Lower - Upper)
Number of admissions reviewed	92	238	330	100.00%	-	27.88%	(23.16% - 32.98%)
Time since HIV diagnosis					**0.649**		
> 1 year before admission	26	72	98	29.70%		26.53%	(18.50%-36.10%)
> 3 months and < 1 year before admission	5	10	15	4.55%		33.33%	(14.17%-60.62%)
Within 3 months before admission	25	71	96	29.09%		26.04%	(17.95%-35.80%)
Undated HIV diagnosis	32	67	99	30.00%		32.32%	(23.50%-42.35%)
No mention of HIV diagnosis/suspicion	4	18	22	6.67%		18.18%	(6.46%-38.90%)
History of previous ART non-adherence					**0.667**		
Yes	17	49	66	20.00%		25.76%	(16.25%-37.71%)
No	75	189	264	80.00%		28.41%	(23.30%-34.36%)
Current ART status					**0.928**		
Reports current ART non-adherence (discontinued)	10	25	35	10.61%		28.57%	(14.76%-45.61%)
Reports irregular ART use	11	27	38	11.52%		28.95%	(16.46%-45.30%)
Reports regular ART use	18	50	68	20.61%		26.47%	(16.91%-38.09%)
Has not initiated ART	14	29	43	13.03%		32.56%	(19.15%-47.63%)
ART use mentioned, regularity not specified	10	30	40	12.12%		25.00%	(12.90%-41.04%)
No mention of ART	25	59	84	25.45%		29.76%	(20.52%-40.38%)
No mention of HIV diagnosis/suspicion	4	18	22	6.67%		18.18%	(6.46%-38.90%)

95% CI - 95% confidence interval
* Pearson's Chi-square test for association.
† Calculated using the adjusted Blaker's exact method

Table 2 shows the hospital CFR stratified by time since diagnosis, history of non-adherence, and current ART status. No significant difference in death distribution was observed based on time since diagnosis [$X^2(4) = 2.473$; $p = 0.649$], history of previous non-adherence [$X^2(1) = 0.185$; $p = 0.667$], or current ARV medication use [$X^2(5) = 1.907$; $p = 0.928$].

Regarding reported substance use histories, 73 (22.12%) patients had a history of alcohol use disorder, with 38 (11.52%) reporting current alcohol use until the date of hospitalization. Regarding tobacco use, 47 (14.24%) patients had a history of tobacco use,

including 2 passive smokers, and 18 (5.45%) reported current use until the time of hospitalization. A history of substance use was present in 44 (13.33%) patients, with cannabis being the most frequent substance (6.67%), followed by cocaine (3.64%), oxi (2.73%), and crack (2.42%). Other unspecified substances were also described (3.33%). However, only 35 (10.61%) records explicitly denied the use of illicit substances, while 251 (76.06%) did not mention its use.

Table 3. Hospital Case Fatality Rate among individuals hospitalized with HIV at João de Barros Barreto University Hospital between 2018 and 2022, stratified by history of alcohol, tobacco, and substance use (n = 330)

						Hospital Case Fatality Rate	
Variables	**Discharges**	**Deaths**	**Total**	**(%)**	**p-value***	**Rate**	**95% CI† (Lower - Upper)**
History of alcohol use					**0.255**		
Yes	57	16	73	21.12%		21.92%	(13.08%-33.14%)
No	181	76	257	85.66%		29.57%	(24.06%-35.56%)
Current alcohol use					**0.167**		
Yes	31	7	38	11.52%		18.42%	(8.37%-33.83%)
No	207	85	292	88.48%		29.11%	(24.06%-34.54%)
History of tobacco use (active or passive)					**0.073**		
Yes	39	8	47	14.24%		17.02%	(7.83%-30.48%)
No	199	84	283	85.76%		29.68%	(24.48%-35.29%)
Current tobacco use					**0.242**		
Yes	15	3	18	5.45%		16.67%	(4.70%-41.20%)
No	181	76	257	77.88%		29.57%	(24.23%-35.55%)
History of substance use					**0.155**		
Explicitly denies substance use	30	5	35	10.61%		14.29%	(5.80%-29.50%)
No mention regarding use	176	75	251	76.06%		29.88%	(24.41%-35.81%)
Reported use	32	12	44	13.33%		27.27%	(15.19%-41.90%)
Specification of substances used**					**-**		
Cannabis	16	6	22	6.67%		27.27%	(12.60%-50.00%)
Cocaine	9	3	12	3.64%		25.00%	(7.19%-54.44%)
Oxi	6	3	9	2.73%		33.33%	(9.77%-68.39%)
Crack	6	2	8	2.42%		25.00%	(4.64%-64.14%)
Other unspecified	7	4	11	3.33%		36.36%	(13.51%-66.71%)

95% CI - 95% confidence interval
* Pearson's Chi-square test for association.
** Multiple responses were permitted; therefore, columns are not mutually exclusive and their sum may exceed the total N.
† Calculated using the adjusted Blaker's exact method

Table 3 presents the hospital case fatality rate stratified by history and current alcohol use, tobacco use, and use of illicit substances. No significant difference in death distribution was found between history of alcohol use disorder [$X^2(1) = 1.298$; $p = 0.255$], current alcohol use [$X^2(1) = 1.911$; $p = 0.167$], history of tobacco use [$X^2(1) = 3.213$; $p = 0.073$], current tobacco use [$X^2(1) = 1.368$; $p = 0.242$], and history of illicit substances [$X^2(2) = 3.725$; $p = 0.155$]. Chi-square for substance specification was not calculated due to low sample size.

Table 4. Hospital Case Fatality Rate among individuals hospitalized with HIV at João de Barros Barreto University Hospital between 2018 and 2022, by Viral Load and CD4 Count at admission.

Variables	Deaths	Discharges	Total	(%)	Hospital Case Fatality Rate	
					Rate (%)	95% CI†
Viral Load (copies/mL)	14	45	59	100%	23.73%	(13.86% - 36.23%)
<500	3	7	10	17%	30.00%	(8.73% - 61.94%)
500 to < 1000	2	0	2	3%	100.00%	(22.36% - 100.00%)
1000 to < 10000	1	2	3	5%	33.33%	(1.70% - 86.46%)
10000 to < 50000	0	5	5	8%	0.00%	(0.00% - 50.00%)
50000 to < 100000	0	5	5	8%	0.00%	(0.00% - 50.00%)
≥ 100000	8	26	34	58%	23.53%	(11.35% - 40.93%)
CD4 Count (cells/mm³)	17	59	76	100%	22.37%	(13.95% - 33.34%)
<100	12	18	30	39%	40.00%	(23.63% - 58.57%)
100-200	3	12	15	20%	20.00%	(5.68% - 46.47%)
200-350	1	11	12	16%	8.33%	(0.43% - 36.58%)
>350 - 500	0	5	5	7%	0.00%	(0.00% - 50.00%)
> 500	1	13	14	18%	7.14%	(0.37% - 31.22%)

Variables	Deaths	Discharges	p-value*	Phi (Φ)	Odds Ratio (OR)	
					Coefficient	95% CI
Viral Load (copies/mL)						
≥ 100000	8	26	0.967	< 0.001	0.97	(0.29 - 3.28)
< 100000	6	19	-	-	-	-
CD4 Count (cells/mm³)						
≤ 200	15	30	0.006	0.317	7.25	(1.52 - 34.54)
> 200	2	29	-	-	-	-

Variables	Time Interval Between Test Result and Hospitalization				
	≤ 1 month	> 1 month to 5 months	> 5 months to 1 year	> 1 year	UTR
Viral Load (copies/mL)	13	25	7	7	7
<500	1	5	2	1	1
500 to < 1000	0	0	0	1	1
1000 to < 10000	0	0	0	1	2
10000 to < 50000	2	1	1	1	0
50000 to < 100000	0	2	1	2	0
≥ 100,000	10	17	3	1	3
CD4 Count (cells/mm³)	12	25	7	6	26
< 100	6	12	5	2	5
100-200	1	6	2	1	5
> 200-350	2	7	0	1	2
> 350 - 500	2	0	0	1	2
> 500	1	0	0	1	12

UTR - Undated Test Results
95% CI - 95% confidence interval
* Pearson's Chi-square test for association.
† Calculated using the adjusted Blaker's exact method

Considering the confidence interval limits (Blaker's exact method), higher fatality was observed among patients with recorded viral load ≥ 500 to < 1,000 copies/mL (100%; 95% CI 22.36% - 100%) and ≥ 100,000 (23.53%; 95% CI 11.35% - 40.93%). Similarly, higher fatality was observed among patients with recorded CD4+ counts < 100 cells/mm³ (40%; 95% CI 23.63% - 58.57%) and 100-200 cells/mm³ (20%; 95% CI 5.68% - 46.47%). The majority of CD4+ (48.68%) and viral load (64.41%) test results were issued within 5 months of the admission date. Table 4 presents in-hospital lethality according to viral load and CD4+ count at admission.

On admission, 59 patients had viral load (VL) testing available, and 76 had CD4+ lymphocyte count testing. A moderate association of higher in-hospital case fatality rate was observed among patients with CD4 ≤ 200 compared to those with CD4 > 200 [$X^2(1) = 7.638$; $p = 0.006$; $\Phi = 0.317$]. Specifically, the odds ratio for death for patients with CD4 ≤ 200 was 7.25 (95% CI 1.52 - 34.54). There was no difference in in-hospital case fatality rate between patients with viral load ≥ 100,000 and < 100,000 copies [$X^2(1) = 0.002$; $p = 0.967$].

There was no significant difference between patients who had CD4 [$X^2(1) = 0.086$; $p = 0.769$] or viral load [$X^2(1) = 0.615$; $p = 0.433$] values available on admission compared to those who did not. There was also no significant difference between patients with available CD4 [$X^2(1) = 0.086$; $p = 0.769$] or viral load [$X^2(1) = 0.615$; $p = 0.433$] values on admission compared to those without tests available at admission.

Table 5. ICD-10 Codes Associated with Higher Hospital Case Fatality Rates among Individuals Hospitalized with HIV at João de Barros Barreto University Hospital.

ICD-10	Deaths	Total	Case Fatality Rate	
			Rate (%)	95% CI† (Lower - Upper)
Other septicemia (A41)	6	6	100.00%	(59.39% - 100.00%)
Gastrointestinal haemorrhage, not otherwise specified (K92.2)	3	3	100.00%	(36.84% - 100.00%)
Disseminated histoplasmosis by *histoplasma capsulatum* (B39.3)	3	3	100.00%	(36.84% - 100.00%)
Unspecified severe protein-energy malnutrition (E43)	4	5	80.00%	(34.26% - 98.98%)
Acute renal failure (N17)	8	14	57.14%	(31.17% - 79.99%)
Sepsis unspecified (A41.9)	8	15	53.33%	(29.03% - 78.50%)
Unspecified bronchopneumonia (J18.0)	9	17	52.94%	(28.22% - 74.70%)
HIV disease resulting in wasting syndrome (B22.2)	2	2	100.00%	(22.36% - 100.00%)
Unspecified bacterial pneumonia (J15.9)	13	38	34.21%	(20.43% - 51.35%)
HIV disease resulting in multiple infections (B20.7)	4	9	44.44%	(16.88% - 74.86%)
Unspecified bacterial meningitis (G00.9)	5	13	38.46%	(16.57% - 66.35%)
Unspecified pneumonia (J18.9)	4	10	40.00%	(15.00% - 71.71%)
Toxoplasma meningoencephalitis (B58.2)	13	58	22.41%	(13.21% - 35.11%)
Brain cryptococcosis (B45.1)	5	17	29.41%	(12.38% - 54.42%)
Histoplasmosis (B39)	2	4	50.00%	(9.76% - 90.24%)
Pneumocystosis (B59)	5	28	17.86%	(7.31% - 35.71%)
Pulmonary tuberculosis, confirmed by unspecified means (A15.3)	3	12	25.00%	(7.19% - 54.44%)
Unspecified acute renal failure (N17.9)	2	6	33.33%	(6.29% - 72.87%)
Bacterial pneumonia not elsewhere classified (J15)	2	6	33.33%	(6.29% - 72.87%)
Pulmonary tuberculosis, confirmed by microscopic examination of sputum, with or without culture (A15.0)	4	23	17.39%	(6.17% - 38.66%)

95% CI: 95% Confidence Interval
† Calculated using the adjusted Blaker's exact method

Regarding in-hospital case fatality rate stratified by diseases described in discharge and death summaries, organized by order of higher case fatality rate by the lower limit of

the confidence interval, higher case fatality rate was observed in patients with records of: Other septicemias (A41; 100.00%; 95% CI 59.39% - 100.00%), Gastrointestinal hemorrhage, unspecified (K92.2; 100.00%; 95% CI 36.84% - 100.00%), Disseminated histoplasmosis due to *Histoplasma capsulatum* (B39.3; 100.00%; 95% CI 36.84% - 100.00%), Severe unspecified protein-energy malnutrition (E43; 80.00%; 95% CI 34.26% - 98.98%), and Acute renal failure (N17; 57.14%; 95% CI 31.17% - 79.99%). Other causes with high case fatality rate are described in Table 5.

4. DISCUSSION

The sample in this study showed a higher prevalence of males among hospitalized individuals (2:1 ratio), reflecting the broader HIV epidemic in Pará where males are predominant. Beyond epidemiology, local cultural aspects might influence men to postpone medical visits, increasing their risk for late diagnosis and urgent hospitalization, which are risk factors for severe outcomes[3,7]. Although female lethality wasn't significantly different in this study, the trend of rising rates in the North and Northeast for females is noted. Vulnerabilities like abusive relationships, difficulty accessing diagnostic services, and poverty may contribute to this[13].

An important point to mention in the discussion of case fatality rates is that persistent non-adherence to ART remains a critical challenge in Brazil[14]. Our study highlighted this, with only 20.61% of hospitalized patients reporting regular ART use and one-fifth of hospitalizations occurring in individuals with a history of non-adherence (nearly half of whom were currently non-adherent). This persistent problem arises from a complex interplay of factors, including structural barriers, stigma, patient-provider relationship gaps, socioeconomic disadvantages, and, critically, substance use[14–16].

We found high rates of current alcohol use (11.2%) among hospitalized PLHIV, correlating with the literature linking it to worse outcomes[17]. Although data on illicit substance use were often absent, positive reports were common when available (e.g., cannabis, 6.67%; cocaine, 3.64%), reinforcing the significant negative impact of substance use on treatment adherence and prognosis[15].

Another topic that requires joint discussion is the relationship between hospitalization and the date of HIV diagnosis. Patients diagnosed more than 1 year before hospitalization (29.70%) include individuals who disengaged from care or never initiated treatment due to challenges like denial or difficulty seeking care (stigma, limited resources), as well as those with therapeutic failure, often linked to lower adherence influenced by structural factors like

inconsistent drug access Current Ministry of Health guidelines recommend screening for opportunistic infections and initiating first-line ART after diagnosis. ART failure is defined by lack of viral suppression within 6 months or viral rebound[19]. Achieving adequate CD4 levels takes time, leaving patients vulnerable to infections leading to hospitalization[20–22].

The group diagnosed within 3 months of hospitalization (29.09%) likely represents late diagnoses, with rapid progression to hospitalization. Studies on late diagnosis impact in Pará are scarce. One of the municipalities in the state showed that 4.7% of PLHIV hospitalizations were due to neurotoxoplasmosis, with 33% developing the condition post-diagnosis, supports this[23]. In this study, 28.7% of documented admissions were diagnosed within 3 months, potentially indicating delayed recognition, impacting ART access and increasing risk of severe complications and death. Brazil has implemented initiatives, but late diagnosis and access persist as challenges, demanding intensified public health interventions, underscored by studies showing high prevalence of late initiation[24].

Our findings highlight that severe immunosuppression (CD4+ lymphocyte count ≤ 200 cells/mm³) was a powerful predictor of in-hospital fatality, demonstrating a significant odds ratio of 7.25 in this cohort. This underscores the critical prognostic impact of immunological status. While viral load is crucial for monitoring ART response, it did not show a significant overall association with case fatality rate in this study, although trends toward higher mortality were noted within specific ranges based on confidence intervals.

Beyond immunological status, key drivers of high in-hospital mortality included septicemias, gastrointestinal hemorrhage, disseminated histoplasmosis, severe protein-energy malnutrition, and acute renal failure. High septicemia mortality reflects severe systemic infection. Malnutrition worsens prognosis[25], while acute renal failure can be linked to HIV or ART toxicity[26]. Other serious conditions like Toxoplasma meningoencephalitis and cerebral cryptococcosis also contributed significantly to mortality[27].

While most baseline immunological assessments (CD4 and viral load) were performed within five months preceding hospitalization, the availability of these tests at admission did not significantly alter case fatality rates. Test timing varied, but availability of tests at admission did not significantly influence CFR, suggesting comorbidities and other clinical factors were more immediate determinants.

This study's limitations should be acknowledged. The retrospective chart review inherently limits precision due to variations in data completeness and clinical documentation. Missing information might indicate either absence or lack of explicit description.

The patient cohort reflects individuals hospitalized at HUJBB and may not fully represent all PLHIV in Pará. Many patients are transferred from other facilities, and lack of standardized information from originating institutions limits evaluation of prior treatment influence. The inclusion criteria favored patients clinically stable enough for transfer, potentially introducing selection bias by excluding those with more acute, untransportable conditions. Futhermore, as an observational study, definitive cause-and-effect relationships cannot be inferred. Associations between factors and outcomes may be influenced by unmeasured confounders.

Finally, the study period encompassed the primary impact period of the COVID-19 pandemic in Brazil, from 2020 to 2022. Due to the study's design, it was not possible to estimate the pandemic's impact on the observed case fatality rate, necessitating future studies to determine the actual rate. Nevertheless, this study can serve as a pandemic snapshot for the patient population treated at this hospital in future research.

Despite these limitations, this study illuminates critical areas for future investigation into the health status and care experiences of hospitalized PLHIV in this setting. Identifying patterns and challenges can inform efforts to improve comprehensive hospital care and strengthen linkages with outpatient services across the territory. The research also underscores opportunities for advancing clinical documentation and encouraging further investigation in relevant areas.

5. CONCLUSIONS

This study reveals a high hospital case fatality rate (HCFR) of 28.12% among HIV-infected individuals hospitalized at João de Barros Barreto University Hospital (HUJBB) in the Brazilian Amazon from 2018 to 2022. The most significant predictor of in-hospital mortality was a CD4+ lymphocyte count ≤200 cells/mm³ at admission (OR=7.25, p=0.006), emphasizing the critical impact of severe immunosuppression on patient outcomes.

While direct statistical associations between mortality and variables such as time since diagnosis or specific histories of substance use were not established in this specific analysis, the findings paint a concerning picture of a patient population with significant vulnerabilities. Notably, only 20.61% of patients with admission records reported regular ART use, with

31.52% of all admissions reporting irregular use or discontinuation. Furthermore, a substantial proportion (29.09%) were diagnosed within three months of hospitalization, strongly suggesting late presentation or rapid progression to advanced disease. The prevalence of substance use, particularly alcohol, although not statistically linked to mortality in this study, remains a critical co-factor known to impede ART adherence and overall health. The primary causes of death – HIV-related complications, sepsis, and respiratory failure – are typical of advanced, unmanaged HIV infection.

A significant limitation was the incompleteness of data in many medical records, which precluded a more granular analysis of variables like specific ART regimens, duration of non-adherence, or detailed substance use patterns. The COVID-19 pandemic is a confounding factor that should also be addressed in further studies. Despite these limitations, the evidence strongly indicates that intensified efforts to improve and sustain ART adherence, facilitate early HIV diagnosis, and ensure continuous, robust outpatient follow-up are paramount to reducing preventable hospitalizations and mortality due to HIV/AIDS in this region. Future research should focus on identifying specific barriers to ART adherence and timely care within this Amazonian context, further investigating the clinical impact of viral load dynamics and potential antiretroviral resistance, and assessing the effectiveness of targeted public health interventions aimed at reaching and retaining vulnerable individuals in comprehensive HIV care.

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