ABCS HEALTH SCIENCES

ORIGINAL ARTICLE

OPEN ACCESS

AIDS in the meeting of the Tapajós and Amazon rivers: deaths in the period 2010-2018 in Santarém, Pará, Brazil

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ABSTRACT

Introduction: The city of Santarém, the regional healthcare center in the western Pará State, lacks studies on the epidemic of the human immunodeficiency virus (HIV), in particular, on the causes of death. **Objective:** To characterize the sociodemographic and clinical profile related to the evolution of HIV infection to death. **Methods:** The sample consisted of 94 medical records of patients from a reference center in the city of Santarém-PA, who died between 2010-2018. Data were collected on the sociodemographic profile, immunological and clinical characteristics of the patients. Data were analyzed using descriptive and inferential statistics, adopting $p<0.05$. **Results:** Most deaths were male (67%), aged between 15-29 years (39%) and diagnosed between 30-44 years (41%), single (54%), mixed race (91.5%), from Santarém (77%) and with sexual intercourse being the main type of exposure (95.7%). Most patients were not being treated at the moment of death (56.4%), the main cause of death was respiratory failure (5%), in which, these individuals had, at the moment of death, TCD4+ lymphocytes <200 cell/mm^3 (26%) and detectable viral load (29%). **Conclusion:** The lifetime from diagnosis to death was 48.45±50,30 months, and immunosuppression in the diagnosis was positively associated with the shortest survival time. However, sex was not associated with the immunological profile, age at the time of diagnosis, and death. There was only a tendency for women towards immunosuppression and detectable viral load.

Keywords: Acquired Immunodeficiency Syndrome; health profile; death.

INTRODUCTION

The infection by the human immunodeficiency virus (HIV) and the development of the Acquired Immunodeficiency Syndrome (AIDS) are relevant public health problems worldwide. Immunosuppression related to HIV/AIDS significantly increases the risk of opportunistic infections by bacteria, fungi, viruses, and protozoa, leading their patients to a debilitating condition and death when in the absence of an early and adequate antiretroviral treatment[1]. In view of its discovery in the 1980s, HIV/AIDS was characterized as a sexually transmitted disease caused only by homosexual activities. However, it is known that HIV/AIDS affects several groups, regardless of sex, skin color, age, social

How to cite this article: Costa et al. AIDS in the meeting of the Tapajós and Amazon rivers: deaths in the period 2010-2018 in Santarém, Pará, Brazil. ABCS Health Sci. 2021;46:e021201. https://doi.org/10.7322/abcshs.2019169.1439

Received: Jan 14, 2020
Revised: Apr 15, 2020
Approved: Jun 04, 2020

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Declaration of interests: nothing to declare

class or sexual orientation, as well as the existence of other routes of transmission[1-3]. Over the years, the epidemic has also spread among people with less education and purchasing power, and an increasing number of places far from the main metropolitan areas[2].

Since the beginning of this epidemic, around 74.9 million people have been infected with HIV, 32 million of whom have already died of AIDS-related illnesses. It is estimated that, currently, 37.9 million people are living with HIV worldwide and that 770,000 died from HIV/AIDS in 2018[4]. Brazil, in particular, has already recorded, since the first registered cases by the end of 2017, a total of 327,655 deaths had HIV/AIDS as the primary cause[5]. There has been a significant reduction in mortality in the country in recent years, mainly due to the availability of free access to diagnosis and treatment for HIV/AIDS by the Ministry of Health, starting in 1996[6,7]. The introduction of antiretroviral therapy (ART) has made it possible to improve the quality and survival of patients, since it reduces the incidence of opportunistic infections and positively regulates the immune system (increased TCD4+ lymphocyte count) of individuals affected by AIDS. Thus, early treatment with ART has been effective in reducing viral transmission, as well as in the rate of morbidity and mortality of individuals[8]. Condition that reinforces the importance of the Paris Declaration with the goal 90-90-90, that is, 90% of people living with HIV diagnosed, of these, 90% are under treatment and that 90% of this group has an undetectable viral load[9].

However, health care for people living with HIV/AIDS does not occur in a universal and equal way in Brazil, which can lead to difficult access to diagnosis and, consequently, to a late start in the use of ART or the non-start of treatment. Such factors, associated with poor adherence to therapy, are decisive for the increase in deaths from HIV/AIDS in the country[10].

Therefore, even with the reduction of mortality from HIV/AIDS in Brazil, the number of people still dying from causes related to it is still large in some Brazilian regions. In general, most states in the North and Northeast regions, with the exception of Roraima and Bahia, increased their HIV/AIDS mortality rates from 2007 to 2017[5].Also, there is strong evidence that the onset of ART occurs lately for a reasonable proportion of people with HIV/AIDS, especially in these regions, a condition that may be related to the high mortality rates of these individuals[11].

The reduction in the number of prevention and testing campaigns for individuals are factors that can increase the time between diagnosis and the start of drug intervention. In addition, in some cases, the scarcity of medication and difficulties related to adherence to treatment are still important factors related to disease progression[7,12].

Thus, considering the increase in the number of deaths in the North region in recent years, with emphasis on the state of Pará, the present study aimed to characterize the sociodemographic and clinical profile related to the evolution of HIV infection until death.

METHODS

This study is a quantitative, descriptive, documentary and transversal research[13]. The research site was the Testing and Counseling Center and Specialized Assistance Service (TCC/SAS) in the municipality of Santarém, Pará, Brazil. It is noteworthy that in the western region of Pará the TCC/SAS is a reference for 20 municipalities and for a population in 1.2 million inhabitants.

The study evaluated 94 (68%) medical records of patients who were followed up by TCC/SAS and who died. Therefore, all medical records of patients who died between January 2010 and December 2018 were adopted as inclusion criteria for the study. Damaged, unreadable or not found medical records were excluded from the sample (n=44).

Data collection was performed with a form containing information such as age, sex, origin, marital status, skin color, date of diagnosis, date of start of ART, date of death, status of treatment at the time of death (being treated, interrupted treatment, never started treatment or abandonment)[14], cause of death, viral load and TCD4+ lymphocyte count.

It is noteworthy that this study is part of a thematic project approved by the Research Ethics Committee of Campus XII - Santarém of the Universidade do Estado do Pará, Brazil, under CAAE: 82729718.7.0000.5168.

The sample of 94 medical records, taking into account the sampling error of 5%, 90% confidence level and heterogeneous sample distribution, proved to be representative. The data were tabulated and organized in spreadsheets for descriptive statistical analysis (median, first quartile - 25%, third quartile - 75%, mean, standard deviation, absolute and relative frequency). Subsequently, the D'Agostino Pearson normality test was applied, which showed non-parametric distribution for the TCD4+ lymphocyte values and viral load. Thus, the Mann-Whitney test was used to compare lymphocyte values and viral load between the time of diagnosis and death, as well as between sexes. The Chi-square test and Odds Ratio (OR) were used to verify the association and the chance of occurrence of the event. For the statistical analysis, the BioEstat 5.3 program was used, adopting a significance level of $p<0.05$.

RESULTS

Table 1 presents information on the distribution of sex, marital status, skin color, reason for seeking care at the TCC/SAS and the type of exposure the patient presented for HIV infection.

According to the origin of the patients who died, 13 municipalities of origin were found, with Santarém, Pará, being the most frequent (77%, n=72), followed by Óbidos (4%, n=4), Oriximiná (4%, n=4), Curuá (2%, n=2), Itaituba (2%, n=2), Novo Progresso (2%, n=2), Land Santa (2%, n=2), Alenquer (1%, n=1), Belterra (1%, n=1), Juruti (1%, n=1), Mojuí dos Campos (1%, n=1), Monte

Alegre (1%, n=1), all municipalities from the state of Pará, and Manaus, Amazon state (1%, n=1).

Table 2 shows the distribution by age group of HIV-infected patients at the time of diagnosis and death. It is noteworthy that the mean age at diagnosis was 34.93±13.21 years and at death, 38.49±12.92 years. In addition, the average life span from diagnosis to death was 48.45±50.30 months. Table 3 shows the distribution of patients' survival time.

The treatment status of patients at the time of death showed that 40.4% (n=38) of the patients were using ART, 33% (n=31) had not started therapy, 23.4% (n=22) had interrupted treatment before death due to abandonment, and 3.2% (n=3) did not have this information in the medical record.

As for the causes that led patients to death, it is worth mentioning that most medical records did not have this variable recorded (77%, n=72). However, among observed records, respiratory failure stood out as the most prevalent (5%, n=5) of the 22 causes recorded, followed by septicemia (4%, n=4), tuberculosis (3%, n=3) , cardiac arrest (2%, n=2), hypovolemic shock (2%, n=2), liver failure (1%, n=1), malnutrition (1%, n=1), external causes (trauma/accidents) (1%, n=1), severe anemia (1%, n=1), neurotoxoplasmosis (1%, n=1) and natural death (not determined) (1%, n=1).

Table 4 shows the distribution of users regarding the values of TCD4+ lymphocytes and viral load at the moment closest to the diagnosis (1st count) and death (last count). It is noteworthy that the values of lymphocytes (p=0.6254) and viral load (p=0.1551) showed no difference between the first and last assessment.

In addition, it should be noted that the median TCD4+ lymphocytes for men at diagnosis was 201 (84-361) cells/mm^3 and at death was 204 (64-408) cells/mm^3, with no difference between these moments (p>0.99). On the other hand, women at the time of diagnosis had values for lymphocytes of 201 (44-377) cells/mm^3 and at death of 123 (44-226) cells/mm^3, there was also no statistical difference between the moments (p=0.3619). Finally, there was no statistical difference in values between genders for diagnosis (p=0.8026) and death (p=0.2183).

When assessing the viral load in males, it was observed at the time of diagnosis 43,432 (6,999-151,754) copies and in the death of 1,171 (0-72,527) copies. It is emphasized that the values were lower at the time of death (p=0.004). For women, the viral load value at the time of diagnosis was 48,711 (1,068-125,470) copies and at death 141,436 (134-596,922) copies, with no statistical difference between the moments evaluated (p=0.3118). There was also no statistical difference between both sexes at the time of diagnosis (p=0.4852) and death (p=0.05).

When the association of sex with the TCD4+ lymphocyte count (< or ≥ 200 cells/mm^3), viral load (detectable or undetectable) and age (≤ or > 40 years), at the time of diagnosis and death, was not found any statistical association (p>0.05). However, attention is drawn to the greater frequency of females, compared to males at

Table 1: Distribution of deaths according to sex, marital status, skin color, reason for seeking treatment and type of exposure of HIV-infected patients, from 2010 to 2018.

Variables	n	%
Sex		
Male	63	67.0
Female	31	33.0
Marital status		
Married	26	27.7
Single	51	54.3
Widowed	1	1.1
Divorced	3	3.2
Not informed	13	13.8
Skin color		
Mixed	86	91.5
Black	3	3.2
White	3	3.2
Not informed	2	2.1
Reason for seeking treatment		
Referred by health service	54	57.4
Knowledge of serological status	5	5.3
Prenatal examination	4	4.3
Prevention	2	2.1
Exposure to risky situation	5	5.3
Suspected sexually transmitted infection	20	21.3
Check previous exam result	1	1.1
AIDS-related symptoms	2	2.1
Not informed	1	1.1
Type of exposure		
Sexual intercourse	90	95.7
Vertical transmission	1	1.1
Not informed	3	3.2

Table 2: Age distribution of patients with HIV/AIDS at the time of diagnosis and death.

Age group	Diagnose		Death	
	n	%	n	%
0 to 14	1	1	1	1
15 to 29	37	39	23	24
30 to 44	30	32	39	41
45 to 59	20	21	21	22
60 to 74	3	3	7	7
Not informed	3	3	3	3

Table 3: Distribution of patients according to survival time from diagnosis to death.

Lifespan (years)	n	%
0 to 2	45	48
3 to 5	19	20
6 to 8	13	14
9 to 11	5	5
12 to 15	6	6
16 to 18	1	1
Not informed	5	5

the time of death, to the presence of immunosuppression (71% *vs* 48%) and detectable viral load (82% *vs* 58%).

As for the association of survival time (≤ or > 40 months) with sex, as well as the TCD4+ lymphocyte count (< or ≥ 200 cells/mm³), viral load (detectable or undetectable) and age (≤ or > 40 years), at the time of diagnosis and at death, there was only significance for the presence of immunosuppression at the time of diagnosis (p=0.0038) (Table 5).

Table 4: Description and frequency of TCD4+ lymphocytes and viral load in the first and last count of HIV-infected patients, Santarém, Pará, Brazil, from 2010 to 2018.

Variables	1st count		Last count	
	n	%	n	%
Lymphocytes TCD4+ (cells/mm³)				
<200	30	32	24	26
≥200	30	32	19	20
Not informed	34	36	51	54
Median (interquartile range)	201 (73-374)		152 (56-388)	
Viral charge				
Undetected	5	5%	15	16%
Detected	61	65%	27	29%
Not informed	28	30%	52	55%
Median (interquartile range)	43,432 (6,082-111,627)		6,071 (0-110,623)	

Table 5: Association of survival time with sex, age, TCD4+ lymphocyte count and viral load at the time of diagnosis and death.

Variables	Survival time				p OR
	≤40 months		>40 months		
	n	%	n	%	
Sex					
Male	39	70	22	67	0.9555
Female	17	30	11	33	---
Diagnose moment					
Lymphocyte TCD4+					
<200 cells/mm³	20	71	9	30	0.0038
≥200 cells/mm³	8	29	21	70	5.83
Age					
≤40 years	34	61	27	82	0.0666
>40 years	22	39	6	18	---
Viral charge					
Detectable	32	97	27	87	0.315
Undetectable	1	3	4	13	---
Death moment					
Lymphocyte TCD4+					
<200 cells/mm³	9	69	14	48	0.3544
≥200 cells/mm³	4	31	15	52	---
Age					
≤40 years	34	61	22	67	0.7381
>40 years	22	39	11	33	---
Viral charge					
Detectable	8	57	18	67	0.796
Undetectable	6	43	9	33	---

OR: odds ratio.

DISCUSSION

The analysis of the 94 medical records of patients who died, followed at the TCC/SAS of Santarém, Pará, Brazil, points to a predominant profile of adults aged between 30 and 44 years, mostly male, single, mixed-race and from this municipality. The location of cases with predominance in Santarém, Pará, Brazil, only confirms that the city is a treatment center for patients in the region. In addition, because TCC/SAS is a reference for the care of HIV/AIDS patients, the high demand for referral of patients from other health services (57.4%) is justified.

With regard to sex, the data found in the literature point to a higher prevalence of HIV/AIDS infection and death in males. That is, from 1980 to 2017, of the total deaths registered in the country, 70.6% correspond to male sex. In addition, data show that 73% of new HIV cases in 2017 occurred in male individuals[5]. This trend has persisted since the beginning of the epidemic with some variations over time, since the proportion between the male and female individuals has suffered constant attenuations in recent years, triggered by an effect called feminization[15]. In Brazil, 2017, the death rate was two men for each woman, a reduction compared to 1985, which was 24.8[5]. One of the factors identified as a contributor to the higher prevalence of men is that, in general, male patients tend to have less adherence to treatment, contributing to the greater risk of death[16].

Regarding the age group at the time of death, a higher prevalence was identified in individuals aged 30 to 44 years (41%), in line with other studies that point to the third decade of life as the age group with the highest number of deaths from HIV/AIDS[8,17]. However, it is important to highlight a growing increase in deaths from HIV/AIDS among younger individuals. In Brazil, there was an increase in case reports among people aged 15 to 24, from approximately 700%, from 2007 to 2017. Among men in the age group of 20 to 24, the AIDS detection rate grew 133% in the same period, from 15.6 to 36.2[5]. This trend is also observed in females. In the present study, the age group from 15 to 29 years represented 24% of deaths, reflecting this scenario. Despite the existence of awareness campaigns and high knowledge about HIV/AIDS prevention and other sexually transmitted infections (STIs) among young people, they are still not prevented efficiently and consciously, highlighting the non-use or discontinued use of the condoms, which justifies this increase[2,18-20].

Regarding marital status, there was a predominance of singles (54%), followed by married people (28%), facts consistent with those found in the studies by Santos et al.[8] and Franco et al.[10] who demonstrated a prevalence of deaths among single people, with 67.6% and 60.4% in each study, respectively. This ends up being associated with higher risk behavior, with several sexual partners and with no preventive measures[1,8]. In addition, the type of exposure was predominantly sexual (95.7%), a data also found in the study by Moura and Faria[21], as well as characterized by national

statistics[5]. Since the beginning of the epidemic, sexual intercourse has been the main route of HIV transmission. Among the determinants involved in the maintenance of its transmission and other sexually transmitted infections is the lack of condoms, associated with low education, multiple partners, and non-adherence prevention methods[18]. The analysis of the type of exposure (homo or heterosexual) was not possible due to lack of information in the medical records.

The Basic Health Units are important interlocutors of TCC/SAS, as its professionals have closer contact with the patients and can do the testing or direct the person to the TCC for the appropriate conducts. In this sense, the present study observed that the main reason for attending the TCC/SAS occurred due to referral to another health service, as well in other studies[21,22]. However, the search for assistance in the Health Unit must be occurring late, and the referral of the patient to the TCC/SAS or the time spent by the patient to attend the consultation must be more extended, as many arrived to confirm the diagnosis and monitoring with low TCD4+ lymphocyte values and detectable viral load.

National statistics indicate that AIDS mortality predominates in mixed skin color[5], as well as noted in this study. In the study by Franco et al.[10], carried out in a hospital in Fortaleza, Ceará, Brazil, they noticed that more than 80% of the patients who died had mixed skin color, of the 146 patients with HIV/AIDS. It is essential to highlight the fact that the distribution of skin color in Brazil is not homogeneous. In the South region, deaths stand out among patients with white skin color, precisely due to the predominance of people considered to be of that race/skin color. In the North region, on the other hand, individuals with brown skin color predominate, and Pará has the highest percentage (above 70%) among the states in this region[8].

Regarding the survival time of these patients, the mean value found was approximately 48 months, with 48% of the sample dying in the range of 0 to 24 months after diagnosis. Medeiros et al.[16] found a median of 15.5 months of survival time and pointed out as determinants in the decrease in survival and quality of life of people living with HIV, late diagnosis, and, above all, non-adherence to ART, which were also found in the present study.

Regarding the treatment status at the time of death, it was observed that most patients were not undergoing treatment (33% had not started and 23.4% had stopped), while only 40.4% of them were using antiretroviral therapy. Several factors may be related to the non-initiation or use of ART, that is, poor adherence or abandonment, the absence of a social support network for patients diagnosed with HIV/AIDS, which is a joint responsibility of family, friends and family and the health team[23]. Thus, early initiation and adherence to treatment are of paramount importance for improving the quality of life and decreasing mortality. Still, it is also one of the most significant challenges in assisting patients with HIV/AIDS. This is because of the different demands regarding behavioral and dietary changes and the use of various medications throughout their lives[10,24].

The TCD4+ lymphocyte count <200 cells/mm^3 at the time of diagnosis was 32% (50% of the present exams), and at death, it was 26% (56% of the present exams). In both moments, it is noted a high frequency of patients with a low TCD4+ lymphocyte count. Also, the frequency of patients with detectable viral load at the time of diagnosis (92% of present test) and death (64% of present test) was high. Taking this into account, it can be inferred that people who sought the service and evolved to death already had some degree of weakness. Thus, attention is drawn at this time to the goal 90-90-90[9], in which Santarém, Pará, Brazil, is not included and that the results of the immunological tests of the patients in this study were against the goal, which should draw the attention of health managers/staff always to be evaluating the action strategy with society and people living with HIV, to provide an early diagnosis, to change the high rate of patients with TCD4+ lymphocytes <200 cells/mm^{3}and well as the non-use ART properly, having a detectable viral load.

In addition, the relationship between the two variables is essential to understand the patient's prognosis and evolution, as a high initial TCD4+ lymphocyte count, combined with an undetectable viral load, shows more favorable outcomes, as they correlate with the absence of opportunistic infections, which are the main causes of death in these patients[16,25-27]. In this sense, the present study demonstrated that the presence of immunosuppression at the time of diagnosis reduces the patient's survival time.

In the association made between sex and the immunological profile, there was a tendency of women, in relation to men, towards immunosuppression (71% *vs* 48%) and detectable viral load (82% *vs* 58%) at the time of death, as well as the highest frequency for immunosuppression (32% *vs* 22%), lower TCD4+ lymphocyte count values (p=0.2183) and higher viral load (p=0.05), however without significance. In a study carried out with patients registered at an outpatient clinic in the city of São Paulo, São Paulo state, Brazil, from 1993 to 2001, it was found that women had lower TCD4+ lymphocyte values than men[28], as well as what was observed in another study conducted in Teresópolis, Rio de Janeiro, Brazil, in which women had significantly lower TCD4+ lymphocyte values and higher viral load, but without significance[29].

The leading cause of death associated with HIV/AIDS was respiratory failure. This is frequent in immunosuppressed patients who had a late diagnosis of HIV, as observed in the study by Melo et al.[30]. Weber et al.[31] point to a new trend in the causes of death worldwide, especially in large centers where there is a large availability of resources and a better living condition. In them, the causes of deaths not related to AIDS grow, in contrast to diseases that previously affected more and were responsible for the deaths of these patients, such as tuberculosis and pneumocystosis. In the present study sample, the causes with the most significant

expression were those related to AIDS. In both studies of Melo et al.[30] and Weber et al.[31], the collection of these data proved to be difficult due to logistical limitations, lack of protocols for filling out medical records, and the complex investigation of these causes. This obstacle was also present in this research because due to insufficient information, it was impossible to list these data in greater detail since 77% of the patients' medical records did not contain the cause of death or the death certificate.

Finally, it is concluded, according to the objective and the proposed method, that there was a predominance of deaths in men, aged 30 to 44 years, in singles, mixed skin color and from the municipality of Santarém, Pará, Brazil. The main reason for patients to seek TCC/SAS services was due to referral to other health services, just as sexual intercourse was the predominant route of HIV transmission. Most of these patients had a survival time of up to 24 months after diagnosis and were not treated at the time of death. The leading cause of death, among those recorded in the medical records, was due to respiratory failure. As for the immunological profile, there was a higher frequency for TCD4+ lymphocyte count <200 cells/mm^3 and detectable viral load, especially for females, compared to males, at the time of death, but without significance. Also, survival time was negatively associated with the presence of immunosuppression at the time of diagnosis.

Thus, the importance of public policies for HIV/AIDS is increasingly clear, to provide actions that favor early diagnosis, introduction, and adherence to treatment, guidance, and monitoring of populations in situations of greater vulnerability for use pre-exposure prophylaxis, condom use, and better integration of the health network to welcome and accompany people living with HIV. In this way, the investment that will be high in the beginning will, over time, represent savings for the health system, as presented by the goal 90-90-90[9].

ACKNOWLEDGMENTS

To the Center for Testing and Counseling and Specialized Assistance Service of the municipality of Santarém, Pará, Brazil, for supporting education and research, and its collaborators who endeavored to provide data collection. To the members of the Amazon Morphofunctional and Metabolic Response Study Group (GERMETA) involved in the thematic project.

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