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Sociodemographic and pharmacoepidemiological profile of people on antiretroviral therapy in the coast of the state of Paraná

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ABSTRACT. The aim of this study was to investigate possible factors related to antiretroviral therapy (ART) that contribute to the understanding of the highest rate of Aids detection on the coast of the state of Paraná, a port region identified administratively as the 1st Regional Health Division (1st HD) in the state of Paraná. Data on the sociodemographic profile of the population undergoing antiretroviral treatment (ART), medication changes, dropout of therapy, proportion of the population undergoing treatment and viral load were obtained through computerized systems. Between July 1, 2018 and June 31, 2019, 1,393 people were on ART in the 1st RS. Of these, 57.6% were male. During this period, 110 people started ART with a predominance of the age group between 30 and 39 years old. ART was switched for 169 people and 211 patient dropouts were detected. The proportion of people diagnosed with HIV without treatment (gap) is still high, however 92.7% people on ART have suppressed viral load. It can be concluded that the lower educational level of the population undergoing treatment, the late diagnosis of those infected and the treatment gap probably contribute to the highest rate of Aids detection in the 1st RS.

Keywords: HIV; Aids; treatment; population; coastal area; Paraná.

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Introduction

HIV infection challenges researchers around the world and remains unresolved (Dantas, Abrão, Costa, & Oliveira, 2015). However, adherence to treatment with antiretroviral drugs can prevent HIV infection from evolving to its most advanced stage, known as Aids (Programa Conjunto das Nações Unidas sobre HIV/Aids [Unaids], 2017).

In 1996, federal law 9313 was enacted, which guaranteed free access to antiretroviral therapy in Brazil through the Unified Health System (SUS) (Brasil, 1996). Studies show that this public policy aimed at controlling HIV infection has contributed significantly to the reduction of mortality and hospitalizations for HIV/Aids in Brazil (Lago & Costa, 2010; Brasil, 2018).

Despite access to therapy and monitoring by health services, the coast of the state of Paraná, administratively identified as the 1st Paranaguá Regional Health Division (1st HD), stands out negatively for maintaining, for years in a row, the highest Aids detection rate of the state (Paraná, 2015). The 1st HD comprises the municipalities of Antonina, Guaraqueçaba, Guaratuba, Matinhos, Morretes, Paranaguá and Pontal do Paraná, adding up to a population of 294,160 inhabitants, dispersed in a coastal and port region of intense commercial activity (Instituto Paranaense de Desenvolvimento Econômico e Social [Ipardes], 2019).

The success of antiretroviral therapy depends heavily on adherence to antiretroviral drugs. Adherence provides a sustained reduction in the HIV virus load, decreases the possibility of transmission of the virus to other people and prevents the clinical evolution of the infection to Aids (Brasil, 2017).

In this context, in 2015, Unaids launched an ambitious treatment target to contribute to the end of the AIDS epidemic, target 90-90-90 (Programa Conjunto das Nações Unidas sobre HIV/Aids [Unaids], 2015). This aims to extend the diagnosis to 90% of people living with HIV, to treat 90% of those infected, and to suppress the viral load of 90% patients using antiretroviral therapy (Unaids, 2017).

Objectives

Therefore, it is relevant to analyze the sociodemographic and pharmacoepidemiological profile of the population undergoing antiretroviral treatment in the 1st HD of Paraná and to identify specific characteristics of this population that can support the development of strategies in health care for people living with HIV/Aids on the coast of the state, with the purpose of contributing to the reduction of the high rates of HIV incidence and Aids detection in that location.

Methodology

This was an observational, descriptive study, with quantitative components, based on reports of clinical follow-up and use of antiretrovirals by people living with HIV/Aids in the 1st Regional Health Division (1st HD) in the state of Paraná, in the period between July, 1st 2018 and June, 30th 2019.

The reports were obtained from the Control System for CD4+/CD8+ and HIV Viral Load Laboratory Tests (SISCEL), the Logistics Control System for Medicines (SICLOM) and the Clinical Monitoring System for People Living with HIV/AIDS (SIMC), all accessed at the Paraná State Drug Center (CEMEPAR) of the Paraná State Department of Health (SESA-PR).

In this study, all people diagnosed with HIV in the 1st HD, using antiretroviral drugs or not, whose records in the SISCEL and SICLOM systems were active in the period covered by the study were considered. By crossing data made possible by SIMC, 1,606 records were found at SISCEL that correspond to people diagnosed with HIV, and 1,393 records of people undergoing antiretroviral treatment, adhering to or dropping out of therapy, accessed by SICLOM. The difference between these values corresponds to the 213 people diagnosed with HIV who had not yet started ART on the 1st HD in the period, called the antiretroviral treatment gap.

The variables of interest obtained from the reports accessed were sex, age group, skin color, education of the general population undergoing treatment in the 1st HD, as well as for people who started ART and those who dropped out of therapy during the study coverage period. Those dropping out of ART were considered to be those who did not show up for more than 100 days in the dispensary units for HIV drugs, as defined by the Clinical Protocol and Therapeutic Guidelines of the Ministry of Health (Brasil, 2018). From this specific population, additional information was collected, also by SICLOM, such as municipality of origin, time of dropout of therapy and line of treatment used before dropout, as a way of assessing the complexity of its treatment and inferring previous failures in ART.

Information on the proportion of people diagnosed who have not yet started ART (gap) in the 1st HD and people on ART with viral loads greater than 50 copies of viral RNA mL^{-1} blood were collected at the end of the study period (on June, 30th 2019) through SIMC.

Data processing took place with the aid of the Excel 2016 software and, for comparisons, descriptive statistics tools were used, such as absolute, relative frequencies, median, minimum and maximum values.

The study was approved by the Research Ethics Committee of the Federal University of Paraná - Health Sciences Sector, according to the opinion number 2620673; CAAE: 82936318.3.0000.0102 and by the Ethics Committee of the state of Paraná - Hospital do Trabalhador/SES/PR according to the opinion number 2.674.606 of May 24th, 2018 (CAAE: 82936318.3.3001.5225).

Results and discussion

HIV infection progresses to Aids mainly among people diagnosed late and without access to or adherence to treatment with antiretroviral drugs.

The Aids detection rate corresponded to 17.8/100,000 inhabitants in Brazil and 16.6/100,000 inhabitants in the state of Paraná (Brasil, 2019). However, the 1st HD of Paranaguá had a high AIDS detection rate of 33.8/100,000 inhabitants, according to the most recent epidemiological bulletin in the state of Paraná (2015). Compared to previous years, a progressive reduction in the rates of AIDS detection is observed throughout Brazil, especially after the recommendation of the Ministry of Health to immediately start the treatment of diagnosed people (Brasil, 2013b). However, despite this, the rate of Aids detection in the 1st HD remained high.

For this reason, this study investigated some variables related to the use of ART in the 1st HD of Paranaguá that may be related to the high rate of Aids detection.

Between July 1st, 2018 and June 31st, 2019, 1,393 people were on ART in the 1st HD. Of these, 802 were male (57.6%) and 591, female (42.4%). For both sexes, the age group between 40 to 59 years old predominated,

representing 54% total sample (male = 52.8%, female = 54.7%), diverging from the predominant age group of 20 to 34 years old (52.7%) among people living with HIV in Brazil (Brasil, 2019).

Regarding the skin color, 67% sample from the 1st HD declared having white skin, in accordance with the IBGE data for Paraná (Instituto Brasileiro de Geografia e Estatística [IBGE], 2017).

In the 1st HD, people between 4 and 7 years of education predominate (43%), which is equivalent to incomplete elementary education. 39.2% male and 49.1% female. However, the missing 16% responses for this variable are noteworthy (Table 1). This result differs from that observed in Brazil, where most infected people have completed high school (Brasil, 2019). The lower educational level is also a factor contributing to the increase in the number of HIV/Aids cases, as this increases the population's distance from access to information about the disease and to prevention and treatment practices (Schaurich & Freitas, 2011).

Table 1. Sociodemographic characterization of the population undergoing antiretroviral treatment in the 1st RS of Paranaguá.

Variables	Total n (%)	Sex	
		Male n (%)	Female n (%)
Age group (years)			
< 15	16 (1.00)	06 (0.80)	10 (1.70)
15 to 19	17 (1.00)	09 (1.20)	08 (1.40)
20 to 29	125 (9.00)	78 (9.80)	47 (7.90)
30 to 39	278 (20.00)	168 (20.90)	110 (18.70)
40 to 49	386 (28.00)	213 (26.50)	173 (29.20)
50 to 59	362 (26.00)	211 (26.30)	151 (25.50)
⩾ 60	209 (15.00)	117 (14.50)	92 (15.60)
Skin color			
Yellow	04 (0.50)	02 (0.25)	02 (0.34)
White	932 (67.0)	595 (74.20)	337 (57.10)
Brown	241 (17.0)	131 (16.30)	110 (18.70)
Black	152 (11.50)	33 (4.10)	119 (20.20)
Not informed / Ignored	64 (5.0)	41 (5.15)	23 (3.66)
Education			
From 1 to 3 years	133 (10.00)	64 (7.90)	69 (11.70)
From 4 to 7 years	604 (43.00)	314 (39.20)	290 (49.10)
From 8 to 11 years	330 (24.00)	214 (26.70)	116 (19.70)
12 and over	91 (6.00)	68 (8.50)	23 (3.90)
Illiterate	14 (1.00)	06 (0.80)	08 (1.20)
Not informed / Ignored	221 (16.00)	136 (16.90)	85 (14.40)

During the study period, 110 people started antiretroviral treatment in the 1st HD (65% male; 35% female). Among these, the age group between 30 and 39 years old predominated, which represented 30% total sample, with little variation between sexes. Considering that people diagnosed with HIV should start antiretroviral treatment immediately, there is a difference of approximately 10 years between the predominant age group in new HIV cases in Brazil and Paraná (20 to 29 years old) and the age group of beginning of treatment in the 1st HD, which may suggest a possible delay in diagnoses, as well as in the onset of therapy (Brasil, 2013b; Paraná, 2015; Brasil, 2019).

Of the patients who started treatment in the mentioned period, 88% used first-line treatment regimens, as expected, such as the combination of tenofovir, lamivudine and dolutegravir (TDF/3TC/DTG). Of these, 91.8% were male and 81.6% were female. However, second-line antiretroviral treatment schemes have also been identified, suggesting therapeutic failure or viral resistance. This line is indicated for patients who have not responded satisfactorily to the initial therapy (Brasil, 2018).

People who start antiretroviral treatment with first-line treatment regimens have more therapeutic options and are more effective in suppressing viral load, as long as they have not been infected with an already resistant virus. However, in situations of vertical transmission, HIV transmission by partners on ART (serodiscordant couples), pregnant women and patients co-infected with tuberculosis the genotyping test is indicated, through which it is possible to identify virus resistance to certain antiretroviral drugs even before starting therapy. Therefore, more complex therapeutic regimens, which characterize other lines of treatment, can be prescribed from the beginning of treatment (Brasil, 2018).

Table 2 lists, therefore, a more mature population that started treatment during the study period and with a first-line therapeutic regimen.

Table 2. Population that started antiretroviral therapy in the 1st RS.

Variables	Total n (%)	Sex	
		Male n (%)	Female n (%)
Age group (years)			
15 to 19	05 (5%)	03 (4.4%)	02 (5.1%)
20 to 29	17 (15%)	14 (19.2%)	03 (7.8%)
30 to 39	32 (30%)	23 (32.4%)	09 (23.6%)
40 to 49	26 (23%)	13 (17.8%)	13 (34.2%)
50 to 59	18 (16%)	11 (15.1%)	07 (18.1%)
⩾ 60	12 (11%)	08 (11.1%)	04 (11.2%)
Treatment lines			
1st line	97 (88%)	66 (91.8%)	31 (81.6%)
2nd line	13 (12%)	06 (8.2%)	07 (18.4%)

Other data investigated in this study refer to the switch of antiretroviral therapy. *The clinical protocol for therapeutic guidelines for the management of HIV infection in adults* (Brasil, 2018) provides for changes in therapeutic regimens, mainly as a result of viral resistance, genotyping, pregnancy, comorbidities or for possible adverse reactions related to the use of antiretrovirals, among other reasons (Brasil, 2018). However, switches motivated by poor adherence to therapy tend to predominate (Carvalho, Barroso, Coelho, & Penaforte, 2019).

In this study, 169 people replaced antiretroviral regimens in the 1st HD during the study period. Of the changes, 77.51% occurred due to adverse reactions, which the system does not detail. 21.90% patients switched therapy for other reasons, such as dropout, unavailability of the drug, genotyping, pregnancy, hepatitis, pulmonary tuberculosis, among other reasons. In only one case, the reason for the switch was not informed. Other studies report similar results (Lima, Arruda, Lima, Oliveira, & Fonteles, 2012; Bernal, Vásquez, Giadalah, Rodríguez, & Villagrán, 2013).

Guidelines on antiretroviral treatment emphasize that, for a better prognosis of treatment, strict adherence to antiretrovirals is necessary, given that irregularity in the use of medications or dropout increases the likelihood of HIV replication, the spread of multidrug-resistant viruses and the evolution of the infection to Aids (Rodrigues & Matsud, 2017). Despite this, dropout of ART is frequent. The Ministry of Health understands as dropout of therapy those cases in which the patient has not been to the health service for more than 100 days to withdraw their antiretroviral drugs (Brasil, 2018).

In the 1st HD, 211 people dropped out of treatment during the study period: 54.98% male and 45.02% female. People aged between 30 and 49 years old predominated (52.13%).

In this study, when assessing the education of people who dropped out of antiretroviral therapy, there was a predominance of people between 4 and 7 years of study (55% sample). Of these, 51.72% were male and 61.05% were female. The illiterate population totaled 12.79% sample. Similar results were reported in other studies (Santos & Seidl, 2011; Silva, Dourado, Brito, & Silva, 2015). It is known that the educational level actively interferes with adherence to treatment, as it is associated with the difficulty of understanding the recommendations of health professionals, little connection with reference services and less awareness about the need for continuous use of the medication; this variable is a decisive factor for non-adherence to treatment (Barreto, Cremonese, Janeiro, Matsuda, & Marcon, 2015).

The treatment dropout time was also investigated in this study. It was observed that 54% patients dropped out of therapy between 0 and 18 months, representing the majority for both sexes (male = 57.76%; female = 60%). Problems in accepting the disease and adverse reactions to antiretroviral drugs are the most frequent causes found in the literature to explain the drop out of antiretroviral therapy. In addition, it is also reported that fragile bonds of patients with health services, with family and friends contributes significantly to this outcome, since the fear of discrimination creates a barrier to adherence to antiretroviral therapy (Nemes et al., 2009; Freitas, Bonolo, Miranda, & Guimarães, 2017).

Paranaguá was the municipality of the 1st HD with the highest number of people dropping out of antiretroviral therapy (64.93% total. Of these, 69.47% were female and 61.21% were male). Another six municipalities that are part of this 1st HD were also mentioned, in addition to residents of the state capital (Curitiba) and the metropolitan region, and other Brazilian states, such as Santa Catarina, Rio Grande do Sul, São Paulo and Sergipe. Obtaining antiretroviral drugs from other cities is allowed, however this distance makes it difficult to link with the reference health service, since multidimensional access to the provision of

specialized care, monitoring of adherence to treatment and the status of the infection, are carried out by this service (Brasil, 2013a; Coelho & Meirelles, 2019).

Considering that Paranaguá is a port municipality with a large flow of travelers from different locations, there is a possibility that some people characterized as dropping out therapy are eventually users in transit, especially those living in distant locations. This modality is foreseen; however, it should be duly identified in SICLOM by the service unit (Brasil, 2010). However, in this study, no service in transit was signaled at SICLOM and the information was counted as dropout.

Before dropout, 56.87% patients used first-line antiretroviral treatment regimens, such as the combination of efavirenz, lamivudine and tenofovir (EFZ/3TC/TDF) used by 43.13% patients, and efavirenz, zidovudine and lamivudine (EFZ/AZT/3TC) used by 12.79%. Regarding the predominant use of first-line antiretroviral therapy regimens, it can be inferred that most of these people dropping out of therapy in the 1st HD were starting HIV treatment. According to the scientific literature, the initial treatment period tends to be the most favorable phase for dropout (Nemes et al., 2009). Nevertheless, it is also noticed that patients who use more complex therapeutic regimens, second- and third-line treatments, are dropping out of antiretroviral therapy (Table 3). This presupposes previous therapeutic and virological failures and the consequence of the infection evolving to AIDS in these patients (Brasil, 2018; Vogler, Alfieri, Gianjacomo, Almeida, & Reiche, 2018).

Table 3. Characterization of the population leaving antiretroviral therapy in the 1st RS of the state of Paraná.

Variables	Total n (%)	Sex	
		Male n (%)	Female n (%)
Age group (years)			
15 to 19	2 (0.95)	1 (0.86)	1 (1.05)
20 to 29	25 (11.85)	10 (8.62)	15 (15.19)
30 to 39	59 (27.96)	29 (25)	30 (14.22)
40 to 49	51 (24.17)	30 (25.86)	21 (22.10)
50 to 59	43 (20.38)	26 (22.41)	17 (17.89)
⩾ 60	31 (14.69)	20 (17.24)	11 (11.58)
Education			
From 1 to 3 years	12 (5.69)	8 (6.89)	4 (4.21)
From 4 to 7 years	118 (55.92)	60 (51.72)	58 (61.05)
From 8 to 11 years	43 (20.38)	27 (23.27)	16 (16.84)
12 and over	7 (3.32)	7 (6.03)	0 (0.00)
Illiterate	27 (12.79)	12 (10.34)	15 (15.79)
Not informed / Ignored	4 (1.89)	2 (1.72)	2 (2.11)
Delay time for returning to the medication dispensary (in months)			
From 0 to 6	43 (18.48)	25 (21.55)	18 (18.95)
From 6 to 12	38 (16.59)	18 (15.52)	20 (21.05)
From 12 to 18	43 (18.96)	24 (20.69)	19 (20.00)
From 18 to 42	14 (6.64)	7 (6.04)	7 (7.38)
From 42 to 48	22 (10.43)	13 (11.21)	9 (9.47)
From 48 to 54	14 (6.63)	6 (5.17)	8 (8.42)
From 54 to 60	16 (7.58)	11 (9.48)	5 (5.26)
> 60	25 (11.83)	16 (13.80)	9 (9.47)
Origin			
Antonina – PR	5 (2.37)	4 (3.45)	1 (1.05)
Guaratuba – PR	13 (6.16)	7 (6.03)	6 (6.31)
Guaraqueçaba – PR	2 (0.95)	1 (0.86)	1 (1.05)
Matinhos – PR	16 (7.58)	10 (8.62)	6 (6.31)
Morretes – PR	3 (1.42)	3 (2.58)	0 (0.00)
Paranaguá – PR	137 (64.93)	71 (61.21)	66 (69.47)
Pontal do Paraná - PR	12 (5.69)	7 (6.03)	5 (5.26)
Curitiba and Metropolitan Region PR	12 (5.69)	9 (7.75)	3 (3.15)
Other states (SC,RS,SP and SE)	11 (5.17)	4 (3.45)	7 (7.35)
Treatment lines			
1st line	147 (69.67)	77 (66.38)	70 (73.68)
2nd line	57 (27.01)	36 (31.03)	21 (22.10)
3rd line	7 (3.32)	3 (2.58)	4 (4.21)

PR – Paraná, SC – Santa Catarina, RS – Rio Grande do Sul, SP – São Paulo and SE – Sergipe.

In this study, the viral load of the population on antiretroviral therapy was also investigated, based on the value recommended by the Ministry of Health of Brazil, which is 50 copies viral RNA mL^{-1} blood (Brasil, 2018).

There were 102 patients with viral load above 50 copies RNA mL^{-1} blood, which represents 7.3% total population under treatment in this region. The median viral load corresponded to 935.5 copies viral RNA mL^{-1} blood (minimum = 51, maximum = 3,304,387), which shows a wide range of values. Monitoring the viral load of people on ART is important because it indicates whether or not the therapy used is successful. Moreover, when the goal of keeping the viral load suppressed is achieved, the risk of transmitting the virus to other people is drastically reduced, as well as the progression of the infection to AIDS (Silva, Duarte, & Lima, 2020).

As previously mentioned, after the diagnosis of HIV infection, the Ministry of Health recommends the immediate start of antiretroviral therapy, regardless of clinical and laboratory parameters. This procedure was implemented in 2013 and aims to reduce the rate of AIDS detection and also to inhibit HIV transmissibility (Brasil, 2013b).

People diagnosed with HIV but who have not yet started using antiretroviral drugs are categorized as a treatment gap and ideally, this should not exceed 10% (Unaids, 2017; Loch et al., 2020). In this study, it was observed that 213 people had not yet started ART at the 1st HD during the study period. This represents 13.3% population diagnosed at the 1st HD. Although it is below ideal, it is better than the national average of 30% in 2013 (Brasil, 2013b).

With respect to viral suppression in the ART population in the 1st HD, 92.7% people undergoing treatment had suppressed viral load, equal to or less than 50 viral copies mL^{-1} blood, during the period of this study. In this way, it reached the ideal proportion that consists of staying above 90% (Unaids, 2017).

Conclusion

In the 1st Regional Health Division of the state of Paraná, the factors related to antiretroviral therapy that can contribute to understand the highest rate of Aids detection in the state of Paraná, were the lowest educational level of the population undergoing treatment, the apparent diagnosis and late onset treatment, and dropouts of therapy. In addition, the use of more complex second-line therapeutic regimens was found among people beginning therapy, which suggests infection with an already resistant virus. Approximately one third of the people who dropped out of ART at the 1st HD used therapeutic regimens of the second- and third-lines of treatment. Besides the fragile bond of these people to the health service, these data demonstrate the occurrence of therapeutic failure, viral resistance due to poor adherence and the greater probability of progression of infection to Aids.

In this context, it is essential that the public authorities invest in health education strategies and in the greater offer of diagnostic tests in the locality. In case of a positive diagnosis, it is necessary to guarantee the immediate start of antiretroviral therapy and the link of these people to the reference health services. In this way, with the proper follow-up, it will be possible to achieve viral suppression, minimize the risk of dropping out of treatment and reduce the number of people whose infection progresses to Aids (Aids detection rate). Viral suppression in those infected will also help to reduce new diagnoses of HIV infections (HIV incidence rate) in the Regional Health Division, as it would make transmission to other people more difficult. These strategies would collaborate greatly to reduce the rates mentioned, the highest in the whole state of Paraná, in addition to providing a better quality of life for this population.

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