ORIGINAL ARTICLE

Effectiveness of antiretroviral therapy in reducing viral load in people living with HIV in Southwest Goiás, Brazil

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ABSTRACT

Introduction: People living with HIV (PLHIV) without adequate treatment experience lymphocyte depletion, thus leading to a state of immunodeficiency. Therefore, to suppress the virus and improve the quality of life of PLHIV, antiretroviral therapy (ART) is necessary, which also leads to reduced transmission and better virus control. **Objective**: To verify the effect of antiretrovirals on viral suppression in HIV-infected patients. **Methods**: This is a descriptive, longitudinal and quantitative study, which evaluated 95 medical records of patients newly diagnosed with HIV infection, between the years 2018 and 2020, monitored by the Testing and Counseling Center and Specialized Outpatient Service (TCC/ SOS), in the municipality of Jataí, Goiás, Brazil. Sociodemographic, clinical, and immunological information was collected from the medical records. The data were analyzed using descriptive and inferential statistics, using the BioEstat 5.3 program, adopting $p<0.05$. **Results**: The study findings showed a predominance of males (71.6%), with a median age of 30 years, single (68.4%), heterosexuals (44.2%), with exposure through sexual intercourse (98.9%). The most commonly used therapeutic regimen was tenofovir + lamivudine + dolutegravir (87.8%), which was shown to be adequate for increasing the CD4+ T lymphocyte count ($p<0.001$) and decreasing the viral load ($p<0.001$) in the period between exams, 9 months and 6 months, respectively. **Conclusion**: According to the proposed method and objective, ART was efficient in reducing the viral load and improving the immune system of PLHIV treated at the TCC/SOS in Jataí, highlighting the importance of early treatment.

Keywords: Acquired immunodeficiency syndrome, Clinical evolution, Opportunistic infections, Sustained virologic response.

INTRODUCTION

According to global statistics, there are around 38.4 million people living with HIV (PLHIV) in the world, among them, 28.7 million have access to antiretroviral therapy (ART), which has reduced mortality from acquired immunodeficiency syndrome (AIDS) by 68% since its peak in 2004[1]. In Brazil, from 2007 to June 2022, there were 434,803 notifications of PLHIV[2], as well as a higher incidence of infection in males compared to females[2,3]. When looking at the distribution by region of the federation, the Central-West region occupies 5th place, with 33,715 (7.7%) reported cases of PLHIV, showing a lower infection rate compared to other regions of Brazil. In the Central-West region, the state of Goiás has the highest number of reported cases of HIV, presenting 13,660 notifications in the period from 2007 to

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https://doi.org/10.11606/issn.2176-7262.rmrp.2024.206561

June 2022, as well as having the highest number of AIDS deaths in the period from 1980 to 2022 (n=7,104; 35.4%). However, in recent years (2011-2021) the mortality rate in the state has reduced by 14.6% (4.1 vs. 3.5/100,000 inhabitants)[2].

In this sense, ART is important in the treatment of HIV infection as it provides the infected patient with a significant reduction in the morbidity and mortality caused by the virus, in addition to promoting an undetectable viral load, at which point there is no sexual transmission of the virus[4,5]. Studies show that individuals who do not achieve viral suppression, due to not using ART, have high, and in some cases earlier, mortality rates as a result of their greater viral loads and low CD4+ T lymphocyte count (CD4+)[6,7]. Furthermore, the effect of ART and its adequate monitoring result in lower death rates even from causes unrelated to AIDS[8]. It should be noted that virological failure is also a determining factor for the high mortality rate in PLHIV[6].

In 2021, considering the proposed 95-95-95 target, around 85% of PLHIV knew their serological status, 88% had access to treatment, 90% achieved viral suppression (<200 copies), and 66% had an undetectable viral load[1]. Furthermore, when the diagnosis of HIV infection is not delayed and ART is initiated as soon as possible, the recovery of the CD4+ count is more efficient, improving the patient's immune system and survival[4], as well as decreasing the time until viral suppression[9].

Studies indicate that viral suppression can be achieved within 11 to 14 months using ART[10-13]. However, the use of ART provides viral suppression for a viral load count below 50 copies[14]. When using ART, statistics reveal that PLHIV demonstrate an improvement in their quality of life, physical size, and mental health, as well as greater independence[15]. In this sense, patients who start taking ART later, compared to those who start early, present high mortality rates[16], as well as having a lower CD4+ count[17]. In this way, ART aims to reduce the viral load and increase the CD4+ count, improving the quality of life of PLHIV[18]. Thus, the objective of the present study is to analyze the effectiveness of antiretroviral therapy in reducing the viral load of people living with HIV, in a reference center in the interior of Goiás.

METHOD

The current study presents itself as descriptive, longitudinal, and quantitative. The study was carried out at the Testing and Counseling Center and Specialized Assistance Service (TCC/SAS), located in the municipality of Jataí, Goiás, Brazil.

The study population consisted of the medical records of 180 PLHIV, belonging to the TCC/SAS of Jataí. To this end, the following inclusion criteria were respected: the patient began their follow-up, due to a diagnosis, at the TCC/SAS of Jataí between 2018 and 2020; had a diagnosis of HIV infection; the medical record was required to contain, at least, information on the date of diagnosis, date of birth, date of starting ART, and sex. The following exclusion criteria were adopted: children under 10 years of age; medical records of patients transferred or who abandoned follow-up (26 excluded); medical records without information from two viral load exams in sequence (58 excluded); and patients not using ART (one excluded). Thus, the sample consisted of the medical records of 95 PLHIV.

It should be noted that the present study was approved by the Research Ethics Committee, under opinion no. 3,380,955, and all ethical secrecy was respected when searching for information in medical records, to avoid identification of the participant.

A spreadsheet was created in the Excel® program to carry out data collection, which contained sociodemographic (date of entry into the TCC/SAS, sex, age, skin color, marital status, sexual orientation, city of residence, education, consumption of alcoholic beverages, smoking, and consumption of illicit drugs) and clinical information (date of diagnosis for HIV infection, type of exposure to HIV, immunodeficiency status, CD4+ count, viral load, and taking ART).

As a reference for the CD4+ count, values of < and ≥200 cells/mm^3 were considered. For viral load, values of ≥50 copies (detectable) and <50 copies (undetectable) were observed[19]. Those with an undetectable load were considered to have zero viral load for statistical analysis.

To be classified as immunodeficient for AIDS, the patient was required to present or have presented an CD4+ count <200 cells/mm^3, or cancer, or a history of opportunistic infection[20].

The data were organized and analyzed using descriptive statistics (minimum, maximum, median, interquartile range – IQR, mean, standard deviation, absolute and relative frequency). The D'Agostino-Pearson normality test was applied for age, CD4+ values, and viral load, and a non-parametric distribution was observed. Thus, the Wilcoxon test was used to compare age between sexes and CD4+ and viral load values between the first and second exams. Fisher's Exact test was applied to verify the difference in the distribution of patients for CD4+ and viral load. The tests were carried out with the support of the BioEstat 5.3 program, adopting a value of $p<0.05$.

RESULTS

The mean age of the sample was 32.97 years (±11.42), varying between 16 and 60 years, with a median of 30 years and an interquartile range (IQR) of 24 to 42 years. Analysis by sex revealed that the mean age for men was 32.43 years (±10.55), ranging from 18 to 60 years, with a median of 29 years and an IQR of 24 to 40 years. In the female group, the mean age was 34.33 years (±13.49), ranging between 16 and 56 years, with a median of 31 years and an IQR of 23 to 45 years. No significant differences were observed between the sexes ($p=0.638$).

Males predominated in the sample, representing 71.6% (n=68) of participants. Table 1 presents the sociodemographic characteristics and lifestyle habits of the participants.

Table 1 – Distribution of people living with HIV in terms of sociodemographic characteristics and lifestyle habits.

Variables	n/%	Variables	n/%
Marital status		**Skin color**	
Single	65/68.4	White	44/46.3
Married	25/26.3	Black	9/9.5
Divorced	2/2.1	Pardo	42/44.2
Separated	1/1.1	**Schooling**	
Not informed	2/2.1	Illiterate	1/1.1
Sexual Orientation		Complete Elementary	0/0
Bisexual	6/6.3	Incomplete Elementary	19/20.0
Heterosexual	42/44.2	Complete Secondary	14/14.7
Homosexual	28/29.5	Incomplete Secondary	9/9.5
Transsexual	2/2.1	Complete Higher	7/7.4
Not informed	17/17.9	Incomplete higher	10/10.5
Consumption of alcoholic beverages		Not informed	35/36.8
Yes	28/29.5	**Resident**	
No	67/70.5	Aporé	3/3.2
Smoking		Caiapônia	6/6.3
Yes	23/24.2	Chapadão do Céu	3/3.2
No	72/75.8	Doverlândia	1/1.1
Use of illicit drugs		Jataí	44/46.3
Yes	13/13.7	Mineiros	35/36.8
No	82/86.3	Santa Rita do Araguaia	2/2.1
Employed		Serranópolis	1/1.1
Yes	70/73.7		
No	25/26.3		

The mean time between diagnosis of HIV infection and initiation of ART was 2.20 months (±2.00), ranging from the same month of diagnosis (zero) to 11 months, with a median of two months and an IQR of one to three months. The mean time between the first and second exams to count CD4+ was 9.97 months (±5.34), ranging from one month to 26 months, with a median of nine months and an IQR of six to 13 months (Table 2).

Viral load demonstrated a mean time between exams of 6.21 months (±3.10), ranging from one to 17 months, with a median of six months and an IQR of four to seven months. This reported information, as well as the clinical characteristics, can be seen in Table 2. Irregular use of ART was noted in only 2.1% (n=2) of patients, with one of the patients using two regimens and the other three antiretroviral regimens.

Table 2 – Distribution of people living with HIV in terms of clinical characteristics and intervals between exams and initiation of antiretroviral therapy.

Variables	
Type of exposure	
Accident with biological material (n/%)	1/1.1
Sexual intercourse (n/%)	94/98.9
Immunodeficiency status	
HIV (n/%)	60/63.2
AIDS (n/%)	35/36.8
Antiretroviral therapy	
TDF+3TC+DTG (n/%)	86/87.8
TDF+3TC+RAL (n/%)	5/5.1
TDF+3TC+EFV (n/%)	4/4.1
TDF+3TC+DRV/r (n/%)	1/1.0
3TC+DTG+DRV/r (n/%)	1/1.0
AZT+3TC+DTG (n/%)	1/1.0
Time until starting antiretroviral therapy	
Minimum (months)	0
Maximum (months)	11
Median (months)	2
Interquartile range (25-75%) (months)	1-3
Mean±standard deviation (months)	2.20±2.00
Time between exams for CD4+ T lymphocyte count	
Minimum (months)	1
Maximum (months)	26
Median (months)	9
Interquartile range (25-75%) (months)	6-13
Mean±standard deviation (months)	9.97±5.34
Time between viral load exams	
Minimum (months)	1
Maximum (months)	17
Median (months)	6
Interquartile range (25-75%) (months)	4-7
Mean±standard deviation (months)	6.21±3.10

TDF – Tenofovir; 3TC – Lamivudine; DTG – Dolutegravir; EFV – Efavirenz; RAL – Raltegravir; DRV/r – Darunavir/ritonavir; AZT – Zidovudine.

Table 3 presents the CD4+ and viral load values at the time of the first and second exams, as well as the comparison between these values. The median CD4+ count increased from the first to the second exam (p<0.001), while the viral load decreased (p<0.001). Furthermore, the number of patients with a detectable viral load decreased in the second exam (100% vs. 22.1%; p<0.001) and the number of patients with CD4+ ≥200 cells/mm^3 improved non-significantly (63.2% vs. 79.4%; p=0.057).

Table 3 – Presentation of the CD4+ T lymphocyte count and viral load in the first and second exams.

Variables	1st exam	2nd exam	p
CD4+ T lymphocytes (cells /mm^3)			
Minimum	4	15	
Maximum	4279	2662	
Median	299	550	<0.001*
Interquartile range (25-75%)	93-505	227-824	
Mean ± standard deviation	445.45±673.98	587.22±404.99	
<200 cells/mm^3 (n/%)	25/36.8	14/20.6	0.057†
≥200 cells/mm^3 (n/%)	43/63.2	54/79.4	
Viral load (copies)			
Minimum	121	0 (IND)	
Maximum	2,188,735	49,474	
Median	28,944	0	<0.001*
Interquartile range (25-75%)	6,315-127,467	0-0	
Mean ± standard deviation	131,924.06± 292,513.56	1,247.20± 6,707.70	
Detectable (n/%)	95/100	21/22.1	<0.001†
Undetectable (n/%)	0/0	74/77.9	

IND – undetectable viral load; *Wilcoxon test; †Fisher's Exact Test.

DISCUSSION

The current study estimated the effectiveness of ART in reducing the viral load of PLHIV and observed, in terms of sociodemographic characteristics, the predominance of males, adults, with white and brown skin color, single, heterosexual, and with incomplete primary education. The highest prevalence of cases in males and among single individuals, as reported in a national epidemiological study[2], may be related to the practice of unprotected sexual intercourse[21], which is less frequent in females[22], the young age group, and involvement with multiple partners[23]. Therefore, awareness strategies about forms of prevention are extremely important to minimize the risk of HIV infection, such as the use of condoms, taking a rapid test[24], and guidance on pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP)[25].

It was observed that sexual contact is the main form of contagion for HIV infection[2,26], as also noted in the present study. This is due to high exposure to the virus, especially when there is no use of condoms between partners[21]. Using condoms incorrectly, or even not using them at all, makes HIV prevention less effective[27], thus contributing to the emergence of new cases[2]. The lack of condom use is possibly caused by little knowledge about safe sex, preventive methods, and the risks of unprotected sex[21].

The data from the present study showed a predominance of heterosexuals. This information is in line with other studies also carried out in the state of Goiás[24,28,29], however, the profile is different to findings for Brazil in general, since in the country the predominance is of men who have sex with men[2]. This characteristic of the present study may be associated with previously highlighted factors, such as not using condoms, and not being aware of the serological status[24,30], and forms of prophylaxis (PrEP and PEP)[25]. Furthermore, in the present study, it was noted that 17.9% of PLHIV did not report sexual orientation and some that were self-reported as heterosexual may have reported this to avoid prejudice[31,32].

The level of education is extremely important, as a lack of good functional health literacy may lead to low adherence to treatment[33], and can affect knowledge about HIV, increasing the risk of infection[34]. In the present study, and nationally[2], a greater distribution of patients with incomplete primary education is observed. In addition to education, another important point to monitor is employment, since in the present study the majority of patients were employed and this reflects in having an income, which places these patients in a situation of a lower risk of vulnerability[23].

In the current study, the majority of the sample was made up of non-smokers, non-alcohol drinkers, and non-drug users, which is important for adherence to ART and to achieve the best treatment results[15]. Smoker patients generally present greater obstacles to treatment, as they already demonstrate poor health, added to which tobacco reduces survival, causing cardiovascular problems[35]. Furthermore, tobacco is also linked to other complications, such as increasing the possibility of the patient having tuberculosis, one of the opportunistic infections that is recurrent in PLHIV[36]. Patients who do not drink alcohol have a good quality of life compared to those who consume alcohol, as high alcohol consumption leads to less awareness of sexual activity, favoring the non-use of condoms, in addition to causing dependence[15].

When reporting on the ART regimen, the most commonly used in the present study was the regimen recommended by the Ministry of Health, TDF+3TC+DTG. However, this regimen must be replaced when there is a contraindication to any of the components. The joint use of TDF+3TC presents advantages in relation to toxicity, CD4+ response, and viral load suppression, providing better treatment results[5]. Furthermore, the TDF+3TC+DTG regimen presents, among patients, good adherence, effectiveness in reducing viral load, mainly to achieve suppression, and few adverse effects[37]. The protease inhibitor DRV/r was prescribed for one of the patients due to renal failure (3TC+DTG+DRV/r) and for the other to provide the option of a more robust regimen, due to the presence of non-Hodgkin's lymphoma (TDF+3TC+DRV/r). DRV/r is linked to the side effects of early liver dysfunction, in addition to headache, nausea, and rash. Furthermore, AZT found

in the AZT+3TC+DTG regimen, also at low frequency, can cause neutropenia and anemia, along with anorexia, headache, nausea, insomnia, and malaise[38].

Regarding the use of ART, the present study demonstrated that the median time to start ART was two months from diagnosis, and the maximum time was 11 months. Starting to take ART earlier is relevant, since the late start of therapy makes the patient more vulnerable to HIV-related diseases and contributes to the advancement of AIDS, reducing the chances of achieving viral load suppression and immunological recovery[20]. Furthermore, PLHIV who are diagnosed late have a lower CD4+ count, which is a bad factor in their evolution. Parallel to this, a study showed that the initial CD4+ count was 590 cells/mm³, in acute infection it reduced to 456 cells/mm³ and in chronic HIV infection it was 377 cells/mm³. This indicates that PLHIV with early HIV infection have a higher CD4+ count, contributing to a good treatment result [39]. Thus, the time elapsed between HIV diagnosis and the start of ART is important, as the faster treatment begins, the faster and more effective the results can be[16]. This supports the effectiveness found in the current study, since the median onset time was not prolonged.

ART improves the CD4+ count[40], especially in patients who initially have a low count[40,41]. The increase in the CD4+ count and decrease in the viral load can be observed in the patient's evolution over a period of one year, counting from their diagnosis, as well as a reduction in the presence of opportunistic infections[26]. Therefore, the rapid introduction of ART is important, especially for patients who have a low CD4+ count, as these individuals have a high risk of death[12]. In this sense, and taking into account a median period of nine months between exams, in the current study an improvement was noted in the CD4+ count (299 vs. 550 cells/mm^3), as well as a reduction in patients with an CD4+ count <200 cells/mm^3 (64.3% vs. 20.0%), showing that the treatment was effective in the immunological evolution of patients.

A low CD4+ count, the onset of opportunistic infections, and cancer are factors for the diagnosis of AIDS[20]. In this sense, more than a third of the sample in the present study had AIDS at the time of diagnosis. Therefore, the proportion of AIDS cases in Brazil is still worrying and, according to the epidemiological bulletin, the state of Goiás has one of the highest proportions of AIDS cases[2]. Furthermore, AIDS patients have a higher mortality rate[42], as well as opportunistic diseases[43], which decrease survival, and increase mortality and viral resistance[44].

Some studies show that the time interval needed to achieve viral load suppression is 12 months[10-12]. However, the present study demonstrated, with a median of six months between the first and second exams, a reduction in viral load (28,944 copies vs. undetectable) and in patients with a detectable viral load (100% vs. 22.1%), demonstrating that patients who underwent the correct treatment with ART had good results in relation to the factors that contribute to improving life quality and expectancy, that is, their viral load reduced until they reached an undetectable viral load, at which point the patient no longer transmits the virus to their partner, and this result contributes to the non-transmission of the disease in general[14,15]. Thus, good adherence to ART improves patient survival, due to its effectiveness in reducing viral load[41] and restoring the immune system[40].

The study has some limitations, such as the small sample, which does not allow generalizations, as well as a better time standard for collecting viral load exams and CD4+ counts, as these were according to the service's routine. Furthermore, it would be interesting to move further along the timeline to monitor patients' progress, in addition to adopting an instrument to assess patients' adherence to the use of ART.

CONCLUSION

It is concluded, according to the proposed objective and method, that PLHIV who were diagnosed with HIV infection in the period 2018-2020 at the TCC/SAS of Jataí, Goiás, presented sexual intercourse as the main type of exposure, more than one third of the sample had AIDS, and the main antiretroviral regimen prescribed was TDF+3TC+DTG. Furthermore, the median time for the introduction of ART was two months, which was shown to be efficient in increasing the CD4+ count and reducing the viral load, in periods of nine and six months, respectively.

Therefore, the importance of early diagnosis and rapid and adequate introduction of ART for viral suppression and improvement in the immune system is highlighted, as well as continuous medical monitoring and strategies to promote adherence to ART, in order to avoid health problems.

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Authors' Participation:

DJSS – Data collection, organization of data, composition of the text, and approval of the final version to be published.

BTW – Data collection, organization of data, composition of the text, and approval of the final version to be published.

GSG – Data collection, interpretation of data, composition of the text, and approval of the final version to be published.

SMB – Data collection, interpretation of data, composition of the text, and approval of the final version to be published

HRMF – Conception and design of the study, composition of the text, and approval of the final version to be published.

EVF – Conception and design of the study, analysis and interpretation of data, composition of the text, and approval of the final version to be published.

LFGS – Orientation, conception and design of the study, analysis and interpretation of data, composition of the text, and approval of the final version to be published.

Funding

The study did not receive financial support.

Conflicts of interest

The authors declare no conflicts of interest.

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Received: jan 10, 2023

Approved:nov 29, 2023

Editor: Profa. Dra. Ada Clarice Gastaldi
