Adherence to antiretroviral drugs: self-reported of missed doses and associated factors in people living with HIV

Adesão aos antirretrovirais: autorrelato de perda de doses e fatores associados em pessoas vivendo com HIV

Denize Lotufo Estevam[1], Carla Gianna Luppi[1,2], Maria Aparecida Silva[1], Artur Olhovetchi Kalichman[1], Danielle Bivanco-Lima[3], Simone Queiroz Rocha[1]

ABSTRACT

Introduction: AIDS has become a chronic disease that may not be sexually transmitted as long as people living with HIV take their medications correctly. Therefore, adherence to antiretroviral drugs remains a central issue for therapeutic success. **Objective:** To describe the prevalence of self-reported missed doses of antiretroviral drugs (MDARV) in people living with HIV and analyze its associated factors. **Methods:** A cross-sectional study was conducted in a specialized service on STI/HIV/AIDS in the city of São Paulo (SP), Brazil. The data sources used were a self-administered form and the Database of the Laboratory Test Control System of the National Network for $CD4^+/CD8^+$ Lymphocyte Count and HIV Viral Load. The dependent variable was the self-report of MDARV by users in the last three days. The independent variables were related to sociodemographic, behavioral, and healthcare-associated characteristics. Poisson regression was used to estimate prevalence ratios and 95% confidence intervals. **Results:** Among the 510 responding participants, the MDARV prevalence in the last three days was 15.9% (95%CI 12.69–19.06). Factors associated with MDARV were detectable viral load, practicing a religion, change of residence in the last year, use of drugs, and more than 11 years of treatment. Knowing $CD4^+$ T lymphocyte count was associated with protection regarding missed doses.**Conclusion:** Monitoring MDARV self-report is a simple tool that can improve comprehensive care for people living with HIV/AIDS.

Keywords: Medication adherence. Self report. HIV. Acquired immunodeficiency syndrome. Viral load.

RESUMO

Introdução: A AIDS se tornou uma doença crônica, e pode não ser sexualmente transmitida desde que as pessoas vivendo com HIV tomem suas medicações corretamente. Desta forma, a adesão aos antirretrovirais permanece uma questão central para a obtenção do sucesso terapêutico. **Objetivo:** Descrever a prevalência de autorrelato de perda de doses da terapia antirretroviral (PDARV) de pessoas vivendo com HIV e analisar os seus fatores associados. **Métodos:** Foi conduzido um estudo transversal em serviço especializado em IST/HIV/Aids do município de São Paulo. As fontes de dados utilizadas foram o formulário autoaplicado e o banco de dados do Sistema de Controle de Exames Laboratoriais da Rede Nacional de Contagem de Linfócitos $CD4^+/CD8^+$ e Carga Viral do HIV. A variável dependente foi o autorrelato dos usuários sobre a PDARV nos últimos três dias. As variáveis independentes foram relacionadas a questões sociodemográficas, comportamentais e associadas ao serviço de saúde. Empregou-se regressão de Poisson para estimar razões de prevalência e intervalos de confiança de 95%. **Resultados:** Dentre os 510 participantes, encontrou-se prevalência de PDARV nos últimos três dias: 15,9% (IC95% 12,69–19,06). Os fatores associados à PDARV foram: carga viral detectável; prática religiosa; mudança de residência no último ano; uso de drogas; e mais de 11 anos de tratamento. O conhecimento da contagem de linfócitos T CD^+4 foi associado à proteção em relação à perda de doses. **Conclusão:** O monitoramento do autorrelato de PDARV é uma ferramenta de simples aplicação que pode melhorar o cuidado integral para as pessoas vivendo com HIV/AIDS.

Palavras-chave: Adesão à medicação. Autorrelato. HIV. Síndrome de imunodeficiência adquirida. Carga viral.

INTRODUCTION

In 2023, the AIDS epidemic completed 42 years and, despite the vast knowledge accumulated about prevention and treatment, it remains a serious public health problem[1].

It is estimated that 39 million people were living with HIV infection in the world in 2022[1], and in Brazil, 40,880 new cases of HIV infection were reported in 2021, with the country recording an average of 36,400 new cases annually of AIDS in the last five years. In Brazil, from 1980 to June 2022, 1,088,536 cases of AIDS were detected[2].

HIV infection is considered a chronic disease and adherence to treatment is a major concern, as it has an impact on outcomes such as virological response, disease progression, and viral resistance. A study carried out in Brazil, including 11,842 patients with chronic diseases, found low adherence in 30.8% of the population studied and a strong relationship with the social component[3]. Among people living with HIV (PLHIV), adherence rates can be influenced by knowledge about the disease, retention in the care offered by the multidisciplinary team, and access to medication.

Among the measures for the prevention and control of HIV infection and AIDS recommended by the World Health Organization (WHO), and adopted by Brazil in 2013[4], we highlight the orientation of the treatment of all PLHIV as soon as possible after the confirmed diagnosis. This strategy, called "treatment as prevention", aims to suppress viral replication and has already been shown to be effective in reducing HIV transmission[5].

To maintain an undetectable viral load, adequate adherence to antiretroviral (ARV) drugs is necessary. Even in the current context, which makes it possible to use regimens with more comfortable dosages, greater flexibility in times of intake and fewer side effects and adverse events in the medium and long term, adherence to ARV is still a challenge in the care of PLHIV[6]. Failures in adherence can lead to viral resistance, triggering a process that ultimately determines the resumption of HIV transmission and the progression of the disease[7].

[1]Centro de Referência e Treinamento DST/AIDS – São Paulo (SP), Brazil. E-mails: dlotufo@crt.saude.sp.gov.br; cgluppi@yahoo.com.br; cida@crt.saude.sp.gov.br; artur.kalichman@aids.gov.br; squeiroz@crt.saude.sp.gov.br
[2]Universidade Federal de São Paulo, Departamento de Medicina Preventiva – São Paulo (SP), Brazil. E-mail: cgluppi@yahoo.com.br
[3]Santa Casa de São Paulo, Faculdade de Ciências Médicas, Departamento de Saúde Coletiva – São Paulo (SP), Brazil. E-mail: danielle.bivanco@gmail.com

Patients' adherence to ARV can be assessed using several strategies: obtaining self-reported adherence, pharmacy dispensing records, pill counting, use of electronic devices such as the Medication Event Monitoring System (MEMS), notes on practitioners' perceptions in medical records, use of standardized questionnaires, and dosage of the serum level of drugs, among others[8]. Self-reported medication use is a simple strategy to be implemented in health services[7] to identify patients with adherence failures that can lead to serious consequences[7,9,10].

OBJECTIVE

This study aimed to describe the prevalence of self-reported MDARV among PLHIV in follow-up at a specialized outpatient clinic in the city of São Paulo (SP), Brazil, in 2017, and to analyze the factors associated with missed doses.

METHODS

Study design and setting

A cross-sectional study was conducted from August to December 2017. The study population consisted of adults with HIV infection enrolled in a specialized care service located in the Southeastern region of the city of São Paulo. This service is an assistance unit of the Health Care Network for PLHIV of the Unified Health System (SUS, *Sistema Único de Saúde*) in Brazil, under State management, a reference for the care of people affected by sexually transmitted infections, HIV/AIDS, and viral hepatitis, and for comprehensive healthcare for transsexuals and transvestites.

Participants

The sample size for the collection of data on adherence was calculated from the universe of adult users with active records at the PLHIV outpatient clinic, defined as if they had used the service at least once between July 1st, 2016, and January 31st, 2017. A total of 6,069 individuals were considered active. The inclusion criteria adopted were age 18 years or older, confirmed diagnosis of HIV infection, and enrollment in this referral service.

Adherence to ARV was estimated at 75%, a value found in a previously published national study[11]. The OpenEpi® program (version 3) was used through the open-source calculator SSPropor. The estimated sample size was 276 respondents from the total population, taking into account the alpha error of 5% (p=0.05). A 20% increase was made in the sample size (estimation of possible losses and refusals), reaching a minimum number of 331 interviewed individuals.

Instruments and data collection

Two data sources were used: primary – self-applied form; and secondary – database of the Laboratory Test Control System of the National Network for $CD4^+/CD8^+$ Lymphocyte Count and HIV Viral Load (SISCEL, *Sistema de Controle de Exames Laboratoriais da Rede Nacional de Contagem de Linfócitos $CD4^+/CD8^+$ e Carga Viral do HIV*).

Data collection from the primary source took place at the scheduled care outpatient clinic and the unscheduled demand service, called "urgent care" (UC). The offer to participate in the research was carried out by trained field investigators, covering all periods of care, and occurred differently in the two types of outpatient clinic: randomized in the outpatient clinic and systematic in the UC. Participants were included after reading and signing informed consent.

The self-administered form consisted of questions about sociodemographic characteristics, data on clinic, behavior, social support, stigma and discrimination, duration of ARV use, and self-reported of MDARV in the last three days. Missed doses were investigated through the question: "Regarding dose missed, have you missed doses in the last three days?" (answer: yes or no). Additionally, data were collected from the last three viral load measurements, through the secondary source (SISCEL), corresponding to each case included.

Variables

The dependent variable was the users' self-report about MDARV in the last three days. The independent variables of interest were gender, age group, skin color/ethnicity, schooling, practicing a religion, current job, change of residence in the last year, interview location, viral load, drug use in the last three months, alcohol use, perception of financial stability, self-perception of health, knowledge of $CD4^+$ T lymphocyte count and duration of ARV use.

The definition used to measure viral load (detectable or undetectable) considered the standard detection limit of the method used to perform the tests in the public health system at the time (40 copies/mL); that is, we considered viral load undetectable when the result was below this threshold and detectable when equal to or above 40 copies/mL[3].

Statistical analysis

Data were entered on the Research Electronic Data Capture® (REDCap) data collection and management platform. The relative and absolute frequencies of the variables, the prevalence of MDARV in the last three days, and the respective prevalence ratios (PR) and 95% confidence intervals (95%CI) were calculated. The statistical package Stata® (version 11.0) was used to perform the analyses. The Poisson regression model, with robust variance estimation, was applied for bivariate and multivariate analyses. The multiple models were organized with the inclusion of all the independent variables analyzed that presented $p<0.20$ in the bivariate analysis, using the Wald test. A significance level of 5% was adopted to maintain the variables in the final model; the selection of variables was performed using the stepwise backward technique. The variables that remained in the model were those that presented a significance level lower than 0.05 by the Wald test.

Ethical approval

The study was approved by the Ethics and Research Committee of the health service where the research was carried out (Opinion Number: 3,760,145; CAAE: 24876619.6.0000.5375). All interviewees were informed about the purpose of the research and signed two copies of the Free and Informed Consent Term, one of which was

made available to the user. Users were advised that the decision to accept or not participate in the research would not impact their access to the service offers, nor the quality of their care.

RESULTS

A total of 570 people were interviewed, of which 52 reported that they had not started using ARV. Of the 518 who reported taking ARV at some point in their lives, 510 responded having MDARV in the last three days, whose prevalence was 15.88 (95%CI 12.69–19.06).

Table 1 presents the prevalence and PRs of MDARV in the last three days according to the main sociodemographic characteristics and interview location. The characteristics associated with higher prevalence of MDARV were practicing a religion 20.07% (PR 1.95, 95%CI 1.07–3.57), change of residence in the last year 23.44% (PR 1.75; 95%CI 1.17–2.63), and place of interview UC 20.47% (95%CI 1.01–2.24).

Table 2 shows the prevalence of MDARV and respective PR with 95%CI according to characteristics related to care and behaviors. The highest prevalence of MDARV was associated with the identification of detectable viral load (41.30%), which corresponded to PR 3.07 (95%CI 2.03–4.66). The other factors that showed the highest prevalence were drug use of 23.00% (PR 1.57; 95%CI 1.02–2.41), alcohol use of 36.00% (PR 2.41; 95%CI 1.37–4.24), fair or poor self-perception of health of 26.14% (PR 1.85; 95%CI 1.21–2.83), and not knowing the $CD4^+$ T lymphocyte count of 24.60%. Duration of ARV use was directly associated with a higher prevalence of MDARV—the longer the time of use, the greater the prevalence of missed dose (χ^2 for trend 4.93465; p=0.03).

Table 1. Sociodemographic characteristics and crude prevalence ratio among people living with HIV according to self-report of missed doses in the last three days. CRT, São Paulo, SP, Brazil, 2017.

Sociodemographic characteristics	Self-report of missed doses in the last three days (n=510)		p-value	cPR (95%CI)
	Total	Yes		
	n	n (%)		
Gender				
Cisgender men	380	54 (14.21)		1.00
Cisgender women	105	22 (20.95)		1.47 (0.94–2.30)
Transgender women	15	4 (26.67)	0.34	1.88 (0.78–4.50)
Transgender men	2	0 (0.00)		0.00 (0.00–0.00)
Missing	8	1 (12.50)		0.88 (0.14–5.60)
Age group (years)				
18–29	56	8 (14.29)		1.00
30–49	252	36 (14.29)	0.48	1.0 (0.49–2.03)
50–80	202	37 (18.32)		1.28 (0.63–2.60)
Self-reported skin color/ethnicity				
White	342	51 (14.91)		1.00
Black	38	6 (15.79)	0.75	1.06 (0.49–2.30)
Mixed color	115	22 (19.13)		1.28 (0.82–2.02)
Indigenous/Yellow	15	2 (13.33)		0.89 (0.24–3.33)
Education level				
Elementary	88	17 (19.32)		1.00
High school	130	22 (16.92)	0.50	0.88 (0.49–1.55)
Undergraduate and above	292	42 (14.38)		0.74 (0.45–1.24)
Practice of religion				
No	107	11 (10.28)		1.00
Yes	294	59 (20.07)	0.01	1.95 (1.07–3.57)
Missing	109	11 (10.09)		0.98 (0.44–2.17)
Currently employed				
No	154	23 (14.94)		1.00
Yes	344	57 (16.57)	0.68	1.10 (0.71–1.73)
Missing	12	1 (8.33)		0.56 (0.08–3.79)
Change of residence in the last year				
None	374	50 (13.37)		1.00
Yes	128	30 (23.44)	0.03	1.75 (1.17–2.63)
Missing	8	1 (12.5)		0.93 (0.15–5.96)
Interview site				
Outpatient clinic	339	46 (13.57)	0.04	1.00
Urgent care	171	35 (20.47)		1.50 (1.01–2.24)
Total	510	81 (15.90)	-	-

cPR: crude prevalence ratio; CI: confidence interval.

Table 2. Health care and behaviors characteristics and crude prevalence ratio among people living with HIV according to self-report of missed doses in the last three days. CRT, São Paulo, SP, Brazil, 2017.

Health care and behaviors characteristics	Self-report of missed doses in the last three days (n=510)		p-value	cPR (95%CI)
	Total	Yes		
	n	n (5)		
Viral load				
Undetectable	462	62 (13.42)		1.00
Detectable	46	19 (41.30)	0.00	3.07 (2.03–4.66)
Missing	2	0 (0.00)		0.00 (0.00–0.00)
Illicit drug use				
No	388	57 (14.69)		1.00
Yes	100	23 (23.00)	0.04	1.57 (1.02–2.41)
Missing	22	1 (4.55)		0.31 (0.04–2.14)
Use of alcohol				
No	475	71 (14.95)		1.00
Yes	25	9 (36.00)	0.02	2.41 (1.37–4.24
Missing	10	1 (10.00)		0.67 (0.10–4.36
Perceived financial stability				
I live comfortably with my earnings	113	13 (11.50)		1.00
Suitable for main needs	203	33 (16.26)		1.41 (0.78–2.57)
Occasionally I need help from relatives and friends	81	20 (24.69)	0.14	2.15 (1.13–4.06)
Difficult to live on my earnings	91	12 (13.19)		1.15 (0.55–2.39)
Missing	22	3 (13.64)		1.19 (0.37–3.82)
Health self-perception				
Good and very good	411	58 (14.11)		1.00
Fair bad or very bad	88	23 (26.14)	0.01	1.85 (1.21–2.83
Missing	11	0 (0.00)		0.00 (0.00–0.00)
Knowing CD4⁺ T lymphocyte count				
No	126	31 (24.60)		1.00
Yes	375	46 (12.27)	0.00	0.50 (0.33–0.75)
Missing	9	4 (44.44)		1.80 (0.82–4.00)
Duration of ARV use (years)				
3 or less	96	9 (9.38)		1.00
4 to 10	115	15 (13.04)	0.03*	1.39 (0.63–3.03)
11 or more	208	39 (18.75)		2.00 (1.00–3.96)
Missing	91	18 (15.88)		2.10 (0.99–4.45)
Total	510	81 (15.90)	-	-

*χ^2 to linear trend= 4.93465. cPR: crude prevalence ratio; CI: confidence interval.

In the multiple models, the following were independently associated with higher MDARV in the last three days: identification of detectable viral load (PR 2.33; 95%CI 1.51–3.57); practicing a religion (PR 1.95; 95%CI 1.09–3.48); change of residence in the last year (PR 2.11; 95%CI 1.42–3.12); drug use (PR 1.82; 95%CI 1.20–2.75); and 11 years or more of ARV use (PR 2.36; 95%CI 1.25–4.42). Knowing CD4⁺ T lymphocyte count was associated with protection in relation to missed doses (PR 0.50; 95%CI 0.32–0.75) (**Table 3**).

DISCUSSION

In this study, a high prevalence of reports of missed doses was found in the three days prior to the interview. It is important to note a significant association of this report with the higher prevalence of detectable viral load in the multivariate analysis, which once again validates the accuracy of this strategy of measuring adherence to antiretroviral therapy (ART).

Despite the numerous ways of measuring adherence and the possible criticisms regarding the self-report method, such as the possibility of users overestimating their adherence, there is evidence that this tool can work as a screening procedure for the evaluation of adherence, being a simple and costless strategy[12].

The correlation between reports of MDARV and detectable viral load has already been addressed several times in the literature[13]. A study analyzing eight cohorts between 1996 and 2013 with 11,689 people, evaluating pharmacy data and self-report as adherence measures, concluded that both methods were strongly associated with virological failure[14]. A meta-analysis including data from 15,351 patients, although from methodologically heterogeneous studies, also concluded that self-reported missing doses was significantly associated with virological response[15], which reinforces the importance of routine investigation of adherence in medical, nursing, and in the pharmacy, actively asking the patients about the correct taking of medications, even in the current days when ARV regimens are more favorable to adherence.

To reflect on issues that can guide health services and professionals towards greater effectiveness in the care of people using ART, we discussed factors independently associated with reporting MDARV

Table 3. Crude and adjusted prevalence ratio of factors associated to self-report of missed doses in the last three days among people living with HIV. CRT, São Paulo, SP, Brazil, 2017.

Variables	Self-report of missed doses in the last three days (n=510)	
	cPR (95%CI)	adjPR (95%CI)
Viral load		
Undetectable	1.00	1.00
Detectable	3.07 (2.03–4.66)	2.33 (1.51– 3.57)
Missing	-	-
Practice of religion		
No	1.00	1.00
Yes	1.95 (1.07–3.57)	1.95 (1.09–3.48)
Missing	0.98 (0.44–2.17)	0.86 (0.40–1.82)
Change of residence in the last year		
None	1.00	1.00
Yes	1.75 (1.17–2.63)	2.11 (1.43–3.12)
Missing	0.93 (0.15–5.96)	1.31 (0.17–9.88)
Illicit drug use		
No	1.00	1.00
Yes	1.57 (1.02–2.41)	1.82 (1.20–2.75)
Missing	0.31 (0.04–2.14)	-
Knowing CD4⁺ T lymphocyte count		
No	1.00	1.00
Yes	0.50 (0.33–0.75)	0.50 (0.32–0.75)
Missing	1.80 (0.82–3.99)	1.06 (0.54–2.06)
Duration of ARV use (years)		
3 or less	1.00	1.00
4 to 10	1.39 (0.63–3.03)	1.49 (0.72–3.10)
11 or more	2.00 (1.00–3.96)	2.36 (1.25–4.42)
Missing	2.10 (0.99–4.45)	2.24 (1.10–4.55)

cPR: crude prevalence ratio; adjPR: adjusted prevalence ratio; CI: confidence interval; ARV: antiretroviral.

in the last three days in this study and that remained significant in the multivariate analysis, namely: the identification of detectable viral load, practicing a religion, change of residence in the last year, drug use, and more than 11 years of ARV use. We also discussed the only factor associated with less missed doses over the past three days, which is the knowledge of CD4⁺ T-cell count.

The association of alcohol and drug use with reports of missed doses is supported by several publications[16-18]. The problematic use of these substances is often related to other vulnerabilities and situations of social exclusion. Such syndemics were associated with detectable viral load in a multicenter cohort study in which the results suggest that the integration of interventions on alcohol and drug use, mental health care, and prevention of sexual risk into standard HIV care may be necessary to optimize treatment and models of "treatment as prevention". Data from an American cohort, with 21,275 patients who responded to a questionnaire on alcohol use disorders during follow-up, showed that a change in the pattern of alcohol use is associated with a change in adherence[18]. Such findings indicate the importance of approaching the use of alcohol and drugs during the assistance provided by the various professionals of the health team to PLHIV, seeking to assess their interference on adherence, and reinforce the role of specialized mental health services in monitoring PLHIV who make problematic use of alcohol and drugs to achieve better outcomes in this population.

The report of change of residence in the last year was also associated with MDARV in the last three days, validating the idea that instability in daily life can lead to failures in adherence. This finding was also identified in a systematic review published in 2016, in which the lack of stable, safe, and adequate housing proved to be a significant barrier factor for care[19].

Practicing a religion was significantly associated with the reporting of MDARV in the last three days. Studies that addressed religion and adherence showed controversial results, suggesting that religious engagement may have positive and negative components[20] that deserve further investigation. Contrary to what was found in this study, a systematic review identified a positive association between religion, spirituality, and clinical outcomes in 67% of the studies included[21]. The results of the HIV Prevention Trials Network (HPTN) 063 cohort study, which involved 749 patients from Brazil, Zambia, and Thailand, showed that 85% of the participants reported religious involvement but this factor was not statistically related to adherence[22]. Although this religious involvement was generally associated with better outcomes, in some places, such as Brazil, it can be a potential barrier for PLHIV with unhealthy alcohol use[22] or for those who, for example, stop treatment due to beliefs in spiritual healing[23].

In our study, being on ARV medication for 11 years or more was associated with reports of MDARV in the last three days. This finding may be related to fatigue resulting from the continuous and prolonged use of ARV drugs[24]. On the other hand, we know that adherence to medication is not a perennial condition in the life of PLHIV on ART and that eventual failures can happen without signifying the abandonment of treatment[25]. Moments of non-adherence can, however, be related to the risk of virological failure, viral resistance, disease progression, and death[7,9], and should be promptly identified and managed with a view to preserving the effectiveness of the therapeutic regimen. A cohort study carried out in Switzerland, with 3,150 treatment-naïve patients who started therapy between 2003 and 2012, with a mean follow-up of 4.7 years, revealed that the self-report (collected in one or two annual consultations) of two or more MDARV in the last four weeks was associated with an increased risk of virological failure and death. The risk of failure rose with at least two missed doses (one dose: hazard ratio [HR] 1.15, 95%CI 0.79–1.67; two doses: HR 2.5, 95%CI 1.31–3.53; more than two doses: HR 5.21, 95%CI 2.96–9.18) and the risk of death was higher with more than two missed doses (HR 4.87, 2.21–10.73)[7]. Persistent viremia correlates with residual inflammation, increased intestinal microbial translocation, and increased cardiovascular risk[9] and even low levels of viremia have been associated with systemic immunoactivation[10]. However, suboptimal adherence, even with an undetectable viral load, is also associated with persistent inflammation and immune activation, factors related to increased morbidity and mortality[9]. In a study in which 24 biomarkers were measured and correlated with self-reported adherence in the last four days, after adjusting for multiple comparisons, tumor necrosis factor-alpha (TNF-α) remained significantly higher (11% increase; $p<0.001$) in patients who reported adherence lower than 100% in this study population[9]. It is concluded that simply asking about adherence can help to identify patients at risk of negative clinical outcomes and offers opportunities for intervention[7].

Knowing the $CD4^+$ T lymphocyte count, which is related to protection regarding missed doses, was significantly associated with reporting lower MDARV in the last three days. This finding seems to explain the active appropriation of information about patients' health and their skills for self-care, which reinforces the importance of health professionals' educational role in achieving better adherence levels. This finding refers to the conceptual model proposed by Fisher & Fisher, in 1992, known as Information-Motivation-Behavioral Skills (IMB)[26], originally used to assess changes in sexual risk behavior for acquiring HIV. In the context of using ART, the adoption of regular adherence would be a function of the knowledge that people have about HIV infection and AIDS and about the risks related to irregular treatment, their motivation to preserve their health and their possibilities to perform specific acts that may converge to the adoption of regular adherence.

This study has limitations inherent to the methodology of cross-sectional analyses. However, it provides important information on factors associated with reports of missed doses that can guide the practice of services for better care for PLHIV.

All factors considered, this work brings significant contributions from the experience of a reference service in the care of PLHIV. It reinforces the validity of the recall and self-report of missing medication doses by users, pointing to a simple strategy for measuring adherence by the services and for the recognition of factors associated with lost doses, which can be used by the services to identify people at risk of failure or already failing to adhere, which constitutes a central challenge both for improving the quality of care for PLHIV/AIDS and for the effectiveness of Brazilian policy to combat the epidemic.

Strengths

One of the strengths of this study is the large sample size, which exceeded the calculation of the sample size by more than 100 participants. In addition, the rigorous randomization of the sample reduced the chance of interviewing only more motivated and higher adherence individuals (who usually have greater interest in participating in research). Also, the check of the viral load in the SISCEL makes the outcome measurement more reliable than the check with the user. Moreover, the analysis of the three most recent measures of viral load observed possible fluctuations and escapes related to adhesion.

Limitations

Missed doses were evaluated only in the last three days, therefore, some non-adherent people may not have been identified by this methodology. Another weakness is the lack of comparison of this method with other adherence assessment tools, besides the viral load test results. However, a meta-analysis that included 38 studies, with 18,010 patients, comparing virological outcomes against any two measures of adherence between monitoring by electronic devices, pill counting, pharmacy refill, self-report, and medical evaluation, concluded that there is no need for expensive or time-consuming adherence measures when the objective is to identify PLHIV at risk of treatment failure, since simple and low-cost adherence measures, such as self-report, predict virological failure better than or as well as objective measures[27].

CONCLUSION

This study evaluated the self-reported MDARV in the last three days among HIV-infected adults and showed its association with detectable viral load, corroborating the importance of a simple and easy-to-implement method to assess the risk of virological failure. In addition, it identified sociodemographic, behavioral, and care factors related to missed doses that can be investigated to identify people at greater risk of irregular adherence to ART.

Approval by the Human Research Ethics Committee

The study was approved by the *Reference and Training Center STD/AIDS (Centro de Referência e Treinamento DST/AIDS)* Research Ethics Committee, where the research was carried out (Opinion Number: 3,760,145; CAAE: 24876619.6.0000.5375).

Participation of each author

DLE: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. CGL: Data curation, Formal analysis, Writing – original draft. MAS: Data curation, Formal analysis, Writing – original draft. AOK: Data curation, Formal analysis, Writing – original draft. DBL: Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. SQR: Formal analysis, Writing – review & editing.

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Conflict of interests

The authors declare no conflicts of interest.

REFERENCES

1. UNAIDS. Estatísticas [Internet]. [cited 2023 Dec 20]. Available from: https://unaids.org.br/estatisticas/
2. Brasil. Ministério da Saúde. Boletim Epidemiológico Especial – HIV/Aids 2021 Internet]. 2021 [cited 2023 Oct 31]. Available from: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/especiais/2021/boletim-epidemiologico-especial-hiv-aids-2021.pdf/view
3. Tavares NUL, Bertoldi AD, Mengue SS, Arrais PSD, Luiza VL, Oliveira MA, et al. Factors associated with low adherence to medicine treatment for chronic diseases in Brazil. Rev Saude Publica. 2016;50(suppl 2):10s. https://doi.org/10.1590/S1518-8787.2016050006150
4. Brasil. Ministério da Saúde. Departamento de HIV, Tuberculose, Hepatites Virais e Infecções Sexualmente Transmissíveis. Protocolos clínicos e diretrizes terapêuticas para manejo da infecção pelo HIV em adultos [Internet]. 2018 [cited on 2021 Nov 11]. Available from: https://www.gov.br/aids/pt-br/central-de-conteudo/pcdts
5. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Antiretroviral therapy for the prevention of HIV-1 transmission. N Engl J Med. 2016;375(9):830-9. https://doi.org/10.1056/NEJMoa1600693
6. Mannheimer S, Hirsch-Moverman Y. What we know and what we do not know about factors associated with and interventions to promote antiretroviral adherence. Curr Infect Dis Rep. 2015;17(4):466. https://doi.org/10.1007/s11908-015-0466-9

7. Glass TR, Sterne JAC, Schneider MP, De Geest S, Nicca D, Furrer H, et al. Self-reported nonadherence to antiretroviral therapy as a predictor of viral failure and mortality. AIDS. 2015;29(16):2195-200. https://doi.org/10.1097/QAD.0000000000000782
8. Orrell C, Cohen K, Leisegang R, Bangsberg DR, Wood R, Maartens G. Comparison of six methods to estimate adherence in an ART-naïve cohort in a resource-poor setting: which best predicts virological and resistance outcomes? AIDS Res Ther. 2017;14(1):20. https://doi.org/10.1186/s12981-017-0138-y
9. Castillo-Mancilla JR, Brown TT, Erlandson KM, Palella Jr FJ, Gardner EM, Macatangay BJC, et al. Suboptimal adherence to combination antiretroviral therapy is associated with higher levels of inflammation despite HIV suppression. Clin Infect Dis. 2016;63(12):1661-7. https://doi.org/10.1093/cid/ciw650
10. Bull ME, Mitchell C, Soria J, Styrchak S, Williams-Wietzikoski C, Legard J, et al. Monotypic low-level HIV viremias during antiretroviral therapy are associated with disproportionate production of X4 virions and systemic immune activation. AIDS. 2018;32(11):1389-401. https://doi.org/10.1097/QAD.0000000000001824
11. Nemes MI, Carvalho HB, Souza MF. Antiretroviral therapy adherence in Brazil: AIDS. 2004;18 Suppl 3:S15-20. https://doi.org/10.1097/00002030-200406003-00004
12. Kabore L, Muntner P, Chamot E, Zinski A, Burkholder G, Mugavero MJ. Self-report measures in the assessment of antiretroviral medication adherence: comparison with medication possession ratio and HIV viral load. J Int Assoc Provid AIDS Care. 2015;14(2):156-62. https://doi.org/10.1177/2325957414557263
13. Da W, Li X, Qiao S, Zhou Y, Shen Z. Evaluation of self-report adherence measures and their associations with detectable viral load among people living with HIV (PLHIV) in China. PLoS One. 2018;13(8):e0203032. https://doi.org/10.1371/journal.pone.0203032
14. Ingle S, Crane H, Glass T, Yip B, Lima V, Gill M, et al. Identifying risk of viral failure in treated hiv-infected patients using different measures of adherence: the antiretroviral therapy cohort collaboration. J Clin Med. 2018;7(10):328. https://doi.org/10.3390/jcm7100328
15. Nieuwkerk PT, Oort FJ. Self-reported adherence to antiretroviral therapy for HIV-1 infection and virologic treatment response: a meta-analysis. J Acquir Immune Defic Syndr. 2005;38(4):445-8. https://doi.org/10.1097/01.qai.0000147522.34369.12
16. Shubber Z, Mills EJ, Nachega JB, Vreeman R, Freitas M, Bock P, et al. Patient-reported barriers to adherence to antiretroviral therapy: a systematic review and meta-analysis. PLoS Med. 2016;13(11):e1002183. https://doi.org/10.1371/journal.pmed.1002183
17. Tran BX, Fleming M, Do HP, Nguyen LH, Latkin CA. Quality of life improvement, social stigma and antiretroviral treatment adherence: implications for long-term HIV/AIDS care. AIDS Care. 2018;30(12):1524-31. https://doi.org/10.1080/09540121.2018.1510094
18. Williams EC, McGinnis KA, Rubinsky AD, Matson TE, Bobb JF, Lapham GT, et al. Alcohol use and antiretroviral adherence among patients living with HIV: is change in alcohol use associated with change in adherence? AIDS Behav. 2021;25(1):203-14. https://doi.org/10.1007/s10461-020-02950-x
19. Aidala AA, Wilson MG, Shubert V, Gogolishvili D, Globerman J, Rueda S, et al. Housing status, medical care, and health outcomes among people living with HIV/AIDS: a systematic review. Am J Public Health. 2016;106(1):e1-23. https://doi.org/10.2105/AJPH.2015.302905
20. Poteat T, Lassiter JM. Positive religious coping predicts self-reported HIV medication adherence at baseline and twelve-month follow-up among Black Americans living with HIV in the Southeastern United States. AIDS Care. 2019;31(8):958-64. https://doi.org/10.1080/09540121.2019.1587363
21. Doolittle BR, Justice AC, Fiellin DA. Religion, spirituality, and HIV clinical outcomes: a systematic review of the literature. AIDS Behav. 2018;22(6):1792-801. https://doi.org/10.1007/s10461-016-1651-z
22. Ransome Y, Mayer KH, Tsuyuki K, Mimiaga MJ, Rodriguez-Diaz CE, Srithanaviboonchai K, et al. The role of religious service attendance, psychosocial and behavioral determinants of Antiretroviral Therapy (ART) adherence: results from HPTN 063 cohort study. AIDS Behav. 2019;23(2):459-74. https://doi.org/10.1007/s10461-018-2206-2
23. Agência de Notícias da Aids. 'A cura do HIV não é com água abençoada da igreja': médicos afirmam que o tratamento antirretroviral é o melhor caminho contra a aids. [Internet]. 2022 [cited 2024 Jun 30]. Available from: https://agenciaaids.com.br/noticia/a-cura-do-hiv-nao-e-com-agua-abencoada-da-igreja-medicos-afirmam-que-o-tratamento-antirretroviral-e-o-melhor-caminho-contra-a-aids/
24. Beer L, Skarbinski J. Adherence to antiretroviral therapy among HIV-infected adults in the United States. AIDS Educ Prev. 2014;26(6):521-37. https:///doi.org/10.1521/aeap.2014.26.6.521
25. Teixeira PR, Paiva V, Shimma E. Tá difícil de engolir? Experiências de adesão ao tratamento antirretroviral em São Paulo [Internet]. [cited on 2021 Nov 11]. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/ta_dificil.pdf
26. Fisher JD, Fisher WA. Changing AIDS-risk behavior. Psychol Bull. 1992;111(3):455-74. https://doi.org/10.1037/0033-2909.111.3.455
27. Almeida-Brasil CC, Moodie EEM, Cardoso TS, Nascimento E, Ceccato MGB. Comparison of the predictive performance of adherence measures for virologic failure detection in people living with HIV: a systematic review and pairwise meta-analysis. AIDS Care. 2019;31(6):647-59. https://doi.org/10.1080/09540121.2018.1554241

Address for correspondence
DENIZE LOTUFO ESTEVAM
Rua Santa Cruz 81 – Vila Mariana
São Paulo (SP), Brazil
CEP: 04121-000
E-mail: dlotufo@crt.saude.sp.gov.br

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