ORIGINAL ARTICLE

Factors related to adherence to antiretroviral treatment in a specialized care facility

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SUMMARY

The objective of this study was to verify the level of adherence to antiretroviral treatment and its associated factors. This is a descriptive cross-sectional study based on data retrieved from medical records. To achieve this, we used a questionnaire composed of sociodemographic and clinical information recorded from patients aged between thirteen and fifty-nine years who attended a specialized service from 2007 to 2014. The chi-square test was performed to verify the association of the outcome with the categorical variables. Continuous variables were compared through the Student t-test. Thirteen variables were analyzed in the bivariate model, resulting in the selection of the following variables to the multivariate model (p<0.20) age of discovery (p=0.12), age (p=0.14), skin color (p=0.12), level of education (p=0.03), time since HIV diagnosis (p<0.001) and AIDS case (p<0.001). Among the six variables selected for the multivariate model, cases of aids (p<0.001) remained significant. We concluded that having aids decreases the probability of non-adherence to antiretroviral treatment by 92%. These results indicate that symptomatic patients have better adherence to therapy.

KEYWORDS: *HIV. Acquired immunodeficiency syndrome. Anti-retroviral agents. Medication adherence. Therapeutics. Health services.*

INTRODUCTION

Antiretroviral therapy (ART) emerged in the 1990s, resulting in an increase in survival rates. Nowadays, the term 'survival' is no longer used because ART has eliminated the prospect of short-term death, ensuring a life expectancy similar to that of non-infected individuals, provided there is proper adherence to therapy[1].

Brasil has been a pioneer in adopting a public policy of universal free access to antiretroviral treatment, even at an international level. In 1996, Brasil implemented high-efficacy antiretroviral therapy, whose greatest success was adopting a regime of three antiretroviral medications (triple therapy)[2]. The universal access to these drugs in Brasil resulted in a change in the characteristic of acquired immunodeficiency syndrome (AIDS), from a disease of high lethality to a controllable chronic disease[3].

The quality of life provided by the universal access to therapy is evidenced by statistical data reproduced by the Global Report of the Joint United Nations Program on Human Immunodeficiency Virus (HIV)/AIDS (UNAIDS)[4], which proved a significant decline in mortality due to aids, not only in Brasil but in all

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other countries. In 2013, there was a reduction of 800,000 deaths[5].

In 2015, UNAIDS established ambitious goals for HIV through a protocol that aims to chart new directions for the treatment of the virus. The goals for 2020 include the knowledge of their seropositive status by 90% of all people living with HIV, uninterrupted antiretroviral therapy for 90% of all people diagnosed with HIV infection, and viral suppression in 90% of all people receiving antiretroviral therapy[4].

Currently, in Brasil, it is estimated that 83% of those infected know their diagnosis, 62% are undergoing medical treatment, and 88% have an undetectable viral load. Thus, in order to achieve the goal established by UNAIDS, it is necessary that those affected by the disease have continued medical monitoring[6].

Considering the above, the objective of this study was to determine the levels of adherence to antiretroviral treatment and the factors related to it by evaluating patients with HIV/Aids in the aged between 13 and 59 years old and treated in a Specialized Care Service (SAE), located in the municipality of Vitória, Espírito Santo (ES), between 2007 and 2014.

METHODS

This is a descriptive, cross-sectional study based on a quantitative approach to identify and assess patients from 13 to 59 years old treated in the Center of Reference for Sexually Transmitted Diseases (STD/AIDS), located in the municipality of Vitória, ES, between 2007 and 2014.

All information was obtained by using a structured form for data collection. The form was divided into two stages, one containing questions related to sociodemographic aspects and the other to the clinical aspects.

We considered a minimum frequency of poor adherence of 5% for any of the categories present among the participants. To obtain a population estimate, considering a confidence interval of 95%, a sample of 102 individuals would be required to discriminate a five-times-higher frequency of poor adherence in a risk category, with 80% of power. Since there were 20 adolescents aged between 13 and 19 years old recorded in the SAE, we decided to include all of them plus a sample of 100 adults, which, in a direct comparison of age ranges, resulted in a ratio of 1:5.

Data were collected from patients' medical records, and we selected those aged from 13 to 59 years. We randomly drew 100 records from the 849 of patients aged between 19 and 59 years, since all adolescents aged between 13 and 19 years were included. The collection period lasted from November 2015 to March 2016.

Regarding the treatment adherence criterion, we classified as adherent members who continued ART without interruptions from the time of diagnosis until the day of data collection, i.e., the criterion used was medication pick-up from the SAE pharmacy. Those who abandoned therapy for any period or permanently were classified as non-adherent.

The categorical variables were represented by their absolute and relative frequencies. The continuous quantitative variables were represented by their central position and variability. Since all fit the Gauss model, we used mean and standard deviation. The bivariate analysis considered a dichotomous outcome (adherence or not), assessing its possible association with several variables. The association of the outcome with the categorical variables was verified by the Chi-square test, except when expected frequencies found were lower than five, in which case the maximum likelihood ratio (more than two categories) was used. Continuous variables were compared by Student's t-test (two groups). To measure the effect, we used the odds ratio with their respective confidence intervals of 95%.

Variables with a p-value of less than 0.2 in the bivariate analysis were included in the multivariate model, which comprised binomial logistic regression. The data were analyzed using Statistical Package for Social Sciences (SPSS), version 17.0, and presented in simple frequency tables.

This study was preceded by the approval of the Research Ethics Committee of the Federal University of Espírito Santo (UFES) (CAAE No. 46032915.9.0000.5060).

RESULTS

Of the 120 forms filled out, 79 (65.8%) belonged to male individuals, and their average age until the day of the collection was 36.3 years. There were 41 females (34.2% of the collected data), with an average age of 38.2 years. The distribution according to skin color revealed that 77 (64.2%) were brown, 22 (18.3%) were white, and 21 (17.5%) were black. Regarding formal education aspects, considering valid records, 27 (27.3%) had not completed primary education, and 24 (24.2%) had completed secondary education (Figure 1). With respect to occupations, we decided to categorize

patients between those who exercise (87 - 76.3%) or not (27 - 23.7%) a profession and then into jobs that require secondary education, corresponding to 66 individuals (57.9%), those that require an university degree, with a total of 21 individuals (18.4%), and those that do not apply, which included 27 individuals (23.7%) who were students, unemployed, or homemakers.

Regarding the distribution of people living with HIV/aids, according to the clinical variables, we found that the main source of infection by the virus was through sex, corresponding to 111 people (97.4%). We observed that the time for the diagnosis of HIV was an average of 63.6 months and 77 individuals (67%) progressed to AIDS. The Viral Load (VL) was undetectable in 67 patients (75.3%). The CD4 lymphocyte count had an average of 608.53 cells/mm3. Regarding a previous history of opportunistic infections, we observed that 66.7% had no history, as shown in Table 1.

Initially, we searched for an association between the adherence or non-adherence and sociodemographic and clinical variables. There was a significant difference ($p<0.05$) concerning the age at the time of diagnosis. Regarding skin color, brown-skinned people showed better adherence when compared to blacks and whites. In relation to formal education, people with higher educational levels showed greater adherence, with statistical significance. As to the clinical variables, we found a significant difference in adherence among those with an AIDS diagnosis ($p<0.001$) (Figure 1). There was significance regarding viral load ($p=0.04$); however, it was not included in the multivariate model because its increased level is a natural consequence of non-adherence and could act as a confounding variable. The prevalence of non-adherence was 43.3% in the sample.

Among the 13 variables analyzed, six were included in the logistic regression model. The results of the analysis (Table 2) showed that an aids diagnosis is associated with better adherence to antiretroviral treatment.

DISCUSSION

In the present study, we observed that an aids diagnosis improves adherence to antiretroviral therapy. Other variables that are considered as potential risk factors for non-adherence, such as education and marital status, showed no significant association with the outcome of interest (adherence).

FIGURE 1. CATEGORICAL VARIABLES INCLUDED IN THE LOGISTIC REGRESSION MODEL

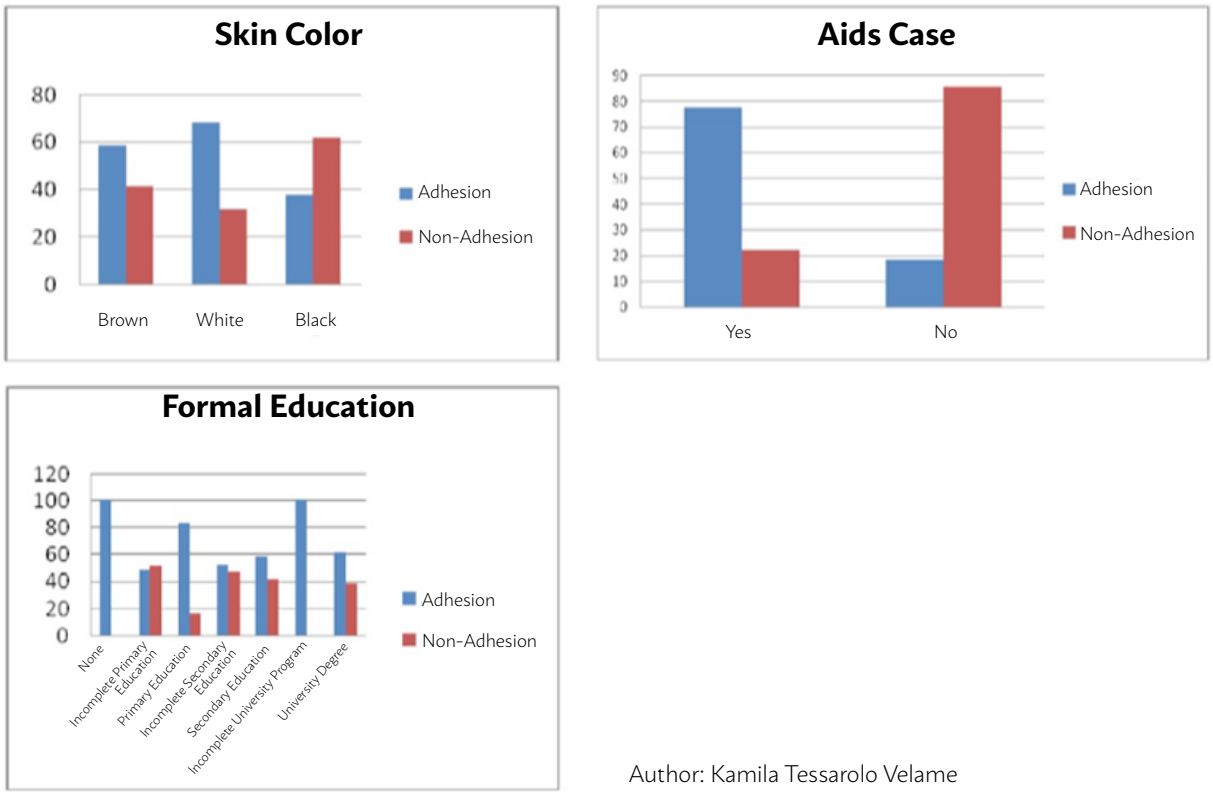

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TABLE 1. CLINICAL AND SOCIODEMOGRAPHIC CHARACTERISTICS OF A SAMPLE OF 120 INDIVIDUALS AGED BETWEEN 13 AND 59 YEARS IN FOLLOW-UP IN THE CENTER OF REFERENCE FOR STD/AIDS* OF VITÓRIA, ES, BRASIL, 2007 TO 2014.

Variables		Adherence n (%)	Non-adherence n (%)	Total n (%)	P-value ¥
Gender	Female	22 (53.2)	19(46.3)	41 (34.2)	0.63a
	Male	46 (58.2)	33 (41.8)	79 (65.8)	
Age (years) mean (SD)		38.2(11.7)	35.3 (9.3)		0.14b
Age of diagnosis (years) average (SD)		34.2(11.1)	29.4 (9.1)		0.12b
Skin color	Brown	45 (58.4)	32(41.6)	77 (64.2)	
	White	15(68.2)	7(31.8)	22(18.3)	0.12a
	Black	8(38.1)	13(61.9)	21 (17.5)	
Marital status	Single	51 (63.0)	30 (37.0)	81 (67.5)	
	Married	11 (45.8)	13 (54.2)	24 (20.0)	
	Divorced/separated	5 (55.6)	4 (44.4)	9 (7.5)	0.4a
	Widow(er)	1 (50.0)	1 (50.0)	2(1.7)	
	Stable union	0 (0.0)	1 (100.0)	1 (0.8)	
Formal education	None	3(100.0)	0 (0.0)	3(3.0)	
	Incomplete primary education	13(48.1)	14(51.9)	27 (27.3)	
	Primary education	5 (83.3)	1 (16.7)	6(6.1)	
	Incomplete secondary education	10(52.6)	9 (47.4)	19(19.2)	0.03a
	Secondary education	14 (58.3)	10(41.7)	24 (24.2)	
	Incomplete university program	7(100.0)	0 (0.0)	7(7.1)	
	University degree	8(61.5)	5 (38.5)	13(13.1)	
Occupation 1§	Yes	51 (58.6)	36(41.4)	87 (76.3)	0.8a
	No‖	15(53.6)	13 (46.4)	28 (24.6)	
Occupation 2^|	Until secondary education	37(56.1)	29 (43.9)	66 (57.9)	
	University degree	15(71.4)	6 (28.6)	21 (18.4)	0.35a
	Does not apply**	15(53.6)	13 (46.4)	28 (24.6)	
Source of	Sexual transmission	64 (57.7)	47 (42.3)	111 (97.4)	
infection	Use of injectable drugs	0 (0.0)	1 (100.0)	1 (0.9)	0.21a
	Occupational	0 (0.0)	1 (100.0)	1 (0.9)	
	Others	1 (100.0)	0 (0.0)	1 (0.9)	
Time of HIV diagnosis (months) average (SD)		54.6 (26)	75.3 (23.7)		<0.00 Ib
Aids case	Yes	60 (77.9)	17(22.1)	77 (67.0)	< 0.001a
	No	7(18.4)	31 (85.6)	38 (33.0)	
Viral load	<50 (undetectable)	55(82.1)	12(17.9)	67 (75.3)	
(copies/ml)	50 to 100,000	10(52.6)	9 (47.4)	19(21.3)	0.04a
	100,001 to 500,000	2 (66.7)	1 (33.3)	3 (3.4)	
Prior history	Yes	23 (57.5)	17(42.5)	40 (33.3)	
of infection	No	45 (56.2)	35 (43.8)	80 (66.7)	0.9a
Total				120/100	

[a]Chi-square test; [b]Student t-test. *STD- sexually transmitted diseases; ¥ - p - probability of significance; SD - standard deviation. Occupation 1§ - categorized as presence or absence of profession; ||No - unemployed, students, and homemakers; Occupation 2 - categorized according to the level of formal education; **Does not apply - unemployed, students, and homemakers. The frequencies were obtained from the record items that contained valid data.

Socioeconomic factors, such as formal education and marital status, have more influence only in situations of extreme poverty since this can make it more difficult to have access to treatment[7].

The results in relation to the variable "case of aids" indicate that the likelihood of non-adherence to antiretroviral treatment is reduced by approximately 92% among individuals who developed the disease. This indicates that symptomatic individuals adhere more often to treatment.

Probably, the presence of symptoms motivates the search for rigorous clinical monitoring due to the expectation of improvement, which, in turn, causes satisfactory adherence to treatment. The absence of symptoms and feeling of well-being are pointed out as causes for not taking their medicine, since patients

TABLE 2. RESULTS FROM THE REGRESSION ANALYSIS OF VARIABLES WITH P < 0.2 AFTER BIVARIATE ANALYSIS OF THE CHARACTERISTICS OF 120 INDIVIDUALS AGED BETWEEN 13 AND 59 YEARS IN FOLLOW-UP IN THE CENTER OF REFERENCE FOR STD/AIDS VITÓRIA, ES, BRASIL, 2007 TO 2014.

Variables	Coefficient (Beta)	Standard error (SE)	Significance (p-value) ¥	Odds ratio Exp (Beta)	Confidence interval (CI 95%)	
					Lower threshold	Upper threshold
Age of diagnosis	.452	.342	.187	1.571	.803	3.074
Age	-.382	.338	.259	.683	.352	1.324
Skin color	.038	.348	.913	1.039	.525	2.054
Formal education	.136	.159	.392	1.146	.839	1.565
Time of HIV diagnosis	-.007	.030	.807	.993	.936	1.053
Aids case	-2.527	.670	.000	.080	.022	.297

*STD - sexually transmitted diseases; ¥ - p - probability of significance; CI - Confidence Interval.

believed it was not necessary, and only resumed taking it once they started to feel bad again[8].

In Brasil, a study conducted in 55 health services specialized in the care for patients with HIV/aids showed large variations in the non-adherence rates throughout the country, ranging from 10.7% to 86.0%. Absenteeism in consultations was a factor that contributed even more to non-adherence and worsened values of CD4 lymphocytes and viral load[9].

The issue of the disease symptoms is highly emblematic in literature and incorporates several dimensions, even those attributed to the occurrence of adverse reactions to medications[10]. The patient cannot see the medication as a trial, just using it when they are symptomatic, believing there will be a spontaneous improvement and, at the same time, blame it for the onset of symptoms. This compromises the correct adherence to treatment[11].

Another important reason for low adherence or even the late start of ART is the stigma. Patients are afraid of being identified as infected by HIV; thus, they avoid care until very late when there are no more choices left, and weakness is inevitable. These aspects reflect a poor understanding of the chronic nature of the disease[12]. In Uganda, a study was conducted that confirms this hypothesis. In it, patients reported difficulties in taking medication when they were close to employers, colleagues, or friends who were not aware of their condition[13]. The irregular follow-up makes it more likely for them to develop symptoms of immunodeficiency. Thus, patients adhere to antiretroviral therapy aiming at a clinical improvement[14].

This study has limitations related to its cross-sectional design, which prevents a proper assessment of causality, and the fact that its sample was calculated to show large effects, thus limiting its ability to identify valid associations of smaller magnitude. In addition, it was not possible to retrieve information about patient behavioral data due to the scarcity of information in the records analyzed.

On the other hand, the importance of the study lies in the fact that it identifies the presence of symptoms as a potential factor that stimulates adherence. In a scenario of an early start of antiretroviral therapy in infected individuals, the results presented here highlight the importance of developing precise strategies to stimulate adherence, since such individuals are more probable of being asymptomatic[15].

CONCLUSION

The AIDS epidemic is currently characterized by the presence of many epidemiological changes in its profile, related to both socioeconomic and clinical aspects. This requires ongoing changes to patient care, which is provided through antiretroviral treatment and various professionals.

The present study fits into the context of the need to establish appropriate strategies to reduce the damages related to HIV infection in individuals. However, there is no intention to exhaust the theme and encompass the full range of issues inherent to a subject as important as the factors that can interfere with adherence to antiretroviral treatment.

Authors contributions

Kamila Tessarolo Velame - Participated in the conception of the study, its design, data collection, data analysis and drafting of the manuscript. Renata de Souza da Silva - Participated in data collection, data analysis, and critical reading of the first version of the manuscript. Crispim Cerutti Junior - Participated in the conception of the study, its design, data analysis, and drafting of the manuscript.

Conflict of interest

There are no conflicts of interest to be declared. Derived from the Master's thesis entitled "Fatores relacionados à adesão ao tratamento antirretroviral em serviço de atendimento especializado", submitted as part of the Graduate Program on Infectious Diseases, at the Federal University of Espírito Santo, Vitória, ES, Brasil.

RESUMO

O objetivo deste estudo foi verificar os níveis de adesão ao tratamento antirretroviral e os fatores associados a ela. Trata-se de um estudo descritivo de delineamento transversal baseado em levantamento de prontuários. Para tanto, foi utilizado um questionário composto de informações sociodemográficas e clínicas de pacientes com idade entre 13 e 59 anos atendidos em um serviço de atendimento especializado nos anos de 2007 a 2014. Foi realizado o teste do Qui-quadrado para verificar a associação do desfecho com as variáveis categóricas. As variáveis contínuas foram comparadas pelo teste t de "Student" (dois grupos). Treze variáveis foram analisadas no modelo bivariado, sendo selecionadas para o modelo multivariado (p<0,20): idade de descoberta (p=0,12), idade (p=0,14), cor da pele (p=0,12), escolaridade (p=0,03), tempo de diagnóstico do HIV (p<0,001) e caso de aids (p<0,001). Das seis variáveis selecionadas para o modelo multivariado, permaneceu significante o fato de o paciente ter aids (p<0,001). Concluiu-se que ter aids reduz a probabilidade de não adesão ao tratamento antirretroviral em cerca de 92%. Os resultados indicam que o indivíduo que é sintomático adere melhor à terapia.

PALAVRAS-CHAVE: *HIV. Síndrome da imunodeficiência adquirida. Antirretrovirais. Adesão à medicação. Terapêutica. Serviços de saúde.*

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