



ORIGINALS

Bilingual edition English/Spanish

Related factors to non-adherence to antiretroviral therapy in HIV/AIDS patients

Factores relacionados con la no adherencia a la terapia antirretroviral en pacientes con VIH/sida

Juan Andrés Arrieta-Martínez¹, Jorge Iván Estrada-Acevedo², Carlos Alberto Gómez³, Juliana Madrigal-Cadavid², Juan Alberto Serna², Paulo Andrés Giraldo², Óscar Quirós-Gómez⁴

¹Fundación Hospital San Pedro, Pasto, Colombia. ²Grupo Farmacoepidemiología y Gestión de Riesgo, +Helpharma IPS, Colombia. ³Grupo Generación de valor en Salud, Omnivida, Medellín, Colombia. ⁴Facultad de Medicina, Universidad CES, Medellín, Colombia.

Author of correspondence

Juliana Madrigal Cadavid
 +helPharma IPS
 Carrera 43a # 34 - 95 Piso 11
 Medellín, Colombia.

Email:
 jmadrigal@helpharma.com

Received 9 July 2021;
 Accepted 1 August 2022.
 Early Access date (10/26/2022).
 DOI: 10.7399/fh.11793

How to cite this paper

Arrieta-Martínez JA, Estrada-Acevedo JI, Gómez CA, Madrigal-Cadavid J, Serna JA, Giraldo PA, et al. Related factors to non-adherence to antiretroviral therapy in HIV/AIDS patients. Farm Hosp. 2022;46(6):319-26.

Abstract

Objective: To identify sociodemographic, clinical, and pharmacological factors associated with nonadherence to antiretroviral treatment in patients with human immunodeficiency virus/acquired immunodeficiency syndrome treated between 2017 and 2020 in four cities in Colombia.

Method: An observational, cross-sectional, retrospective study was conducted of a population of patients with human immunodeficiency virus/acquired immunodeficiency syndrome treated between 2017 and 2020. The Morisky-Green scale, the simplified medication adherence questionnaire, and the simplified scale to detect adherence problems to antiretroviral treatment were applied to determine patient adherence. A binomial multiple logistic regression was performed to evaluate the factors that best explain nonadherence.

Results: A total of 9,835 patients were evaluated, of whom 74.4% were men, 71.1% were aged between 18 and 44 years, 76.0% had attended at most secondary school, 78.1% were single, and 97.6% resided in an urban area. After applying three different scales to each patient, 10% of the study population were identified as nonadherent to treatment. The risk of nonadherence was significantly higher in patients who presented any drug-related problem or had an adverse reaction to antiretroviral drugs.

Conclusions: The variables most strongly associated with nonadherence

Resumen

Objetivo: Identificar los factores sociodemográficos, clínicos y farmacológicos asociados a la no adherencia al tratamiento antirretroviral en pacientes con infección por virus de la inmunodeficiencia humana/sida atendidos entre 2017 y 2020 en diferentes ciudades de Colombia.

Método: Se realizó un estudio observacional, de corte transversal y retrospectivo, con una población de pacientes con infección por virus de la inmunodeficiencia humana/sida atendidos entre 2017 a 2020. Se aplicaron las escalas Morisky-Green, el cuestionario simplificado de adherencia a la medicación y la escala simplificada para detectar problemas de adherencia al tratamiento antirretroviral, para determinar la adherencia de los pacientes. Se realizó una regresión logística múltiple para evaluar los factores que mejor explican la no adherencia.

Resultados: Se evaluaron 9.835 pacientes, de los cuales el 74,4% eran hombres, el 71,1% tenían una edad entre 18 a 44 años, el 76,0% cursó como máximo hasta secundaria, el 78,1% eran solteros y el 97,6% residían en zona urbana. Se encontró una proporción de no adherencia al tratamiento del 10% después de aplicar tres escalas diferentes a cada paciente. Las personas que presentaron algún problema relacionado con los medicamentos tuvieron un riesgo significativamente mayor de no ser adherentes, al igual que aquellos que tuvieron alguna reacción adversa a los medicamentos antirretrovirales.

KEYWORDS

Medication adherence; HIV; Anti-HIV agents; Drug-related side effects and adverse reactions.

PALABRAS CLAVE

Cumplimiento de la medicación; VIH; Fármacos anti-VIH; Efectos colaterales y reacciones adversas relacionados con medicamentos.



Los artículos publicados en esta revista se distribuyen con la licencia
 Articles published in this journal are licensed with a
 Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License.
<http://creativecommons.org/licenses/by-nc-sa/4.0/>
 La revista Farmacia no cobra tasas por el envío de trabajos,
 ni tampoco por la publicación de sus artículos.

rence to antiretroviral treatment were drug-related problems, adverse drug reactions, a history of nonadherence to treatment, and psychoactive substance use.

Introduction

Human immunodeficiency virus (HIV) continues to be a global public health problem. According to figures provided by the World Health Organization (WHO), at the end of 2018, there were approximately 38 million people with HIV. Over time, this disease has claimed more than 32 million lives¹. Human immunodeficiency virus is a chronic infection. Resources are aimed at increasing its prevention and improving access to health care. Its control at the individual level depends largely on adherence to antiretroviral treatment (ARV)^{2,3}.

According to the WHO, and based on the definitions of Haynes and Rand⁴, adherence to treatment can be understood as "The degree to which a person's behaviour (taking medication, following a diet, and making lifestyle changes) corresponds to the recommendations agreed upon by a health care provider". In HIV/acquired immunodeficiency syndrome (AIDS) patients, the rapid rate of virus replication and mutation requires high adherence to drug treatment to reduce the viral load and ensure that drug therapy is effective^{3,5}.

ARV treatment is the most effective intervention in terms of survival and reduced morbidity and mortality in HIV patients⁶. However, a significant percentage of patients still present virological treatment failure^{7,8}, mainly due to nonadherence to therapy. Adherence to ARV treatment can be affected by multiple factors. Several studies have shown how these factors can vary according to the population in which they are studied. In general, low adherence to ARV treatment has been found to be associated with variables such as low educational levels, sexual orientation (homosexual), age (younger people), low income, unemployment, and time on treatment^{9,10}. Similarly, associations have been found between nonadherence to ARV treatment and the use of psychoactive substances such as cannabis, cocaine, methadone, heroin, and alcohol^{10,11}.

In Colombia, the Ministry of Social Protection and Health affirms that pharmaceutical chemists are responsible for evaluating and monitoring adherence to ARV; however, no specific methodology has been defined¹² and pharmacists are responsible for measuring adherence by using different methodologies, such as questionnaires/scales and dispensing records¹³.

Variability in the factors that lead to nonadherence to ARV treatment makes it relevant to evaluate these factors in specific populations and thus identify and focus health interventions on those aspects that can have a positive impact on adherence, thus improving health outcomes for patients.

The objective of this study was to identify the sociodemographic, clinical, and pharmacological factors associated with nonadherence to ARV treatment in HIV patients treated in health care provider institutions in Colombia.

Methods

An observational, cross-sectional, retrospective study was conducted of patients diagnosed with HIV. Between 2017 and 2020, the study included patients with active ARV treatment who had agreed to participate in a pharmacotherapeutic follow-up program in a Colombian health institution in the cities of Medellín, Cali, Bogotá, and Barranquilla. We excluded minors when the individuals responsible for them did not authorize participation in the pharmacotherapeutic follow-up program.

During the pharmacotherapeutic follow-up consultation, pharmacists measured adherence in each patient by administering the Morisky-Green scale⁴, the Simplified Medication Adherence Questionnaire (SMAQ)¹⁵, and the simplified scale to detect problems with adherence (ESPA) to ARV treatment¹⁶. After completing the three scales, patients with a result of nonadherence on at least one of the scales were nonadherent. Three different scales were used to measure adherence to reduce potential information bias because experience has indicated that patients tend to memorize the questionnaires and respond intuitively.

Conclusiones: Los problemas relacionados con el uso de medicamentos, las reacciones adversas a medicamentos, los antecedentes de no adherencia al tratamiento y el consumo de sustancias psicoactivas fueron las variables que más se asociaron con la no adherencia al tratamiento antirretroviral.

A database was used to include and store the variables identified during the medical and pharmaceutical consultations regularly attended by patients. For the purposes of analysis, these variables were first grouped into sociodemographic ones, such as age, sex, educational level, marital status, area of residence, occupation, economic dependence, health regime, sexual preference, children and partner, and socioeconomic level. The latter variable was measured according to housing conditions and environment on a scale of 1 to 6 as defined by the National Administrative Department of Statistics of Colombia, where 1 indicates the worst conditions and 6 is the best conditions. We also included clinical variables (stage at admission, psychoactive substance use, psychological illnesses, emergencies in the last year) and pharmacological variables (time on treatment, ARV regimen, a history of nonadherence, adverse drug reactions [ADRs], polymedication, and drug-related problems [DRPs]). Definitions provided by the WHO were used to classify ADRs. The identification and classification of DRPs and their interventions were based on the Dader method, which defines DRPs as negative clinical outcomes resulting from pharmacotherapy that for many reasons lead to the nonachievement of the therapeutic objective or to the appearance of unwanted effects.

We conducted a univariate analysis. Qualitative variables are expressed as absolute and relative frequencies (simple and cumulative) and quantitative variables are expressed as summary measures, such as central tendency, dispersion, and position (Kolmogorov-Smirnov normality test). We performed contingency tables and the chi-square test and used Odds Ratios (OR) and their respective 95% confidence intervals (95%CI) to measure statistical power.

The variables that showed statistical differences in the bivariate analysis were entered into a multivariate model for explanatory purposes (binary logistic regression: 95% confidence interval; alpha = 0.05). R statistical software was used.

As stated in Act No. 260 of June 2, 2021, this study was approved by the Institutional Ethics Committee for Human Research of University CES. It was also endorsed by the Scientific Management of the insurer and the research committee of the health institution.

Results

The analysis included a total of 9,835 patients with HIV/AIDS on ARV treatment. Of these patients, 74.4% were men, 71.1% were between 18 and 44 years of age, 76.0% had at most secondary education, 78.1% were single, 97.6% resided in urban areas, 72.4% had a medium socioeconomic level (levels 3 and 4), and 82.1% did not have an active partner. Table 1 summarizes the general characteristics of the study population. Most patients received the ARV treatments abacavir/lamivudine plus efavirenz (27.2%) and emtricitabine/tenofovir plus efavirenz (21.8%). Figure 1 shows the different treatments in the study population.

In total, 10.0% of patients were classified as nonadherent. This population was sociodemographically characterized by being male (69.9%), less than 45 years of age (80.7%), without a partner (79.9%), having a medium socioeconomic level of at least 3 (67.9%), being economically independent (87.0%), affiliated to the contributory health regime (95.0%), and having homo/bisexual sexual tendencies (63.1%) (Table 2).

Regarding the clinical and pharmacological variables, the nonadherent patients differed in terms of having an HIV diagnosis (not yet classified as AIDS) at admission (67.1%), not consuming alcohol (65.8%), not smoking tobacco (85.1%), and denying the consumption of psychoactive substances (88.9%). Of the nonadherent patients, 100% had a history of nonadherence, 50% had presented with medication-related problems (Figure 2), and 12.4% had presented with adverse reactions (Table 3).

The multivariate analysis found significant associations between nonadherence and DRPs, ADRs, a history of nonadherence, health affiliation regime, age (at most 45 years), sexual preference (heterosexual), psychoac-

Table 1. General characteristics of the HIV patient population on antiretroviral treatment (2017-2020)

Variable		n	(%)
Sex	Male	7,317	74.40
	Female	2,518	25.60
Age, years	At least 65	292	2.97
	45 to 64	2,507	25.49
	18 to 44	6,995	71.12
	At most 18	41	0.42
Educational level	University	783	7.96
	Technical/technology	1,570	15.96
	Secondary school or lower	7,482	76.08
Marital status	Single/widowed/separated	8,078	82.14
	Partnered/married	1,757	17.86
Socioeconomic level*	High	303	3.08
	Medium	7,126	72.46
	Low	2,406	24.46
Alcohol consumption	Yes	2,640	26.84
	No	7,195	73.16
Tobacco consumption	Yes	871	8.86
	No	8,964	91.14
Psychoactive substance consumption	Yes	565	5.74
	No	9,270	94.26
Bipolar affective disorder	Yes	132	1.34
	No	9,703	98.66
Depression	Yes	431	4.38
	No	9,404	95.62
Anxiety	Yes	276	2.81
	No	9,559	97.19
Pharmacological group	2 ITIAN + 1 ITINN	6,332	64.38
	2 ITIAN + 1 IP	2,332	23.71
	Other	1,171	11.91
Adverse drug reactions	No	9,521	96.81
	Yes	314	3.19
Polymedication	No	8,675	88.21
	Yes	1,160	11.79
Forgetting to collect medications	No	9,120	92.73
	Yes	715	7.27
Problems related to the use of medications	No	8,799	89.47
	Yes	1,036	10.53

*Socioeconomic levels groups: 1-2, low; 3-4, medium; level, and 5-6, high.

ITIAN: Nucleotide analogue reverse-transcriptase inhibitor; ITINN: non-nucleotide reverse-transcriptase inhibitor; IP: protease inhibitor.

tive substance use, socioeconomic level (2 or lower), and polymedication. The latter variable was a "protective factor" for adherence (adjusted OR: 0.68; CI: 0.49-0.94). Of note, table 4 shows that the ratio of nonadherence to adherence is 8 times higher in patients with DRPs than in those without DRPs (adjusted OR: 8.11; CI: 6.47-10.17). Adverse reactions and history of nonadherence also acted as risk factors (adjusted OR: 1.86; CI: 1.46-2.38 and adjusted OR: 2.01; CI: 1.41-2.85, respectively).

Discussion

In total, 10% of the study population were identified as nonadherent. This percentage is lower than the percentages reported by Sung-Hee Kim *et al.*¹⁷ (47%, 38%, and 33% in North America, Europe, and South America, respectively). However, it should be noted that most of the studies referred to in their work used viral load and dispensing records to measure adherence. Although some of the scales used to measure adherence have not been

Figure 1. Distribution of the study population according to antiretroviral scheme.

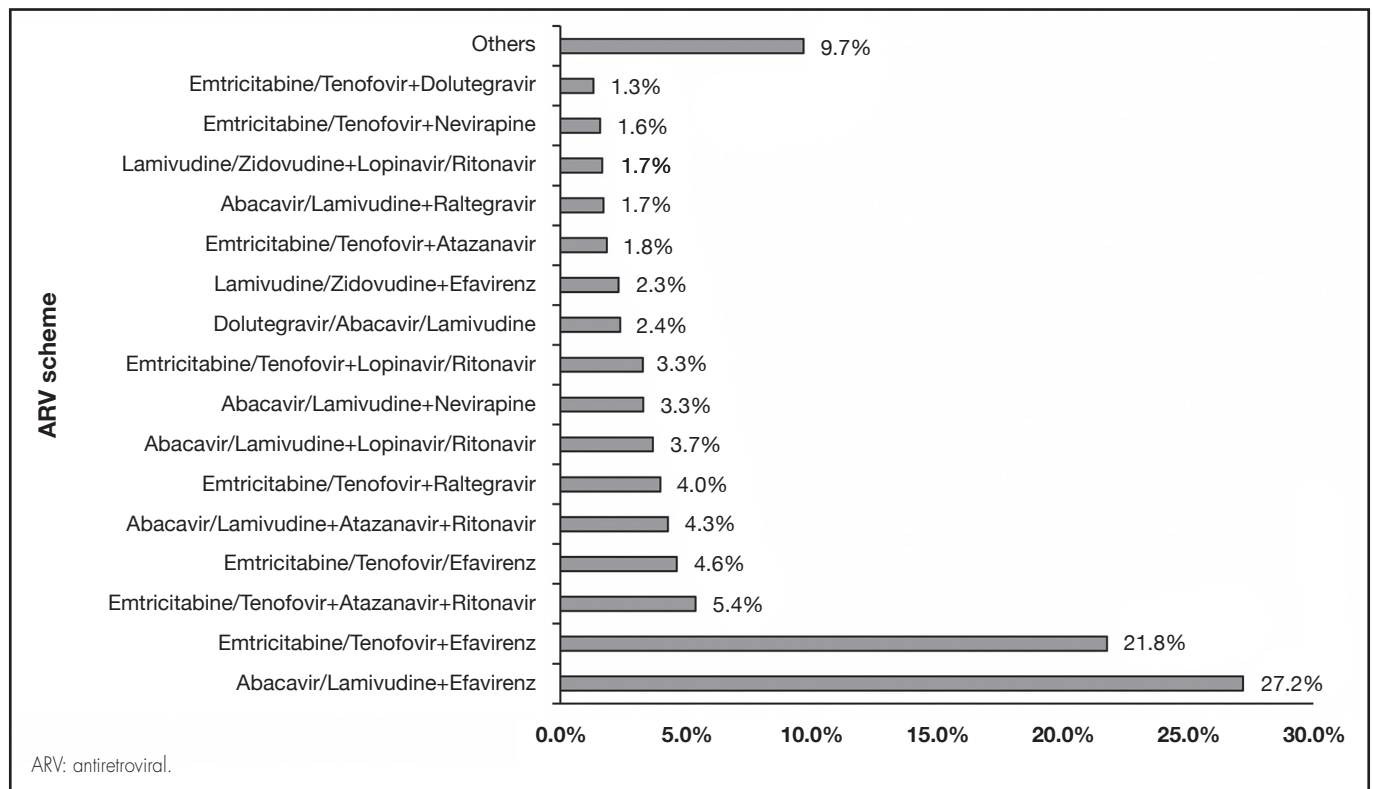


Figure 2. Main medication-related problems identified during pharmacotherapeutic monitoring.

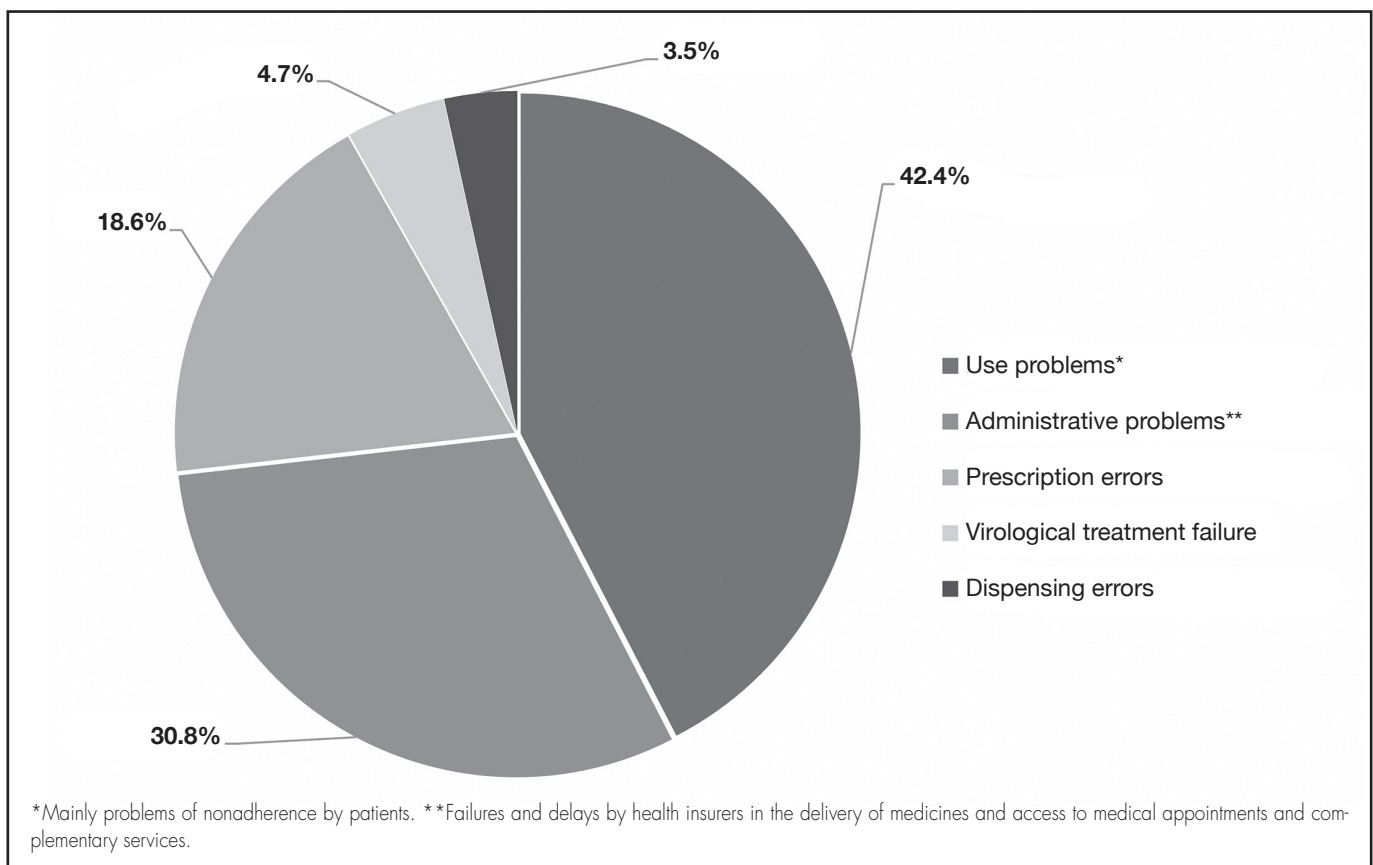


Table 2. Sociodemographic characteristics associated with nonadherence in HIV patients on antiretroviral treatment (2017-2020)

Sociodemographic characteristics	Nonadherent	Adherent	χ^2	P-value
	n (%)	n (%)		
Sex				
Male	685 (69.90)	6,632 (74.90)	11.30	< 0.01
Female	295 (30.10)	2,223 (25.10)		
Age				
At least 45 years	189 (19.29)	2,610 (29.47)	44.49	< 0.01
At most 44 years	791 (80.71)	6,245 (70.53)		
Education				
At least technical	227 (23.16)	2,126 (24.01)	0.30	0.58
At most secondary	753 (76.84)	6,729 (75.99)		
Marital status				
Partnered	197 (20.10)	1,560 (17.62)	3.54	0.05
Nonpartnered	783 (79.90)	7,295 (82.38)		
Area of residence				
Urban	953 (97.24)	8,646 (97.64)	0.43	0.51
Rural	27 (2.76)	209 (2.36)		
Social level				
At least level 3	665 (67.86)	6,764 (76.38)	34.27	< 0.01
At most level 2	315 (32.14)	2,091 (23.62)		
Economic dependence				
No	835 (86.98)	7,838 (90.52)	11.81	< 0.01
Yes	125 (13.02)	821 (9.48)		
Health regime				
Contributory	928 (94.98)	8,596 (97.41)	17.83	< 0.01
Subsidized	49 (5.02)	229 (2.59)		
Sexual preference				
Homo/Bisexual	436 (63.10)	4,703 (73.51)	33.37	< 0.01
Heterosexual	255 (36.90)	1,695 (26.49)		
Children				
Yes	9 (0.97)	118 (1.43)	0.98	0.32
No	920 (99.03)	8,135 (98.57)		
Carer				
Yes	232 (24.14)	1,681 (20.12)	8.34	< 0.01
No	729 (75.86)	6,678 (79.88)		

validated in HIV patients, it should be noted that they are widely used given the high cost or lack of availability of other methods¹⁸.

A systematic review and meta-analysis of 53 studies conducted in Latin America and the Caribbean¹⁹ showed that overall adherence to treatment was 70%: thus, the percentage of nonadherent patients was higher in those studies than in our study. Suárez *et al.*²⁰ evaluated adherence to ARV treatment in patients in the Caribbean region of Colombia. They used the Morisky-Green test as a measure and found that 89.0% were nonadherent. Adherence levels are highly variable and depend mainly on the population studied (variability between regions) and the measurement instrument used²¹.

The presence of adverse reactions represents a strong barrier to adherence to ARV treatment. Associations were found between nonadherence to ARV therapy and adverse drug reactions and DRPs. These results are consistent with recent findings obtained by Urizar *et al.*²², who found that patients receiving ARV treatment in a hospital in Paraguay were eight times more likely to be nonadherent to treatment when adverse reactions occurred. Similarly, Pérez and Viana²³ found that the risk of nonadherence to ARV treatment was four times higher in patients who had adverse drug reactions.

In this study, DRPs were the most relevant factor associated with nonadherence. This result is significant given that few studies have evaluated the association between nonadherence to ARV treatment and the presence of DRPs. In general, the most frequently evaluated variable has been the presence of adverse drug reactions; however, Ospina *et al.*²⁴ conducted a review in 2011 and found that, regarding medication, safety problems (including adverse drug reactions) only form a small percentage of all the potential problems that can occur during medication use.

Overall, the available evidence suggests that treatment adherence worsens as the number of pills the patients must take increases²⁵. According to our results, and contrary to expectations, it is striking that polymedication (taking more than five drugs, including ARVs) was found to be a protective factor for adherence. The reasons for this situation remain unclear; however, polymedicated patients are generally older, which may explain adherence in this group of patients.

Significant associations were also found between nonadherence and other sociodemographic factors (being less than 45 years of age and low income). The results suggest that young people are at increased risk of nonadherence. This situation may be related to social behaviour and the

Table 3. Clinical and pharmacological characteristics associated with nonadherence in HIV patients on antiretroviral treatment (2017-2020)

Variables	Nonadherent		Adherent		χ^2	P-value
	n (%)		n (%)			
Diagnosis at admission	HIV	658 (67.14)	6,222 (7.27)	3.94	0.04	
	AIDS	322 (32.86)	2,633 (29.73)			
Alcohol consumption	No	645 (65.82)	6,550 (73.97)	29.45	< 0.01	
	Yes	335 (34.18)	2,305 (26.03)			
Tobacco consumption	No	834 (85.10)	8,130 (91.81)	48.39	< 0.01	
	Yes	146 (14.90)	725 (8.19)			
PAS consumption	No	871 (88.88)	8,399 (94.85)	57.03	< 0.01	
	Yes	109 (11.12)	456 (5.15)			
Bipolar affective disorder	No	962 (98.16)	8,741 (98.71)	1.61	0.20	
	Yes	18 (1.84)	114 (1.29)			
Schizophrenia	No	959 (97.86)	8,567 (96.75)	3.21	0.07	
	Yes	21 (2.14)	288 (3.25)			
Depression	No	946 (96.53)	8,458 (95.62)	1.92	0.16	
	Yes	34 (3.47)	397 (4.38)			
Anxiety	No	960 (97.96)	8,599 (97.11)	2.03	0.15	
	Yes	20 (2.04)	256 (2.89)			
History of nonadherence	No	0 (0.00)	7,471 (84.37)	886.38	< 0.01	
	Yes	980 (10.0)	1,384 (15.63)			
Adverse reactions	No	859 (87.65)	8,662 (97.82)	291.84	< 0.01	
	Yes	121 (12.35)	193 (2.18)			
Polymedication	No	887 (9.51)	7,788 (87.95)	5.31	0.02	
	Yes	93 (9.49)	1,067 (12.05)			
ARV treatment time	At least 2 y	620 (63.40)	5,334 (6.38)	3.23	0.07	
	1-2 y	358 (36.60)	3,500 (39.62)			
Emergencies	No	374 (38.16)	3,471 (39.20)	0.36	0.54	
	Yes	606 (61.84)	5,383 (6.80)			
PRM	No	480 (48.98)	8,319 (93.95)	1884.40	< 0.01	
	Yes	500 (51.02)	536 (6.05)			

ARV: antiretroviral; HIV: human immunodeficiency virus; PAS: psychoactive substances; PRM: problems related to medication.

Table 4. Variables that explain nonadherence in patient with HIV/AIDS under antiretroviral treatment (2017-2020)

Variables	Raw OR (95%CI)	Adjusted OR* (95%CI)
Female sex	1.28 (1.10-1.48)	1.13 (0.92-1.40)
Age (at most 45 years)	1.66 (1.42-1.95)	1.54 (1.21-1.95)
Socioeconomic level (at most level 2)	1.53 (1.33-1.77)	1.24 (1.02-1.53)
Economic dependence (yes)	1.43 (1.17-1.75)	1.12 (0.84-1.49)
Health regimen (subsidised)	1.98 (1.45-2.72)	1.61 (1.02-2.54)
Sexual preference (heterosexual)	1.62 (1.37-1.91)	1.51 (1.22-1.86)
Diagnosis at admission (AIDS)	1.16 (1.02-1.33)	0.99 (0.80-1.22)
Carer (yes)	0.79 (0.69-0.93)	0.95 (0.75-1.20)
Alcohol consumption	1.48 (1.28-1.70)	1.13 (0.92-1.40)
Tobacco consumption	1.96 (1.62-2.38)	1.19 (0.88-1.61)
Psychoactive substance consumption	2.31 (1.85-2.87)	1.49 (1.07-2.07)
Polymedication (yes)	0.77 (0.61-0.96)	0.68 (0.49-0.94)
History of nonadherence	6.73 (5.86-7.73)	1.86 (1.46-2.38)
Adverse reactions	6.32 (4.98-8.02)	2.01 (1.41-2.85)
Duration ARV treatment (1-2 years)	0.72 (0.61-0.85)	0.88 (0.71-1.06)
PRM	16.17 (13.88-18.83)	8.11 (6.47-10.17)

*Adjusted ORs with significant associations are shown in bold.

ARV: antiretroviral; CI: confidence interval; OR: odds ratio; PRM: problems related to medication.

young patients' environment, which may be less strict in terms of the importance of adherence to taking medications. This result is very similar to that found in a systematic review conducted by Ghiddei *et al.*²⁶, who found that older patients were at a lower risk of nonadherence. Income level is widely recognized as a factor that can act as a strong barrier to patient access to medical appointments and medications^{9,11}.

In Colombia, people access health services through affiliation with the General Social Security Health System. In 2018, according to data provided by the national health survey, 93.5% of Colombians were affiliated with the system: 58.0% were affiliated through the contributory regimen (employed people contribute resources to the health system) and the remaining 42.0% were affiliated through the subsidized regimen (unemployed people receive coverage by the state)²⁷. The affiliation regimen is related to the income of the individuals; in general, people affiliated with the subsidized regimen have scarce economic resources and are not actively employed. According to our results, there is an association between being affiliated with the subsidized regimen and an increased risk of nonadherence to treatment. This may be explained by the relationship between the affiliation regimen and the lack of formal work and scarce economic resources.

The results also suggest that adherence to medication is lower in heterosexual patients than in homo/bisexual patients. It remains unclear if there is an association between sexual preference and an increase in nonadherence. Neupane *et al.*²⁸ found that adherence was higher among women than among men (OR: 10.5; CI: 1.8-60.1), although no association was found with sexual preference.

No differences in adherence were found between people who consumed alcohol and tobacco (after multivariate analysis); however, an association was found between the consumption of psychoactive substances and nonadherence to ARV treatment. These results differ from those obtained by Velloza *et al.*²⁹, who conducted a systematic review and found that patients who consumed alcohol were at a higher risk of nonadherence (OR: 2.47; CI: 1.58-3.87). Similar results were obtained by González-Álvarez *et al.*³⁰ They found that the risk of nonadherence was higher among alcohol-consuming patients (OR: 4.33; CI: 1.16-16.21), whereas they found no differences in adherence among cocaine-, cannabis- and heroin-consuming patients.

These disparities in the results may be due to differences and variability in the dynamics of the consumption of alcohol, tobacco, and psychoactive substances among the study populations. It may be the case that the percentage of alcohol and tobacco use is higher than that reported in the study, given that patients may avoid providing information that they feel is inappropriate to disclose to their treating physicians.

It is noteworthy that a history of anxiety and depression appeared to be factors associated with adherence, although without reaching statistical significance. This result contrasts with those found in a systematic review conducted in India¹⁰, which found that patients with depressive symptoms were at an increased risk of nonadherence to ARV treatment. It is noteworthy that no information was included on the level of control of psychological disorders in the study patients, given that the management or otherwise of these comorbidities directly affects adherence to ARV treatment.

Other results suggest that patients who have previously been assessed as nonadherent are more likely to be associated with new nonadherence behaviour. According to the results shown in Table 4, patients who at some

points have been assessed as nonadherent are almost twice as likely to continue to present adherence problems in the future.

Finally, it is important to highlight the diversity of factors that can lead to inadequate adherence to ARV treatment. There is a need for comprehensive management and interventions directed at modifiable variables and at patients who are at increased risk of nonadherence, with pharmaceutical education being a high priority given the impact of adverse drug reactions and the need for the prevention of DRPs.

This study has some limitations. The three scales used to measure levels of adherence are indirect methods and there will always be a risk that patients, in the attempt to avoid stigmatization, will answer the questions based on what they consider to be the most appropriate response. It would have been useful to have incorporated other types of measurement, such as dispensing records and cross-checking them against the qualitative results of adherence to further ensure that patients classified as nonadherent are in fact nonadherent. On the other hand, there may have been information bias regarding some relevant variables, such as alcohol, tobacco, and psychoactive substance use, because there is always a risk that patients may fail to provide adequate information, especially when, in this case, such information was collected during the normal care process rather than during a study.

In conclusion, the variables that were most strongly associated with nonadherence to ARV treatment were DRPs, adverse drug reactions, a history of nonadherence to treatment, and psychoactive substance use.

Funding

No funding.

Acknowledgments

We would like to thank Helpharma and the health care sponsor for their support and access to the information needed to conduct the study.

Conflicts of interest

No conflicts of interest.

Contribution to the scientific literature

This study provides new information by analysing variables derived from pharmacotherapeutic follow-up and their relationship with nonadherence —such as problems related to medication— and integrates these variables into a multivariate model that includes other social, demographic, and clinical factors.

The results may help in the development of interventions to prevent and manage nonadherence to antiretroviral treatment in a population of almost 10,000 patients with human immunodeficiency virus/acquired immunodeficiency syndrome. They may also open the door to designing a predictive model of nonadherence, which will help to improve health outcomes in the population studied and apply timely interventions in nonadherent patients. Thus, it will be possible to avoid the negative clinical outcomes associated with nonadherence, such as virological treatment failure and resistance to antiretroviral drugs.

Bibliography

- Organizacion Mundial de la Salud. VIH/sida [internet] [accessed 02/23/2022]. Available at: <https://www.who.int/es/news-room/fact-sheets/detail/hiv-aids>
- Antiretroviral Therapy Cohort Collaboration. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. *Lancet HIV*. 2017;4(8):e349-56. DOI: 10.1016/S2352-3018(17)30066-8
- Morillo-Verdugo R, Polo R, Knobel H. Documento de consenso para mejorar la adherencia a la farmacoterapia en pacientes con infección por el virus de la inmunodeficiencia humana en tratamiento antirretroviral. *Farm Hosp*. 2020 (Julio-Agosto);44(4):163-73.
- Pan American Health Organization. Adherencia a los tratamientos a largo plazo: pruebas para la acción. [Internet] 2004 [accessed 02/23/2022]. Available at: <https://iris.paho.org/handle/10665.2/41182>
- May MT, Gompels M, Delpech V, Porter K, Orkin C, Kegg S, *et al*. Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy. *AIDS Lond Engl*. 2014;28(8):1193-202. DOI: 10.1097/QAD.000000000000243
- Hanhoff N, Vu Q, Lang R, Gill MJ. Impact of three decades of antiretroviral therapy in a longitudinal population cohort study. *Antivir Ther*. 2019;24(3):153-65. DOI: 10.3851/IMP3287

7. Ahmed M, Merga H, Jarso H. Predictors of virological treatment failure among adult HIV patients on first-line antiretroviral therapy in Woldia and Dessie hospitals, Northeast Ethiopia: a case-control study. *BMC Infect Dis.* 2019;19(1):305. DOI: 10.1186/s12879-019-3924-4
8. Sithole Z, Mbizvo E, Chonzi P, Mungati M, Juru TP, Shambira G, et al. Virological failure among adolescents on ART, Harare City, 2017: a case-control study. *BMC Infect Dis.* 2018;18(1):469. DOI: 10.1186/s12879-018-3372-6
9. Safren SA, Biello KB, Smeaton L, Mimiaga MJ, Walawander A, Lama JR, et al. Psychosocial predictors of non-adherence and treatment failure in a large scale multi-national trial of antiretroviral therapy for HIV: data from the ACTG A5175/PEARLS trial. *PLoS One.* 2014;9(8):e104178. DOI: 10.1371/journal.pone.0104178
10. Paramesha AE, Chacko LK. Predictors of adherence to antiretroviral therapy among PLHIV. *Indian J Public Health.* 2019;63(4):367. DOI: 10.4103/ijph.IJPH_376_18
11. 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. DOI: 10.1371/journal.pmed.1002183
12. Ministerio de Salud y Protección Social, Empresa Nacional Promotora del Desarrollo Territorial e Instituto de Evaluación Tecnológica en Salud. Guía de Práctica Clínica basada en la evidencia científica para la atención de la infección por VIH/SIDA en personas adultas, gestantes y adolescentes. Versión para profesionales de salud [internet]. Bogotá D.C. Colombia; 2021 [accessed 05/30/2022]. Available at: <chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/PP/ET/gpc-vih-adultos-version-profesionales-salud.pdf>
13. Pagès-Puigdemont N, Valverde-Merino M. Métodos para medir la adherencia terapéutica. *Ars Pharm.* 2018;59(3):163-72. DOI: 10.30827/ars.v59i3.7387
14. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care.* 1986;24(1):67-74. DOI: 10.1097/00005650-198601000-00007
15. Knobel H, Alonso J, Casado JL, Collazos J, González J, Ruiz I, et al. Validation of a simplified medication adherence questionnaire in a large cohort of HIV-infected patients: the GEEMA Study. *AIDS Lond Engl.* 2002;16(4):605-13. DOI: 10.1097/00002030-200203080-00012
16. Ventura-Cerdá JM, Mínguez-Gallego C, Fernández-Villalba EM, Alós-Almiñana M, Andrés-Soler J. Escala simplificada para detectar problemas de adherencia (ESPA) al tratamiento antirretroviral. *Farm Hosp.* 2006;30(3):171-6. DOI: 10.1016/S1130-6343(06)73968-X
17. Kim SH, Gerver SM, Fidler S, Ward H. Adherence to antiretroviral therapy in adolescents living with HIV: systematic review and meta-analysis. *AIDS Lond Engl.* 2014;28(13):1945-56. DOI: 10.1097/QAD.0000000000000316
18. Spinelli MA, Haberer JE, Chai PR, Castillo-Mancilla J, Anderson PL, Gandhi M. Approaches to Objectively Measure Antiretroviral Medication Adherence and Drive Adherence Interventions. *Curr HIV/AIDS Rep.* 2020;17(4):301-14. DOI: 10.1007/s11904-020-00502-5
19. Costa JM, Torres TS, Coelho LE, Luz PM. Adherence to antiretroviral therapy for HIV/AIDS in Latin America and the Caribbean: Systematic review and meta-analysis. *J Int AIDS Soc.* 2018;21(1):e25066. DOI: 10.1002/jia2.25066
20. Suárez-Villa M, Lastre-Amell G, Rodríguez-López J, Rada LN, Navas SR, Britto MR. Adherencia a fármaco-terapia antirretroviral para el tratamiento del VIH/SIDA en la costa Caribe colombiana. *Rev Latinoam Hipertens.* 2018;13(2):20-5.
21. Reyes-Flores E, Trejo-Álvarez R, Arguijo-Abrego S, Jiménez-Gómez A, Castillo-Castro A, Hernández-Silva A, et al. Adherencia terapéutica: conceptos, determinantes y nuevas estrategias. *Rev Méd Hondur.* 2016;125-32. DOI: 10.51581/rccm.v23i2.287.
22. Urizar CA, Jarolin-Montiel M, Ayala-Servin N, Centurión-Wenninger C, Montiel-Garce D. Factores asociados a la no adherencia del tratamiento antirretroviral en pacientes con VIH en un hospital de Oaraguay. *Rev Científica Cienc Médica.* 2020;23(2):166-74.
23. Barrera-Espinoza RW, Gómez-Gonzales WE, Girón-Vargas A, Arana-Escobar M, Nieva-Villegas LM, Gamarra-Bustillos C, Auqui-Canchari M, et al. Factores asociados a la no adherencia terapéutica a los antirretrovirales en personas con VIH/sida. *Horiz Med (Lima)* 2021;21(4):e1498 [internet]. [accessed 02/23/2022]. Available at: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0375-07602020000200003
24. Ospina Andrea S, Benjumea G Dora M, Amariles M Pedro. Problemas de proceso y resultado relacionados con los medicamentos: evolución histórica de sus definiciones. *Rev. Fac. Nac. Salud Pública* 2011;29(3):329-40 [internet] [accessed 02/23/2022]. Available at: http://www.scielo.org.co/scielo.php?pid=S0120-386X2011000300014&script=sci_abstract&lng=es
25. Nachega JB, Parienti JJ, Uthman OA, Gross R, Dowdy DW, Sax PE, et al. Lower pill burden and once-daily antiretroviral treatment regimens for HIV infection: A meta-analysis of randomized controlled trials. *Clin Infect Dis.* 2014;58(9):1297-307. DOI: 10.1093/cid/ciu046
26. Ghidei L, Simone MJ, Salow MJ, Zimmerman KM, Paquin AM, Skarf LM, et al. Aging, antiretrovirals, and adherence: a meta analysis of adherence among older HIV-infected individuals. *Drugs Aging.* 2013;30(10):809-19. DOI: 10.1007/s40266-013-0107-7
27. Instituto Nacional de Estadística. Encuesta nacional de calidad de vida (ECV). España; 2019 [internet] [accessed 02/23/2022]. Available at: <https://www.dane.gov.co/index.php/estadisticas-por-tema/salud/calidad-de-vida-ecv/encuesta-nacional-de-calidad-de-vida-ecv-2019>
28. Neupane S, Dhungana GP, Ghimire HC. Adherence to antiretroviral treatment and associated factors among people living with HIV and AIDS in CHITWAN, Nepal. *BMC Public Health.* 2019;19(1):720. DOI: 10.1186/s12889-019-7051-3
29. Velloza J, Kemp CG, Aunon FM, Ramaiya MK, Creegan E, Simoni JM. Alcohol Use and Antiretroviral Therapy Non-Adherence Among Adults Living with HIV/AIDS in Sub-Saharan Africa: A Systematic Review and Meta-Analysis. *AIDS Behav.* 2020;24(6):1727-42. DOI: 10.1007/s10461-019-02716-0
30. González-Álvarez S, Madoz-Gürpide A, Parro-Torres C, Hernández-Huerta D, Mangado EO. Relación entre la adherencia al tratamiento antirretroviral en pacientes VIH+ y el consumo de alcohol, asociado o no al uso de otras sustancias. *Adicciones.* 2017;31(1):8-17. DOI: 10.20882/adicciones.916