Prevalence and Risk Factors Associated with Adherence to Antiretroviral Therapy in HIV-Infected Adults in a Tertiary Care Hospital in Mexico

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Abstract

Background: Human immunodeficiency virus (HIV) infection has become a disease in epidemiological transition since the introduction of antiretroviral therapy (ART); however, its control depends on adherence to therapy. There are some studies in Mexico regarding such adherence but they have had heterogeneous results. We aimed to determine the prevalence of ART adherence and risk factors associated with non-adherence among HIV-infected adults in a tertiary care hospital in Mexico.

Methods: This was a cross-sectional study conducted at the Hospital de Infectología, "La Raza" National Medical Center, Mexico City. The subjects of the study were HIV-infected adults after at least 6 months on ART. They answered a questionnaire involving socio-demographics, biochemical, and clinical variables. Adherence was measured using the simplified medication adherence questionnaire

Results: Three hundred seventy-six HIV-infected patients were included in the study. The median age was 35 years (interquartile range, IQR, 29-44) and most of them were men (79.3%). Among the participants, 73% (95% confidence interval, CI, 68.2-77.4%) adhered to the medications prescribed. Factors associated with good adherence were being male (odds ratio, OR, 0.43; 95% CI, 0.22-0.83) and the absence of alcohol use (OR, 0.27; 95% CI, 0.12-0.58); factors associated with non-adherence were a history of ≥2 ART regimens (OR, 1.95; 95% CI, 1.05-3.62), time spend attending medical care or receiving drugs (OR, 2.40; 95% CI, 1.22-4.70), and persistent viremia (OR, 2.72; 95% CI, 1.42-5.19; P<0.005).

Conclusion: In the era of ART as prevention for transmission of HIV as well as treatment for HIV-positive individuals irrespective of CD4 cell counts, the importance of adherence has grown. Treatment failure reduces future treatment options and therefore long-term clinical success as well as increases the possibility of developing drug resistant mutations. Being male and a lack of alcohol use were factors associated with higher rates of adherence, whereas previous use of ART, more ARV regimens, and a longer time waiting for medical care or drugs, were associated with nonadherence in this HIV-infected population. Incomplete ART adherence is associated with persistent viremia.

Keywords: HIV; ART; Adherence; Virological failure; Risk factors; HIV-1 viral load; CD4+ cells count

Introduction

In Mexico, antiretroviral therapy (ART) coverage for human immunodeficiency virus (HIV) infection is about 85%; the aim is to achieve optimal and prolonged HIV-1 RNA viral load suppression, if possible to <50 copies/mL, and patient adherence is necessary [1,2]. ART suppresses the HIV-1 RNA viral load, leading to immunological recovery and clinical improvements [3,4]. Success in achieving good outcomes relies on high levels of ART adherence: preferably 95% or more to suppress HIV replication, and 80% or more to protect the immune system [5,6].

The World Health Organization defines adherence as the degree to which people's behavior taking medication, keeping on a diet, and changes in lifestyle corresponds with agreed recommendations from a health care provider. Poor adherence compromises health improvements and leads to the wastage of treatment resources that are already limited [7,8]. Non-adherence to recommended therapies is a global problem and has been observed for all diseases, but adherence to ART differs among countries according to clinical, economic, and socio-demographic factors [9]. A meta-analysis of 19 case-controlled studies found that adherence to ART was significantly lower in patients with adverse reactions to antiretroviral drugs than among those without them [10].

A cross-sectional study conducted in Barcelona, Spain, in 2002 used the simplified medication adherence questionnaire (SMAQ) to validate adherence and applied it to 3004 HIV-infected patients. The test consists of six questions and the study found a prevalence of ART adherence of 68% in that population [11]. A study conducted in Mexico on 93 HIV-infected patients found that 43% of participants were nonadherent; however, factors associated with nonadherence were not evaluated [12]. In our country, information about ART adherence, the impact that it has on HIV-infected patients, and the associated risk factors is still limited. The aim of this study was to determine the prevalence of ART adherence and the risk factors associated with

nonadherence in this HIV-infected population.

Methods

Design

A cross-sectional study was conducted to assess the adherence to ART among HIV-1-infected patients who attended the hospital de Infectología, "La Raza" National Medical Center.

Patients

The subjects of the study were people infected with HIV-1 >18 years old, on ART for at least 6 months; and ≥ 2 determinations of CD4+ T cell count and HIV-1 RNA viral load during the regimen, separated by 8-12 weeks. Patients with major psychiatric disorders or with incomplete information were excluded.

Measurements

In the context of HIV, ART can be defined as the "ability of the person living with HIV/AIDS to be involved in choosing, starting, managing, and maintaining a given therapeutic medication regimen to control HIV replication and to improve immune function. Adherence to ART was assessed through a structured questionnaire during direct interviews with the participants. The SMAQ questionnaire was used to evaluate the prevalence of adherence to ART in this population. Another questionnaire, "Rule AMAI NSE 8 × 7", was applied to determine the patients' sociodemographic characteristics such as gender, age, place of residence, alcohol use, use or supply of recreational drugs, marital status, partner status, educational level, and time spent waiting for medical care [13,14].

Medical records were reviewed to collect patient information about the time of the HIV infection diagnosis, history of ART regimens, clinical stage according to CDC and CD4+ cell counts, and HIV-1 RNA viral load. Virologial failure was defined as two determinations of HIV-1 RNA viral load with more than 200 copies/mL, blip was defined as a single detectable viral load.

Statistical analyses

Patients were stratified by age, gender, marital and socioeconomic status, educational level, and antiretroviral regimen used. Groups were compared according to adherence level. The Kolmogorov–Smirnov test was used to determine normality of distribution of the data. Baseline characteristics were summarized using medians and interquartile ranges (IQRs) for continuous variables and proportions for categorical variables. Risk factors associated with adherence were tested using a bivariate analysis, which estimated crude odds ratios (ORs) and 95% confidence intervals (CIs). Fisher's exact test and Chi-squared tests were also applied. Independent risk factors associated with adherence were identified in the binomial logistic regression model that included statistically significant variables from the bivariate analysis. All analyses were carried out using IBM SPSS (v. 21.0; IBM Corp., Armonk, NY, USA) and EpiData (v. 3.8; EpiData Association, Odense, Denmark) software. P values <0.05 were considered significant.

Results

Of the 387 patients invited, 376 agreed to participate; 79% were men. The median age was 35 years (IQR, 29-44). Most of the patients were living in Mexico City (60%), 65.2% were married, and 54.3% were men who had sex with men (MSM). Twenty-nine percent had completed high school, and 44.1% were employees (Table 1). Bivariate analysis was applied to investigate associations between all potential variables from this study, and self-reported adherence (Table 2).

Adherence measurement

The overall prevalence of ART adherence was 73% (95% CI, 68.2-77.4), and this was evaluated in different categories (Table 3).

Characteristics	N	%
Sex		
Male	298	79.3
Age (y)		
18-29	100	26.6
30-39	133	35.4
40-49	81	21.5
≥50	62	16.5
Sexual preference		
Heterosexual	152	40.4
MSM	204	54.3
Bisexual	20	5.3
Marital status		
Single	245	65.2
Married	56	14.9
Living with partner	46	12.2
Other	29	7.7
Educational level		
Lack of schooling	2	0.5
Elementary school	26	6.9
Junior high school	98	26.1
High school	109	29.0
Degree studies	95	25.3
Postgraduate studies	46	12.2
Concomitant conditions		
Diabetes	8	2.1
Hypertension	9	2.4
Chronic Gastritis	9	2.4
Ischemic Cardiopathy	3	0.8
Others	21	5.6
Receiving treatment for concomitant conditions		
Yes	75	19.9
No	301	80.1
Cumulative exposure to antiretroviral drugs		
First ART regimen	290	77.2
1 to 3 changes of ART regimen	43	11.4
>3 ART regimens	43	11.4
Occupation		
Housework	16	4.3
Employee	166	44.1
Professional	76	20.2
Housewife and employee	39	10.4
Others	79	21.0
Residence area		
Distrito Federal and Estado de México	358	95.2
Other State	18	4.8
Socioeconomic status		
High	91	24.2
Medium	224	59.6
Low	61	16.2

y, years; CI, confidence interval; MSM, men who have sex with men; χ², Chi-squared test; P<0.05

Table 1: Baseline characteristics (N=376).

Variable	OR	95% CI	P value
Age			
18-29 y	0.55	0.25-1.21	0.096
30-39 y	0.38	0.18-0.80	0.006
40-49 y	0.94	0.40-2.24	0.542
≥50 y	1		
Gender			
Female	1		
Male	0.63	0.37-1.08	0.065
Occupation			
Housework	1		
Housewife and employee	1.78	0.54-5.80	0.251
Laborer	12.5	2.19-71.36	0.002
Professional	8.5	2.50-28.9	0.009
Current smoker			
No	0.49	0.29-0.84	0.007
Yes	1		
Alcohol consumer			
No	0.42	0.26-0.68	<0.001
Yes	1		
Recreational drug user			
No	0.38	0.16-0.88	0.023
Yes	1		

y, years; OR, odds ratio; CI, confidence interval.

Table 2: Bivariate analysis of risk factors associated with ART adherence.

Characteristics	N	Adherence (%)	95% CI
	376	73.0	68.2-77.4
Gender			
Male	223	74.8	69.7-79.9
Female	51	65.3	54.1-76.5
Age			
18-29 y	100	72.0	62.7-81.3
30-39 y	133	63.9	55.3-72.4
40-49 y	81	81.4	72.4-90.5
>50 y	62	82.2	71.9-92.5
Sexual preference			
Heterosexual	152	62.0	61.4-76.7
MSM	204	75.9	69.8-82.0
Bisexual	20	70.0	45.7-88.1
Marital status			
Single	245	72.6	66.8-78.4
Married	56	75.0	62.7-87.2
Living with partner	46	63.0	48.0-78.0
Widowed	23	86.9	66.4-97.2
Separated from partner	6	83.3	35.8-99.5
Educational level			
Lack of school	2	50	1.2-98.7
Elementary school	26	73.0	54.1-92.0
Junior high school	98	68.3	58.6-78.0
High school	109	68.8	59.6-77.9
Degree	95	76.8	67.8-85.8
Postgraduate studies	46	84.7	73.3-96.2
Residence area			
Distrito Federal	224	70.0	63.8-76.3
Estado de México	134	76.1	68.5-83.7
Others	18	83.3	58.5-96.4
Socioeconomic status			
High	91	73.6	64.0-83.2
Medium	224	74.1	68.1-80.0
Low	61	67.2	54.6-79.8

N, number of patients; y, years; MSM, men who have sex with men; CI, confidence interval

Table 3: Prevalence of adherence to ART in patients with HIV.

Characteristics	N	Adherence (%)	95% CI
Current ARV regimen			
TDF/FTC + NVP	29	86.2	68.3-96.1
ABC/3TC + EFV	27	81.5	61.9-93.7
TDF/FTC + EFV	98	80.6	72.2-88.9
ABC/3TC + LPV/RTV	27	77.8	57.7-91.3
TDF/FTC + LPV/RTV	45	68.9	54.2-83.5
TDF/FTC + ATZ/RTV	19	68.4	43.4-87.4
ABC/3TC + NVP	22	68.2	45.1-86.1
TDF/FTC + FPV/RTV	17	58.8	32.9-81.5
ZDV/3TC + LPV/RTV	19	52.6	28.8-75.5
Others	73	65.8	54.1-77.3
Adverse events related with current ARV treatment			
Adverse effects	56	85.7%	75.65-95.77
Time spent waiting for medical care or to receive drugs			
<30 min	157	68.2	60.54-75.75
30-60 min	131	76.3	68.67-83.99
>60 min	88	76.1	66.66-85.61

N, number of patients; CI, confidence interval; TDF, tenofovir; FTC, emtricitabine; NVP, nevirapine; ABC, abacavir; 3TC, lamivudine; EFV, efavirenz; LPV, lopinavir; RTV, ritonavir; ATZ, atazanavir; FPV, Fosamprenavir.

Table 4: Prevalence of adherence according to ART regimen.

The prevalence of adherence was calculated according to ART usage. Some ARV treatment had highest rate of adherence (Table 4).

For virological and immunological responses, the prevalence of adherence was higher (74.8%) in patients with a CD4+ cell count of 200-500/μL (95% CI, 68.2-81.4), and 75.1% of those patients did not show virological failure (95% CI, 70.5-79.7; Table 5).

Other factors were found to be associated with higher adherence by multivariate analysis. These were male gender (OR, 0.43; 95% CI, 0.22-0.83) and absence of alcohol use (OR, 0.27; 95% CI, 0.12-0.58). Factors associated with non-adherence were a history of 2 ART regimens (OR, 1.95; 95% CI, 1.05-3.62), a longer time waiting for medical care or lack of suitable ART drugs (OR, 2.40; 95% CI, 1.22-4.70), and persistent viremia (OR, 2.72; 95% CI, 1.42-5.19; P<0.005; Table 6).

Discussion

We aimed to investigate the prevalence of and risk factors associated with adherence to ART. There was a high level of adherence in these patients with HIV/AIDS (73%; 95% CI, 68.2-77.4%).

Treatment adherence requires patient commitment, and the physician needs to explain the importance of both factors for achieving therapeutic success. Good adherence is associated with better outcomes, including an improved quality of life, higher CD4+ cell count, and lower health care costs [2]. We found here that male gender and absence of alcohol use were positively and significantly associated with better adherence, whereas a history of ≥ 2 ART regimens and lack of supply of the necessary drugs were factors associated with non-adherence. Non-adherence was directly associated with the presence of persistent viremia.

Our study is similar to the study of Mbopi-Kéou et al. that analyzed a population of 356 patients and found a calculated adherence of 51.5% and a declared adherence of 80.2% [14]. Margalho et al. in a study conducted in 2011 in Portugal found lower levels of non-adherence to ART compared with our data. They applied two measuring instruments and calculated a non-adherence rate of 17.5% [15], whereas in our study 27% of the subjects were non-adherent to ART.

In other studies, including ours, most of the subjects were men. For example, Piña-López et al. reported that 68.8% were men and 58.1% were not married [16], similar to our patients, where 65.2% were single. For educational level, they observed that over half of the patients (54.9%) had completed high school; by contrast, we found that only 26.1% of patients had completed junior high school and 29% had completed high school (Table 1). In Mexico, studies conducted in the north of the country in 2006 by Peñarrieta et al. and Piña-López et al. reported different rates of adherence (50-52%). These used the adherence questionnaire VPAD24 [12,17]. In our study, we decided to use the SMAQ questionnaire because it is easier to use, with a sensitivity of 72% and specificity of 91% [13]. In this way, we aimed to capture the true nonadherent population in a large Latin American sample of HIV-positive patients.

Characteristics	N	%	95% CI
CD4+ cell count/μL			
>500	135	74.0	66.3-81.8
200-500	179	74.8	68.2-81.4
<200	62	64.5	51.8-77.2
HIV-1 RNA viral load in copies/mL			
<20	270	80.0	75-84.9
20-199	81	65.4	54.4-76.4
200-999	12	33.3	9.9-65.1
>1000	13	7.7	0.2-36.0
Persistent viremia			
Yes	26	30.8	11.1-50.4
No	334	77.2	72.6-81.8
Blip	16	50.0	24.6-75.3
Virological failure			
Yes	14	14.2	1.7-42.8
No	362	75.1	70.5-79.7

N, number of patients; CI, confidence interval
Blip, only one HIV-1 RNA viral load elevation less than 1,000 copies/mL

Table 5: Prevalence of adherence to ART: immunological and virological variables.

Characteristics	OR	95% CI	P value
Gender			
Female	1		
Male	0.43	0.22-0.83	0.012
Alcohol consumption			
Yes	1		
No	0.27	0.12-0.58	0.001
Number of prior ART regimens			
1	1		
≥2	1.95	1.05-3.62	0.033
Time spend attending medical care or receiving drugs (more than 30 minutes)			
No	1		
Yes	2.403	1.22-4.70	0.011

OR, odds ratio; CI, confidence interval

Table 6: Multivariate analysis of factors associated with ART adherence.

Difficulty in accessing antiretroviral drugs is a clear risk factor for nonadherence, and institutions should take more control of this. Regarding the subjects' prior ART experience, a history of ≥ 2 regimens was a risk factor for persistent non-adherence, and we found that these patients showed virological failure more frequently.

In our study, adverse events were not statistically significant, in contrast to a meta-analysis of 19 studies conducted by Al-Dakkak et al., who found lower adherence in patients with adverse effects to ART compared with those without [10].

Our results are similar to those of some clinical trials when they found a higher frequency of virological failure in women, factors associated with non-adherence, antiretroviral discontinuation, and poor virologic response in univariate analyses were being the primary caregiver for children, unemployment, and transportation difficulties, respectively, and the major sex-based differences in response may be due to higher discontinuation rates in women [17,18].

It is well known that adherence depends on the regimen simplicity. Several studies have evaluated this association and concluded that decreasing the pill burden and dosing frequency is associated with increased adherence [19]. In our study, treatment regimens that had greater adherence were tenofovir/emtricitabina plus nevirapina, followed by abacavir/lamivudina plus efavirenz and tenofovir/ emtricitabina plus efavirenz and those who had lower adherence rate were protease inhibitors based regimens. This results were similar to those reported by Sterrantino et al. [20], who conclude that 30% of patients with protease inhibitors based regimen did not adhere to ART and only 26% and 25% of patients in a once daily and twice daily regimen, respectively, did not adhere. In this study, 30%, 19% and 14% of patients did not adhere to protease inhibitors regimen, once daily and twice daily regimens, respectively. This better adherence with simple regimens and mostly free of protease inhibitors is associated with a lowest number of pills, the dose frequency and the adverse effects which have the greatest impact on patients´ perceived ability to adhere to ARV medication regimen. Cohen et al, has been shown that patients on a once daily single tablet regimen consistently achieve higher adherence levels than patients on 2 pills per day regimens and that single tablet regimen was significantly better at achieving >90% adherence rates when compared with other multi-pill regimens, despite an once daily schedule [21]. In our medical care center do not have single tablet regimens but simple regimen such as tenofovir/ emtricitabine plus Nevirapina, abacavir/lamivudina plus Efavirenz and tenofovir/emtricitabine plus Efavirenz were associated with high adherence to ART in this study.

Finally, in contrast with a systematic review by Lankowski AL et al., when they found that geographic and transportation-related barriers were associated with worse outcomes throughout the continuum of HIV care. These associations were observed with lack of transportation and inability to afford the cost transportation. Our population lived in cities with access to transportation to arrive the HIV clinic, only 4% were living in other states [22].

In conclusion in the era of ART as prevention for transmission of HIV as well as treatment for HIV-positive individuals irrespective of CD4 cell counts, the importance of adherence has grown. Treatment failure reduces future treatment options and therefore long-term clinical success as well as increases the possibility of developing drug resistant mutations. The overall prevalence of ART adherence in these HIV-infected adults was 73%. Being male and a lack of alcohol use were factors associated with higher rates of adherence, whereas previous use of ART, more ARV regimens, and a longer time waiting for medical

care or drugs, were associated with nonadherence in this HIV-infected population. Incomplete ART adherence is associated with persistent viremia.

In summary, we assessed risk factors that could help us to identify patients at risk of nonadherence. These factors could be modified in many patients to increase the possibility of virological success.

Competing Interests

We don't have conflict of interest.

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