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Predictors of Nonadherence to Highly Active Antiretroviral Therapy Among HIV-Infected South Indians in Clinical Care: Implications for Developing Adherence Interventions in Resource-Limited Settings

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Abstract

In light of the increasing availability of generic highly active antiretroviral therapy (HAART) in India, further data are needed to examine variables associated with HAART nonadherence among HIV-infected Indians in clinical care. We conducted a cross-sectional analysis of 198 HIV-infected South Indian men and women between January and April 2008 receiving first-line non-nucleoside reverse transcriptase inhibitor (NNRTI)-based HAART. Nonadherence was defined as taking less than 95% of HAART doses in the last 1 month, and was examined using multivariable logistic regression models. Half of the participants reported less than 95% adherence to HAART, and 50% had been on HAART for more than 24 months. The median CD4 cell count was 435 cells per microliter. An increased odds of nonadherence was found for participants with current CD4 cell counts greater than 500 cells per microliter (adjusted odds ratio [AOR]: 2.22 [95% confidence interval {CI}: 1.04–4.75]; $p = 0.038$), who were on HAART for more than 24 months (AOR: 3.07 [95% CI: 1.35–7.01]; $p = 0.007$), who reported alcohol use (AOR: 5.68 [95%CI: 2.10-15.32]; $p = 0.001$), who had low general health perceptions (AOR: 3.58 [95%CI: 1.20-10.66]; $p = 0.021$), and who had high distress (AOR: 3.32 [95%CI: 1.19-9.26]; $p = 0.022$). This study documents several modifiable risk factors for nonadherence in a clinic population of HIV-infected Indians with substantial HAART experience. Further targeted culturally specific interventions are needed that address barriers to optimal adherence.

Introduction

For over a decade, increasingly well-tolerated highly active antiretroviral therapy (HAART) has dramatically changed HIV-associated morbidity and mortality and has improved the quality of life of HIV-infected individuals.[1–4] Recent global initiatives have concentrated on expanding access to HIV treatment in resource-limited settings[5]; so, by the end of 2008, close to 4 million people were receiving HAART.[6] In India, it is estimated that 2.47 million individuals are currently living with HIV.[7] In 2004, the Indian government began providing HAART, consisting of an initial regimen of stavudine or zidovudine, lamivudine, and nevirapine, free of charge as part of its National AIDS Control Program, with the objective of initiating 100,000 people on treatment by 2007.[8] The government had aimed to provide HAART to 300,000 adults and 40,000 children over the next 5 years as part of its second phase.

However, the success of HAART, associated with viral suppression, immunologic recovery, and avoiding the development of resistant virus, depends on optimal medication adherence.[9] Hence, promoting optimal adherence is necessary

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for the success of HAART. Treatment nonadherence can also overlap with other self-care behaviors, such as continued unsafe sexual practices; and the cooccurrence of nonadherence and HIV transmission risk behavior could lead to the spread of drug-resistant virus.[10,11] Data from the developed world have suggested an association between treatment nonadherence and continued HIV transmission risk behavior.[12–14] Studies conducted in resource-limited settings have shown that HIV-infected individuals can maintain high levels of adherence to HAART.[15–23] Despite expanding access to HAART in India, quantitative studies examining behavioral correlates of adherence remain limited.[24] We had earlier undertaken one qualitative study[25] and one chart review study[26] to assess barriers and facilitators of HAART adherence in South India, which were conducted before the further reduction in cost and roll-out of subsidized HAART. However, these studies were limited in that the qualitative study was hypothesis generating, and the chart review was limited to data that were in patients' medical records. Further quantitative data from India are needed in light of the expanded access to HAART through the government roll-out and to examine whether associations of nonadherence found in other settings apply to this social context.

In the current study, we examined sociodemographic, behavioral, and clinical risk factors of HAART nonadherence among 198 HIV-infected South Indians in clinical care. We also estimated population attributable fractions and assessed effect modification (interaction) associated with significant potentially modifiable risk factors for nonadherence. The findings of the current study can inform the development of further culturally tailored adherence interventions for HIV-infected Indians in clinical care.

Methods

Setting and study population

Between January and April 2008, we enrolled 247 HIV-infected patients receiving outpatient HIV clinical care at YRG Center for AIDS Research and Education (YRG CARE), Voluntary Health Services (VHS), a large community-based HIV care facility in Chennai, India. Among these 247 participants, 198 had been prescribed HAART for at least 3 months, and the current analysis is only on these 198 participants. All participants were HIV-infected, more than 18 years of age, and had been enrolled in HIV clinical and preventive care for at least 6 months prior to the date of study enrollment. We attempted to select the current study sample to match the larger population of patients receiving HIV clinical care at YRG CARE in 2008 on gender, age, current CD4 cell count, and HAART status.

Services at YRG CARE include integrated medical services for the treatment of HIV and related illnesses, prevention programs, and nutrition counseling. YRG CARE has clinical protocols for treatment, which are consistent with World Health Organization (WHO) treatment guidelines,[27] consisting of first-line non-nucleoside reverse-transcriptase inhibitor (NNRTI)-containing regimens. Patients were generally advised to initiate HAART before CD4 cell counts fell below 200 cells per microliter or when CD4 cell counts ranged between 200–350 cells per microliter with an AIDS-defining illness. Standard of care involved seeing providers every 3–6 months or as clinically indicated and adherence and risk reduction counseling at each clinic visit following initiation of HAART.

Data were collected under the approval of the Institutional Review Boards (IRB) at YRG CARE, Brown University, and the Miriam Hospital.

Data collection

HIV-infected patients completed a structured interviewer-administered questionnaire about demographics, psychosocial status, sexually transmitted infections (STI) symptoms, and behavioral practices. After determining eligibility and consent, the questionnaire was delivered in either Tamil or English; the Tamil questionnaire was translated from the original English version and then back-translated into English to ensure consistency between the two versions. The questionnaire was piloted among 20 patients to assess cultural suitability. Interviewers received training in eliciting information on sensitive topics in a nonjudgmental manner. Additional clinical data and information of primary partner's HIV status (concordant versus discordant) were obtained via an observational database.

Behavioral measures

Patient demographics included age, gender identification, gender, residential status (urban versus rural), education, employment, marital status, number of children, and migrant status (defined as whether travels regularly for employment or is a truck driver). General health perceptions were measured by asking participants "How do you feel about your current health?" to indicate their overall health using a percentage scale from 0 (worst) to 100 (best).[28] Scores were then divided into three categories—low, intermediate, and high—such that approximately 25% of participants were grouped in the low and high categories and approximately 50% were grouped in the intermediate category. The split yielded ranges of 0–70 for low, 70–90 for intermediate, and 90–100 for high. Distress was measured using a visual analogue scale (i.e., distress thermometer) by asking participants "How much distress have you been experiencing in the past week. By distress, I am referring to any pain and suffering that you have been feeling during this past week."[29] The 10-point distress visual analogue scale was split into three categories—low, intermediate, high—such that approximately 25% of the participants were grouped in the low and high categories and about 50% in the intermediate category. The split yielded ranges of 0–1 for low, 1–6 for intermediate, and 6–10 for high. Sexual behavior over the past 3 months was assessed by inquiring about sexual frequency (regardless of the number of partners), and frequency of condom use for each sex act. Among sexually active participants who did not use condoms, we asked further questions about type of sex acts for which condoms were not used. Alcohol use, defined as number of times used alcohol over the past month, was measured with a frequency scale.[30] Among participants who reported alcohol use over the past month, alcohol abuse was assessed using the CAGE Scale.[31] HAART adherence over the past month was measured using a visual analogue scale based on asking the question, "What percent of the time did you take your medications exactly as your doctor prescribed them over the last month?" (11 response categories, 0, 10, 20,... 100%),[32] which has been shown to be an effective method in other resource-limited settings.[21]

Medical chart review data We also conducted a medical record review, through utilizing the YRG CARE Chennai HIV Natural History Study Observational Database.[33,34] This database, updated daily, collects information on patient demographics, including probable route of HIV infection, date of HIV diagnosis, and ART history; clinical assessments, including data related to the occurrence of opportunistic infections and adverse events (AEs); and laboratory data. We confirmed ART history and obtained relevant clinical data, including CD4 cell count at time of enrollment to care, at the time of initiating HAART, and at the time of survey assessment (measurement within 6 months of date of survey), and past STIs diagnosed by clinic physicians. The medical record was considered the referent measure for inconsistencies between patient self-report and medical record data documented by clinic physicians.

Definitions of variables used in analyses

The outcome of HAART adherence during the past month was calculated based on dividing percentages from the 30-day visual analogue scale.[32] Because this variable was highly skewed, we dichotomized adherence, coding participants achieving less than 95% adherence as "1" and those 95% or more adherence as "0." This cutoff point is consistent with prior research that has used categorical classifications, and that suggests a high level of HAART adherence is necessary for adequate viral suppression.[35] Unlike protease inhibitor-based regimens, NNRTI-based regimens may require lower levels of adherence to achieve viral suppression.[36]

We defined sexually active as having engaged in anal or vaginal intercourse either with a primary or nonprimary partner in the last 3 months. Participants who had not engaged in anal or vaginal intercourse in the last 3 months were defined as not being sexually active. We defined unprotected sexual intercourse as having engaged in at least one act of anal of vaginal intercourse without a condom with a primary or nonprimary partner in the last 3 months, which is in accordance with indicators used in other studies.[37,38] In terms of primary relationship status, a concordant relationship was defined as the HIV-infected patient enrolled in care and his/her primary partner were both HIV-infected, and a discordant relationship was defined as the primary partner of the HIV-infected patient enrolled in care had tested HIV negative up to the study date.

Statistical analysis

Descriptive statistics were calculated with mean and standard deviation for variables that were normally distributed; and the median and interquartile range (IQR) were calculated for variables influenced by extreme values. We first compared sociodemographic, clinical, and behavioral characteristics stratified by participant gender to see whether characteristics varied across men versus women, and then examined odds ratios (OR) of these characteristics associated with HAART nonadherence. Multivariable logistic regression models were used to assess predictors of HAART nonadherence. Significance was determined using the likelihood ratio test (LRT). Colinearity of included covariates was assessed.

We used a stepwise model to identify independent sociodemographic, behavioral, and clinical predictors of HAART nonadherence in which variables initially associated with nonadherence that reached a threshold value ($p < 0.20$) were examined, and those associated with HAART non-adherence ($p < 0.10$) in a multivariable model were retained. After introducing the primary predictors based on the stepwise model, each covariate was introduced into the model to assess confounding, which was assessed based on a change of at least 0.10 or 10% of the non-log–transformed β coefficients of the independent predictors. The following sociodemographic variables were included in the final multivariable model: gender, age (>30 years versus ≤30 years), and current employment status (employed versus not employed); clinical variables: current CD4 cell count (<350 cells per microliter, 350–500 cells per microliter, versus >500 cells per microliter) and time on HAART (<12 months, 12–24 months, versus >12 months); and behavioral variables, general health perceptions (low, intermediate, versus high), distress (low, intermediate, versus high), alcohol use in the past month, sexually active in the last 3 months, and reported unprotected sex in the last 3 months.

We also examined adjusted interaction effects (effect measure modification) through conducting stratified analyses to assess whether the alcohol-adherence association was moderated by patient characteristics.[39] The population attributable fraction (PAF) of HAART nonadherence associated with significant preventable risk factors in the final model was estimated from the adjusted odds ratio (AOR).[40] The adjusted PAF and its confidence intervals (CI) were obtained using the *aflogit* command in STATA.[41] All data analyses were conducted using STATA (STATACORP, version 10.0, College Station, TX) software. A 95% confidence interval and a 5% level of significance were used to interpret statistical significance. All statistical tests were two-tailed.

Results

Approximately one third (31.5%) of the participants were female and most participants (85.9%) were 30 years of age or older. The primary mode of HIV transmission was via heterosexual intercourse (>95%). Over three fourths of participants were married (83.3%) and had children (79.3%). Over half of the participants (58.1%) were in a HIV-concordant primary relationship. Almost three fifths (58.6%) of participants reported being sexually active, of whom 12.1% reported unprotected sexual intercourse. Only two participants reported having sexual intercourse with their nonprimary sex partner in the last 3 months.

The median CD4 cell count at the time of enrolling to care was 248 cells per microliter (IQR: 100–339), and the median CD4 cell count at the time of initiating HAART was 220 cells per microliter (IQR: 150–285). At the time of the current study, the median CD4 cell count was 435 cells per microliter (IQR: 273–585).

Characteristics of study population stratified by participant gender

Table 1 presents participant sociodemographic, behavioral, and clinical characteristics stratified by gender. Men were more likely to be older, not have children, to be currently employed, and have low general health perceptions. Almost all participants who used alcohol (96.7%) were men. Women were more likely to be in a HIV concordant relationship and to be *Herpes simplex* type 2 antibody-positive. Both men and

Table 1. Characteristics of HAART-Experienced HIV-Infected South Indians Stratified by Gender ($N = 198$)

Characteristic	Proportion by gender, %		Odds ratio, OR (95% CI); p value
	Men (n = 136)	*Women* (n = 62)	*(Men as outcome vs. women)*
Sociodemographic and behavioral characteristics			
Age			
≥30 years	94.1	67.7	7.61 (3.12–18.57); <0.0001
<30 years	5.9	32.3	1.00
Has children			
No	25.0	11.3	2.61 (1.08–6.29); 0.031
Yes	75.0	88.7	1.00
Education			
University or>	19.9	11.3	1.39 (0.89–2.17); 0.144
<secondary	80.1	88.7	1.00
Currently employed			
No	5.1	54.2	0.35 (0.26–0.48); <0.0001
Yes	94.9	45.8	1.00
Residential status			
Urban	65.4	66.1	0.96 (0.51–1.82); 0.925
Rural	34.6	33.9	1.00
Truck driver/travels for work			
No	15.4	100.0	—
Yes	84.6	0.0	
Currently lives with spouse			
No	16.9	24.2	0.63 (0.30–1.32); 0.230
Yes	83.1	75.8	1.00
Alcohol use in the last month			
Yes	23.5	1.6	18.76 (2.50–140.82); 0.004
No	76.5	98.4	1.00
Partner HIV status			
Concordant	52.2	71.0	0.44 (0.23–0.85); 0.014
Discordant	47.8	29.0	1.00
General health perceptions			
Low	28.6	21.0	2.40 (1.01–5.67); 0.046
Intermediate	52.9	46.8	1.98 (0.95–4.11); 0.065
High	18.4	32.3	1.00
Distress			
High	22.8	33.9	0.59 (0.26–1.35); 0.218
Intermediate	50.0	41.9	1.06 (0.50–2.24); 0.879
Low	27.2	24.2	1.00
Sexually active			
Yes	60.3	54.8	1.25 (0.68–2.29); 0.470
No	39.7	45.2	1.00
Reported unprotected sex			
Yes	5.9	3.2	1.21 (0.36–3.98); 0.754
No	94.1	96.8	1.00
Clinical characteristics			
HSV-2 antibody positive			
Yes	15.4	29.0	0.44 (0.21–0.91); 0.028
No	84.5	70.0	1.00
Current CD4 cell count			
>500 cells/per microliter	58.1	72.6	0.36 (0.11–1.15); 0.087
350–500 cells/per microliter	27.9	21.0	0.61 (0.17–2.14); 0.446
≤350 cells/per microliter	14.0	6.5	1.00
Time on HAART			
>24 months	55.7	44.1	1.27 (0.59–2.72); 0.528
12–24 months	19.1	30.5	0.63 (0.26–1.49); 0.295
<12 months	25.2	25.4	1.00
Time in clinical care			
>24 months	69.1	72.6	0.92 (0.37–2.29); 0.872
12–24 months	17.6	14.5	1.18 (0.38–3.67); 0.769
<12 months	13.2	12.9	1.00

HAART, highly active antiretroviral therapy; HSV-2, *Herpes simplex* virus 2; CI, confidence interval.

women had similar levels of education, residential status, cohabitation status, distress, sexual activity, reported unprotected sex, current CD4 cell count, time on HAART, and time in clinical care. No participants reported drug use.

Patterns of treatment adherence

Half of the participants (50.5%) reported 100% HAART adherence, 31.8% reported 90% HAART adherence, 10.8% reported 80% adherence, and the remainder (7.1%) reported 70% adherence or below. Almost one third of participants (28.8%) reported initiating HAART as soon as they were enrolled into HIV clinical care. Over one fourth of participants (28.3%) had been on HAART for 12 months or less, 21.7% between 12–24 months, and 50% longer than 24 months. The most common HAART regimens included: lamivudine plus stavudine plus nevirapine (31.0%), lamivudine plus stavudine plus efavirenz (19.9%), zidovudine plus lamivudine plus efarvirenz (17.3%), and nevirapine plus zidovudine plus lamivudine (11%). The proportion of participants who were nonadherent was similar across different HAART regimens.

Patterns of alcohol use

Table 2 presents patterns of alcohol use and dependence as well as participant characteristics associated with alcohol use. In the last month, 16.7% of participants reported alcohol use. Among these participants who used alcohol, over two thirds (67.7%) reported using alcohol once a week or more and a tenth (9.1%) had a CAGE score of at least 3. Participants who used alcohol were more likely to be men, in a HIV-concordant primary relationship, and be currently employed.

Table 2. Patterns of Alcohol Use and Characteristics of Participants who Used Alcohol ($N = 33$)

Patterns of alcohol use	*Proportion (%)*
Frequency of alcohol consumption	
≤2 times a month	33.3
Once a week	57.6
>2 times a week	9.0
CAGE score	
+1	45.5
+2	27.3
+3	9.1
Characteristics of those who used alcohol	*OR (95% CI);* p *value*
Gender	
Men	18.77 (95% CI: 2.95–776.38); $p = 0.0001$
Women	1.00
Partner HIV status	
Concordant	2.17 (95% CI: 0.90–5.62); $p = 0.06$
Discordant	1.00
Employment status	
Employed	4.96 (95% CI: 1.16–44.38); $p = 0.0197$
Unemployed	1.00

OR, odds ratio; CI, confidence interval.

Association between HAART nonadherence and selected sociodemographic, behavioral, and clinical risk factors

Almost half (49%) of the 198 participants had below 95% adherence, and these participants are classified as nonadherent in the current analysis. Participants who had been HAART-experienced for greater than 24 months were more likely to be nonadherent than participants who had been on HAART for less than 24 months (OR: 2.01 [95% CI: 1.03–3.92]; 0.040; Table 3). Participants who reported low (OR: 4.94 [95% CI: 2.05–11.92]; $p < 0.0001$) and intermediate (OR: 3.69 [95% CI: 1.68–8.09]; $p = 0.001$) general health perceptions were more likely to be nonadherent compared to participants who reported high general health perceptions. Similarly, participants who reported high (OR: 3.29 [95% CI: 1.47–7.36]; $p = 0.004$) and intermediate (OR: 2.24; 95% CI: 1.10–4.54); $p = 0.025$) levels of distress were more likely to be nonadherent compared to participants who reported a low level of distress. Participants who reported alcohol use were more likely to be nonadherent compared to participants who had not used alcohol (OR: 3.93 [95% CI: 1.67–9.24]; $p = 0.002$).

Participants who were sexually active were less likely to be nonadherent compared to those who were not sexually active (OR: 0.49 [95% CI: 0.27–0.87); $p = 0.016$). Participants who were sexually active were less likely to have low general health perceptions (OR: 0.23 [95% CI: 0.09–0.58]; $p = 0.002$) and a high level of distress (OR: 0.34 [95% CI: 0.15–0.78); $p = 0.011$) compared to participants who were not sexually active. Although not statistically significant, the few participants who reported unprotected sex were more likely to be nonadherent than participants who reported only protected sex (OR: 2.49 [95% CI: 0.62–9.91]; $p = 0.196$). Among nonadherent participants, of a total of 84 reported anal/vaginal sex acts in the last 3 months, only 25 (29.8%) were protected with condoms, but all sex acts were with a HIV-concordant primary partner. Among adherent participants, out of a total of 17 reported anal/vaginal sex acts, none were protected with condoms, 5 of which were with a HIV discordant primary partner.

Nonadherent participants were not significantly more likely to have a past diagnosis of tuberculosis compared to adherent participants (70.4% versus 61.0%; $p = 0.163$).

Multivariable analysis of risk factors of antiretroviral nonadherence

In the final multivariable model, participants with current CD4 cell counts greater than 500 cells per microliter were over two times more likely to be nonadherent compared to participants with lower CD4 cell counts (AOR: 2.22 [95% CI: 1.04–4.75]; $p = 0.038$; Table 3). Participants who had been on HAART for longer than 24 months were over three times more likely to be nonadherent compared to participants who had been on HAART for a shorter period of time (AOR: 3.07 [95% CI: 1.35-7.01]; $p = 0.007$). Participants who reported alcohol use were over five times more likely to be nonadherent compared to participants who had not used alcohol (AOR: 5.68 [95% CI: 2.10–15.32]; $p = 0.001$). Participants who reported low (AOR: 3.58 [95% CI: 1.20-10.66]; $p = 0.021$) and intermediate (AOR: 3.32 [95% CI: 1.28-8.63]; $p = 0.014$) general health perceptions were over three times more likely to be nonadherent compared to participants who reported high general health perceptions. Similarly, participants who

Table 3. Unadjusted and Adjusted Sociodemographic, Behavioral, and Clinical Predictors of Nonadherence to HAART Among HIV-Infected South Indians ($N = 198$)

	Proportion nonadherent		*Unadjusted analysis OR (95% CI); p value*	*Adjusted analysis OR (95% CI); p value*
	No (%) n = 98	*Yes (%) n = 100*	*Unadjusted (bivariate) association*	*Adjusted (multivariable) association*
Gender				
Female	28.6	34	0.78 (0.42–1.41); 0.411	1.25 (0.49–3.17); 0.635
Male	71.4	66	1.00	1.00
Age				
≥30 years	85.7	86	0.98 (0.44–2.17); 0.954	0.48 (0.16–1.41); 0.186
<30 years	14.3	14	1.00	1.00
Current employment				
No	16.3	26.0	0.55 (0.27–1.11); 0.098	0.41 (0.15–1.11); 0.080
Yes	83.7	74.0	1.00	1.00
Current CD4 cell count				
>500 cells/per microliter	45.9	35.0	1.51 (0.80–2.85); 0.202	2.22 (1.04–4.75); 0.038
350–500 cells/per microliter	19.4	25.0	0.89 (0.42–1.89); 0.770	1.57 (0.64–3.88); 0.322
≤350 cells/per microliter	34.7	40.0	1.00	1.00
Time on HAART				
>24 months	57.1	43.0	2.01 (1.03–3.92); 0.040	3.07 (1.35–7.01); 0.007
12–24 months	20.4	23.0	1.34 (0.60–3.00); 0.471	2.24 (0.84–5.94); 0.103
<12 months	22.4	34.0	1.00	1.00
General health perceptions				
Low	32.6	34.0	4.94 (2.05–11.92); <0.0001	3.58 (1.20–10.66); 0.021
Intermediate	56.1	46.0	3.69 (1.68–8.09); 0.001	3.32 (1.28–8.63); 0.014
High	11.2	34.0	1.00	1.00
Distress				
High	32.7	20	3.29 (1.47–7.36); 0.004	3.32 (1.19–9.26); 0.022
Intermediate	50.0	45	2.24 (1.10–4.54); 0.025	1.75 (0.73–4.19); 0.206
Low	17.3	35	1.00	1.00
Alcohol use				
Yes	25.6	8.0	3.93 (1.67–9.24); 0.002	5.68 (2.10–15.32; 0.001
No	74.5	92.0	1.00	1.00
Sexually active				
Yes	50.0	67.0	0.49 (0.27–0.87); 0.016	0.58 (0.29–1.14); 0.113
No	50.0	33.0	1.00	1.00
Unprotected sex				
Yes	7.1	3.0	2.49 (0.62–9.91); 0.196	1.63 (0.32–8.12); 0.550
No	92.9	97.0	1.00	1.00

OR, odds ratio; CI, confidence interval; HAART, highly active antiretroviral therapy.

reported a high level of distress were more likely to be nonadherent compared to participants with lower levels of distress (AOR: 3.32 [95% CI: 1.19–9.26]; $p = 0.022$). Although not statistically significant, participants who were sexually active were less likely to be nonadherent compared to those who were not sexually active (AOR: 0.58 [95% CI: 0.29–1.14]; $p = 0.113$), and also participants who were currently unemployed compared to those who were employed (AOR: 0.41 [95% CI: 0.15–1.11]; $p = 0.080$). Participant gender, age, and reported unprotected sex were not significant predictors of HAART nonadherence.

The adjusted association between alcohol consumption and nonadherence was two times greater among sexually active participants (AOR: 10.44 [95% CI: 2.61–41.63]; $p = 0.001$) compared to those who were not sexually active (AOR: 5.39 [95% CI: 0.66–43.49]; $p = 0.114$).

The adjusted PAF for alcohol use was 11.4% (95% CI: 0.05–0.17), for low/intermediate general health perceptions was 37.3% (95% CI: 0.02–0.60), for high/intermediate distress was 24.0% (95% CI: −0.05–0.45), and for CD4 cell count greater than 500 cells per microliter was 10.0% (95% CI: −0.01–0.20).

Discussion

The current study documents several modifiable risk factors for nonadherence, namely alcohol use and psychosocial status, in a population of HIV-infected Indians in clinical care with substantial experience to NNRTI-based HAART. Participants who had recently used alcohol as well as those with increasingly higher distress and lower general health perceptions were more likely to be nonadherent. It is of concern that participants with higher CD4 cell counts and a longer time period of HAART experience were less likely to be adherent, suggesting possible treatment exhaustion and the need for sustained efforts to emphasize continued adherence over time. In accordance with earlier studies in resource-limited studies,[17] demographic characteristics, such as age, gender, occupation, and residential status, did not predict treatment adherence.

The current study found that only about half of the participants had greater than 95% adherence, which is lower than most studies conducted in resource-limited settings and closer to adherence levels documented in North America.[15] A recent study from western India conducted at private health clinics found that among patients paying for treatment out-of-pocket, three fourths of patients had 95% adherence or higher.[24] Earlier studies monitoring treatment adherence from resource-limited setting have generally been conducted soon after patients initiated HAART, when patients were experiencing dramatic increases in health status. However, in the current study, half the population had been HAART-experienced for over 2 years, suggesting the need for sustained efforts to maintain high levels of adherence well after the initial immune-restorative effects of treatment. In light of the continued decrease in prices of generic HAART and the Indian government treatment roll-out at the time of the current study, we had anticipated a higher level of treatment adherence. Cost of treatment has frequently been cited as a major barrier to adequate adherence in resource-limited settings,[15] including in our patient population.[25,26] Further longitudinal studies are needed to elucidate how treatment adherence may vary over time based on changing patient clinical and behavioral characteristics, as well as policies over the provision of accessible treatment.

Participants who reported alcohol use were at a substantially increased likelihood of being nonadherent. Alcohol use can diminish qualify of life, decrease adherence to medical regimens, and is a prevalent concern among HIV-infected individuals.[39,42] Data have suggested the deleterious consequences of alcohol use on markers of immunological functioning and viral suppression, which could be moderated by nonadherence.[43,44] In the current study, we were interested in conditions under which alcohol use was more likely to influence adherence, and participants who were sexually active were more likely to use alcohol and be nonadherent. The prominence of the alcohol-adherence association that was documented in men is concordant with a recent meta-analysis.[39] The findings of this study suggest that proactive screening and referral for counseling about alcohol use should be a component of HIV care in this regional setting, including support for provider-based training.[45]

Participants with lower levels of general health perceptions and higher levels of distress were more likely to be nonadherent. Earlier studies from varying regional settings have identified psychological distress as a barrier to optimal adherence.[46,47] Further in-depth studies in this patient population are needed to understand the impact of psychological function on treatment adherence, and psychosocial interventions (e.g., cognitive behavioral therapy) should be examined.[48] Having sex is an important part of overall health and quality of life, including patients infected with HIV.[42] In the current study, participants who were sexually active were less likely to be nonadherent. Participants who were sexually active generally had lower levels of distress and higher general health perceptions. However, although not significant, participants who were nonadherent were more likely to report unprotected sex. It is possible that a larger sample size than the current study would be required to detect a significant effect of unprotected sex on treatment nonadherence.

There are several limitations to note. We did not have plasma viral load measurements to correlate with the adherence data because these tests were not standard of care in this resource-limited setting. Recent data from India suggest that providers should rely on validated measures of HAART adherence rather than using their own assessment of patient adherence when plasma viral load monitoring is not readily available.[49] The current study was cross sectional in design, and hence may not reflect the dynamic nature of adherence, which can vary over time. We assessed adherence based on patient self-report using a validated instrument, while commonly utilized,[21] it may not perfectly reflect actual adherence levels. Prior research among this patient population has suggested that self-report may be an acceptable method in a clinic-based assessment situation.[50] Despite a relatively small sample size, we documented associations of sufficient magnitude. We also attempted to make the results of the current sample generalizable to patients receiving outpatient care in this HIV clinic population through matching the sample on relevant demographic and clinical characteristics. The sample included a diverse population of HIV-infected Indians from urban and rural locations as well as varying levels of socioeconomic status.

Due to the limited availability of second-line treatment in addition to the lack of adequate virologic monitoring in India, both primarily driven by cost considerations, maintaining optimal adherence on first-line HAART is critical to ensure long-term treatment efficacy. We identified severable modifiable behavioral risk factors of ART adherence in this patient population with substantial treatment experience, suggesting that health care providers could play a central role in integrating adherence interventions into follow-up HIV care to improve patient treatment outcomes. Continued monitoring of treatment-experienced Indian patients and further targeted culturally specific interventions will need to be developed that address long-term barriers to optimal adherence. As programs to expand the coverage of HAART continue in India, optimizing patient adherence via understanding unique regional factors will be a crucial part of a comprehensive treatment strategy.

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Author Disclosure Statement

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