Original Article

Assessment of self-reported adherence to ART and patient's virological/CD4 response in a tertiary care clinic and government free ART clinic

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Abstract

Introduction: Treatment adherence to antiretroviral treatment (ART) is critical in reducing morbidity, mortality, and improving the survival in HIV patients. ART is a life-long commitment, and the variety of factors can influence treatment adherence. We studied the factors affecting treatment adherence in the private sector and public sector outdoor clinic in Ahmedabad, India. The primary objective of this study is to compare the level of adherence and factors that influence adherence to ART in patients attending government run free ART program and private setup. **Methods:** We conducted a cross-sectional study of 8 weeks among HIV-infected patients who were receiving ART from private clinic and free ART center from July 2019 to September 2019. We enrolled all consecutive patients >18 years of age attending both clinics. Statistical analysis was carried out using the SPSS software version 25.0. Multiple logistic regression was used to identify the factors that were independently associated with adherence to ART. **Results:** The study enrolled 306 patients, 151 (49.34%) from the outpatient department of private hospital, and 155 (50.65%) from the free ART center. Patients attending private clinics were more likely to have been diagnosed with HIV since ≥10 years compared to free ART center. Higher opportunistic infection rates were found in free ART center (64.51%). Treatment adherence was significantly lower in the patients attending free ART center ($P = 0.004$). Patients taking concomitant medications for other comorbid conditions (≥4 pills/day) were more likely to exhibit inadequate adherence ([odds ratio] 1.216, 95% confidence interval 1.0171–1.454). Univariate analysis showed that age, education, habits of alcohol, tobacco, number of pills, and duration of disease played a significant role in predicting adherence to ART ($P < 0.05$). **Conclusions:** Patients attending private clinic are surviving longer with HIV diagnosis, have fewer opportunistic infections, and have better treatment adherence compared to free ART clinic.

Key words: Antiretroviral treatment adherence, antiretroviral treatment in India, private sector, public sector, virological response and antiretroviral treatment adherence

INTRODUCTION

Modern antiretroviral medicine has transformed HIV in to a chronic manageable infection with near normal life expectancy and zero HIV transmission.[1,2] Pharmacological treatment has

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evolved from a multiple pills per day with associated high toxicities, to less toxic single pill per day. The National AIDS Control Organization (NACO) provides free antiretroviral treatment (ART) according to the current NACO guidelines which is in accordance with the current WHO HIV treatment guidelines.[3] Private clinics in India generally follow national guideline to treat patients and also adopt the treatment regimens according to the current international guidelines. HIV patients can have many social challenges apart from medical such as stigma, poverty, depression, substance abuse, and cultural beliefs which can affect their QOL not only from the physical health aspect, but also from mental and social health point of view making it necessary to routinely assess the effects of treatment and quantifying the return on health-care investment.[4,5] Self-reported adherence measures would be useful both in the clinical management of individual patients and in monitoring adherence in patient populations.[6,7] The cost of therapy is also a factor apart from pill burden, drug toxicities, and substance abuse leading to treatment interruption.[8] An adherence to ART of 95% is required by a patient to achieve maximal viral suppression associated with near normal life.[9-12] Nonadherence is related to the development of ART resistance, progression to AIDS, and death.[3-15] However, in the clinical practice, the maintenance of optimal ART adherence is challenging due to various reasons. We conducted a study to know any difference in the level of adherence and QOL in patients taking ART from the government and private sectors.

Objectives

The primary objective of this study is to compare the level of adherence and factors that influence adherence to ART in patients attending free ART program and private setup. The secondary objective was to evaluate health-related quality of life in patients receiving ART and to evaluate the prescribing the pattern of drugs used to treat HIV in private set up and in ART center

METHODS

Study design and criteria

We conducted a cross-sectional study of 8 weeks among patients receiving ART in a private outpatient clinic and ART center at a teaching hospital in Ahmedabad from July 2019 to September 2019. We enrolled all consecutive patients, who consented, attending both clinics during the study period. The inclusion criteria were patients >18 years of age of either gender and diagnosed with HIV. Patients refusing to participate were excluded.

Data collection and instruments

Data were collected by two investigators, one at each setup. Sociodemographic data, comorbidities, and drugs prescribed were entered in standard case record form. Structured interviews were conducted for 15–20 min, prior to each patient's visit with their physician. Adherence was assessed using the self-reported baseline correlates of adherence Adult AIDS Clinical Trials Group[16] questionnaire. Patients were categorized as being "non-adherent" if they reported skipping medications within past 2 weeks. Score of ≥95% was considered to be highly adherent.

Health-related quality of life (HQoL)[17] was assessed using WHO-HIV BREF Quality of Life scale, which consists of 31 five-point Likert scale items, which are grouped into six domains of HQoL; referred to as physical, psychological, level of independence, social, environmental, and spiritual.

Statistical analysis

The analysis was carried out using the IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corporation. The characteristics of adherent and nonadherent participants were compared using the Chi-square tests for the categorical variables. The Mann–Whitney test was used to compare the data between the groups for continuous variables. Spearman correlation was used to compare adherence with group variables. Multiple logistic regression was used to identify the factors that were independently associated with adherence to ART. $P < 0.05$ was considered statistically significant.

Ethical consideration

Informed consent was obtained from all the participants. NHL Institutional Review Board and Gujarat State AIDS Control Society (GSACS) approval were obtained for this study.

RESULTS

The study population consisted of 306 patients, 151 (49.34%) from the private clinic, and 155 (50.65%) from the ART Center with ages ranging from 19 to 75 years. Table 1 depicts the sociodemographic and clinical characteristics of study participants at private and public ART clinics. Statistically significant differences in education and adherence patterns were seen at two centers ($P = 0.002$). Comorbidities such as Type 2 diabetes mellitus, hypertension, coronary heart disease, and hypothyroidism were similar in participants from ART center (43, 27.7%) and private setup (48, 31.7%). Patients attending private

clinic were more likely to have been diagnosed with HIV (≥10 years) compared to ART center. In contrast, patients attending ART center had been diagnosed with HIV since ≥5 years and were more likely to have a history of high-risk exposure, and report that not having enough wages was an important barrier to care. Patients' treatment were monitored with viral load assay at private clinic while CD4 count was used at ART center [Table 1].

Prescription analysis

Majority of patients (65.16%) at ART center were receiving a single pill of Tenofovir (300 mg) + Lamivudine (150 mg) + Efavirenz (600 mg), whereas 50.99% of patients in the private setup were receiving single pill of Tenofovir (300 mg) + Emtricitabine (200 mg) + Efavirenz (600 mg). Annual costs per patient per year in the private setup summed up to an average of Rs. 20400 ($284) for the most commonly prescribed combination of Tenofovir + Emtricitabine + Efavirenz which was also a reason in 25.82% patients nonadherent to their treatment. Thus, the cost of treatment was an insurmountable obstacle to adherence. Gastrointestinal adverse drug reactions were described by 46 (29.6%) and 33 (21.8%) and cutaneous (rash, dryness, and itching) in 41 (27.15%), and 32 (20.64%) patients in private and ART center, respectively.

Quality of life indicators

In the ART center, the social relationships domain recorded the lowest mean score (13.90 ± 4.33) and highest mean score was observed in the Spirituality/Religion/Personal Beliefs domain (17.20 ± 2.18), whereas in private clinics, the environment health domain recorded the lowest mean score (14.55 ± 5.84) and highest mean score was observed in the physical health domain (15.91 ± 3.00) [Table 2]. When the average scores of QoL were analyzed in regard to therapeutic adherence, we verified that the individuals classified as "non-adherent" in both setups presented significant differences in social relationship domains ($P = 0.008$) signifying being not satisfied with their personal relationships and with the support they get from friends/relatives. Statistically significant differences were seen in spiritual domain ($P = 0.0001$) which looks at participant's inclination toward meaningful life, bothered by people blaming them for their HIV status, concerns about future and death. Negative correlation was present between QoL with duration of disease and habits in both settings, but the differences between the two settings were not statistically significant ($P > 0.05$). Thus, longer duration of disease and indulging in habits both have a negative impact on QoL.

Table 1: Sociodemographic and clinical characteristics of HIV-infected persons receiving antiretroviral therapy at private and public antiretroviral therapy clinics in Gujarat, India (*n*=306)

Category	Free ART center (*n*=155)	Private setup (*n*=151)
Mean age±SD (years)	39.8±11.6	49±12
18-35, *n* (%)	62 (40)	15 (9.9)
36-54, *n* (%)	76 (49.03)	47 (31.12)
≥55, *n* (%)	17 (10.96)	89 (58.94)
Female-to-male ratio	1:1.71	1:2.30
Male	98 (63.22%)	106 (69.53)
Female	57 (36.77%)	46 (30.46)
Weight (kg), mean±SD	55.85±11.94	67.83±11.07
Duration of disease (years), mean±SD	5.21±3.53	10.7±5.84
Educational status, *n* (%)		
Illiterate	37 (23.87)	-
11th or less	74 (47.74)	81 (53.64)
High school graduate	27 (17.41)	20 (13.24)
2 year college	1 (0.6)	17 (11.25)
College graduate	16 (10.3)	27 (17.88)
Master's degree	-	6 (3.9)
Habits, *n* (%)		
Tobacco/smoking	80 (61.93)	42 (27.8)
Alcohol	24 (15.4)	31 (20.5)
Number of pills a day (including other than ART), *n* (%)		
≤3	121 (78.06)	95 (62.9)
≥4	34 (21.93)	56 (37.1)
History of comorbidities, *n* (%)	43 (27.7)	48 (31.7)
History of opportunistic infections, *n* (%)		
Tuberculosis	94 (60.64)	25 (16.55)
Pulmonary	79	9
LNTB	7	11
Abdominal	8	5
Oropharyngeal candidiasis	3 (1.9)	13 (8.6)
Herpes virus (Simplex + Zoster)	3 (1.9)	5 (3.3)
Pneumocystic pneumonia	-	2 (1.3)

ART: Antiretroviral therapy, SD: Standard deviation, LNTB: Lymph node tuberculosis

Table 2: The mean scores of domains of health-related quality of life using WHO-HIV BREF

Domain	Mean±SD		*P*
	Free ART center	Private	
Physical health	15.67±2.45	15.91±3.00	0.239
Psychological health	14.96±2.36	15.14±3.30	0.258
Level of independence	16.06±1.39	15.76±2.75	0.815
Social relationship	13.90±4.33	14.88±3.86	0.101
Environment health	14.94±3.75	14.55±5.84	0.465
Spirituality health	17.20±2.18	15.25±3.35	0.001*

*P<0.05. SD: Standard deviation

Self-reported medication adherence and its correlates

By self-report out of 306 patients, 125 (80.6%) in ART center and 128 (84.76%) participants in the private setup were certain in taking medications but only 96 (61.9%) in ART center and 129 (85.43%) in private setup reported adherence of >95% to therapy. Hundred percent adherence was reported by 64 (41.2%) patients in ART center and 66 (43.70%) patients in private setup. There was a statistically significant difference in adherence between the ART center and private settings ($P = 0.004$) adherence being lower in the ART center setup. Participants who were taking concomitant medications for other comorbid conditions (≥4 pills/day) were more likely to exhibit inadequate adherence (odds ratio [OR] 1.216, 95% confidence interval [CI] 1.0171–1.454). When comparing their age groups, middle-aged (36–54 years) and old-aged (>55 years) patients showed a significant association with suboptimal adherence than their younger counterparts (OR 1.58, 95% CI 1.03–1.75 and OR 1.15, 95% CI 1.01–1.46). Longer duration of disease was also associated with suboptimal adherence (OR 1.20, 95% CI 1.02–1.35). Self-reported medication adherence and its correlates are depicted in Table 3.

Among patients with low adherence, the most common reasons for missing doses in patients presenting to the public and private setup were either they were "away from home" followed by "busy with other things." The frequency of presentation of reasons is described in Table 4.

In regard to time since the diagnosis, 83 (53.54%) participants from ART center and 35 (23.17%) participants from private reported <5 years since the diagnosis with mean 10.7 ± 5.84 years since the diagnosis in the private set up. In terms of clinical characteristics for the CD4 T-cells count, most participants 107 (69.03%) had >350 cells/mm^3. The viral load was undetectable to <20 copies per ml for 117 (77.48%) participants, whereas 3 (2%) individuals presented >100,000 copies per ml. Compared with nonadherent participants, adherent participants were more likely to have virological suppression and improved CD4 counts (OR 2.38 95% 0.77–10.2 and OR 8.6 95%CI 0.9–9.8) [Table 5].

Intuitively, it seems reasonable to suppose that prescription of a large number of pills per day will tend to reduce adherence, and indeed in the present study, we found that adherence was worse in patients who had to take 4 or more pills per day. Negative correlation was present between adherence with duration of disease, number of pills per day, and habits in both settings, but the differences between the two settings were not statistically significant ($P > 0.05$). Adherence was positively correlated with QoL in both the settings, suggesting higher adherence can lead to better QoL with statistically significant difference seen in settings ($P < 0.05$)

DISCUSSION

In our study of 306 HIV-infected persons seeking care at ART center and private clinics in India, we observed significant differences between ART center and private clinic attendees, varied levels of HIV disclosure among the two groups, and low levels of ART adherence and poor quality of life among persons attending public setup. Compared to their private counterparts, HIV participants cared

Table 3: Self-reported adherence to antiretroviral therapy

Hospital setting	Male (%)	Female (%)	Total (%)	*P*
Free ART center				
Optimal adherence				
Yes	58 (37.4)	38 (24.51)	96 (61.9)	0.004*
No	40 (25.8)	19 (12.25)	59 (38.06)	
Forgot doses in the last week				
Yes	16 (10.3)	5 (3.2)	21 (13.54)	
Forgot doses in the past 2 weeks				
Yes	24 (15.48)	14 (9)	38 (24.51)	
Private				
Optimal adherence				
Yes	90 (59.6)	39 (25.82)	129 (85.43)	0.0045*
No	16 (10.5)	6 (3.9)	22 (14.56)	
Forgot doses in the last week				
Yes	6 (3.9)	1 (0.6)		
Forgot doses in the past 2 weeks				
Yes	10 (6.6)	5 (3.3)		

*P<0.05. ART: Antiretroviral therapy

Table 4: Reasons for nonadherence (*n*=306)

Reasons	Free ART center (%)	Private (%)
Were away from home?	58.7	47.01
Were busy with other things?	36.12	33.11
Simply forgot?	30.3	29.8
Patient ran out of pills?	3.2	25.82
Had problem taking pills at specified time (with meals, empty stomach, etc.?)	18.06	21.85
Felt depressed/overwhelmed?	6.4	17.21
Had too many pills to take?	7	16.55
Wanted to avoid side effects?	7.7	13.24
Did not want others to notice you taking medication?	12.25	20.5
Had a change in daily routine?	2.5	15.89
Felt like drug was toxic/harmful?	3.2	11.25
Felt asleep/slept through the dose time?	9	18.54
Felt ill or sick?	4.5	16.55
Felt good?	4.5	13.9

ART: Antiretroviral therapy

Table 5: Immunological and virological correlates of adherence

	Adherent	Nonadherent	OR (95% CI)
RNA copies			
<20	101	16	1 (reference)
20-200	19	2	0.66 (0.14-3.13)
>200	9	4	2.38 (0.77-10.2)
CD4			
<200	1	4	8.6 (0.9-9.8)
200-349	15	23	3.27 (1.15-4.45)
350-499	26	18	1.48 (0.6-3.3)
>500	43	20	1 (reference)

OR: Odds ratio, CI: Confidence interval

for in government health-care facilities were more likely to have lower levels of employment and lower educational levels (71.6%), more tobacco use and smoking (61.93%) and more prevalence of opportunistic infections (64.51%), low mean body weight (55.85 ± 11.94 kg), and less duration since HIV diagnosis (5.21 ± 3.53 years). Longer mean duration (10.7 ± 5.84 years) since HIV diagnosis and still under care with a good quality of life in the private set up is assuring and support the notion that HIV-infected patients adhering their ART can have prolong and good quality of life just like any other chronic illnesses requiring treatment and monitoring. Educational barrier is also one of the factor suggesting that the lower levels of adherence is correlated with their lower education levels ($P = 0.02$).[18] Other studies have shown the low levels of education as an important factor associated with nonadherence.[19,20] In contrast, a study in Bangalore, India, found education had no effect on adherence.[21]

The awareness regarding a positive effect of life-long ART on their health was higher in private (80.79%) as compared to ART center setting (63.87%). Some studies have identified side effects of ART medications as the significant barriers to good adherence.[22] In this study, 44.11% reported some form of signs and symptoms to their treatment, further analysis did not identify these factors as being significantly related to nonadherence. Nevertheless, where possible ART programs should increase the availability of regimens with fewer adverse reactions.[23]

Of the population sample, we studied majority of them were males in both settings (66.6%). This largely reflects the pattern of the heterosexual epidemic in India, where many men became HIV-infected from high-risk sexual behaviors while away from the home.[24] Efforts to make ART access equitable to both men and women is essential as ART becomes more accessible throughout the country.

Based on the self-report questionnaire, 59 (38.06%) in ART center and 22 (14.56%) of participants in private reported poor ART adherence. This is a matter of concern as poor adherence severely compromises efficacy and is linked with the likelihood of the drug resistance. Studies have found a large number of pills per day to be the principal obstacle to good adherence and to be associated with poorer quality of life as found in our study.[25] The variables age, habits of alcohol/smoking/tobacco, number of pills, and duration of disease played a significant role in predicting adherence to ART. Our survey also demonstrated a trend toward a lower percentage of female (25.16%) patients adherent to ART because in many societies, particularly in India still men are perceived to be the major source financially and also are often given priority

within the family to access care and medications, particularly if resources are limited. Furthermore, women may also have a harder time leaving their family duties and traveling long distances to access care.[26] In the private settings, running out of pills was among the other common reasons for nonadherence, posing an economic burden.

The results show that all the individuals scored well in the QoL domains according to clinical variables, especially in the spirituality and physical domains, for ART center and private settings, respectively. According to Mannheimer *et al*.,[5] QoL can influence treatment adherence since people with a higher QoL also have a greater tendency of adhering to treatment. The relationship between treatment adherence and QoL should be more thoroughly explored.

The authors such as Wu[27] have pointed out that optimization of quality of life in HIV patients is essential for achieving good adherence to therapy regimens, and thus for reducing morbidity and mortality. Strategies in improving adherence to the treatment should be implemented which include using mass media in bringing awareness and disseminating information, training counsellors, establishing patient provider relationship, not prescribing complex regimens, assessing and addressing any cultural beliefs or misinformation, addressing possibilities of developing potential side effects and managing them, not being judgmental when discussing nonadherence and examining barriers and reasons for nonadherence, encourage the use of reminder tools (e.g., using pill boxes, diaries, cell phone alarms, and reminders from the text messages), not neglecting patients reporting perfect adherence and most importantly promote social support – including appropriate disclosure and the involvement of a designated treatment-adherence partner, peers, family members, partner, and friends.[28]

Strengths and limitations

This is the first study across our country which compares the adherence with ART in private and public setup, thus our results can be somewhat generalizable to persons-seeking treatment at both setups. Our comprehensive evaluation of determinants that affect nonadherence in both setups could be of use to optimize ART services. Furthermore, our study highlighted the multidimensional nature of interference of quality of life with poor adherence.

The study has some limitations. First, is its cross-sectional methodological design and thus causal associations and changes in nonadherence indicators over time cannot be observed. Second, is we used self-reported questionnaire for monitoring adherence which can underestimate or overestimate adherence. As of now we do not have any gold standard tool to assess adherence which also necessitates rigorous development and testing of measures of adherence as a research priority. Furthermore, we did not have access to information on participants' CD4 count or viral load before ART initiation, which are the critical predictors of virological response.

CONCLUSIONS

HIV infection is no longer considered as a life-threatening debilitating infection in modern ART era. The availability of less complex single-pill regimen and better tolerated newer generation antiretroviral agents have improved adherence to medication. Like patients in developed countries, Indian patients in private as well as public sector hospitals are surviving longer with the good quality of life. Our results showed that only 61.9% versus 85.4% of HIV-infected individuals had adequate adherence to ART comparing both government and private settings, respectively, and there were the modifiable risk factors affecting low adherence inferring on a continuous need to monitor the ART adherence of people living with HIV/AIDS.

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Conflicts of interest

There are no conflicts of interest.

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