

Adherence to highly active antiretroviral therapy in Hyderabad, India: barriers, facilitators and identification of target groups

Abstract

We assessed the barriers and facilitators to HAART adherence and determined their prevalence among HIV/AIDS patients in Hyderabad, India. We conducted a cross-sectional study among HIV-infected adults prescribed HAART and receiving care from nine outpatient clinics. Depression was screened using Patient Health Questionnaire 9 and facilitators of HIV medication adherence were assessed using an 11-item scale which yielded a total positive attitude to disease score. Prevalence ratios of non-adherence between different categories of potential risk factors were calculated. We compared mean "facilitators to adherence" scores between the adherent and non-adherent population. Multivariable Poisson regression with robust variance was used to identify independent risk factors. Among the 211 respondents, nearly 20% were non-adherent, approximately 8 percent had either moderately severe or severe depression and mean score for combined facilitators to medication adherence was 33.35 (± 7.88) out of a possible 44 points. Factors significantly associated with non-adherence included older age, female sex worker, moderate to severe depression, and the combined facilitators to medication adherence score. These data from a broad range of clinical settings in Hyderabad reveal that key groups to focus on for adherence intervention are female sex workers, older persons and those with depression.

Keywords

HIV, adherence, nonadherence, female sex workers, Hyderabad, India, medication, highly active antiretroviral therapy, barriers, facilitators

Introduction

Medication non-adherence has been associated with greater rates of hospital re-admission, increased cost of health care expenditures, progression of disease, lower quality-of-life, development of co-morbidities,¹⁻⁴ and death⁵ among HIV/AIDS patients. As a result, adherence to antiretrovirals has emerged as an attractive point of intervention toward promoting better health outcomes in persons infected with HIV.⁶⁻⁸ However, for many highly active antiretroviral therapy (HAART) regimens, high levels of adherence are needed to derive sustained clinical benefit.⁹ Additionally, poor levels of HAART adherence are associated with rapid development of drug resistance,¹⁰ requiring the need for expensive and sometimes less convenient second-line therapies.

An estimated 2.1 million people live with HIV/AIDS in India.¹¹ HIV/AIDS is concentrated among high risk groups with rates as high as 8.82 percent in transgenders, 7.14 percent in injection drug users (IDU), 4.43 percent in men who have sex with men (MSM) and 2.67 percent in female sex workers (FSW). These prevalence statistics are in contrast to the antenatal clinic attendee prevalence (0.40 percent), considered a proxy for the general population.¹² In India, 43% of HIV/AIDS patients with

a CD4+ count <350 cells/mm³ are on antiretroviral therapy. The total number of people receiving ART is approximately 500,000 and most receive ART from the public sector.¹³

Andhra Pradesh is a south Indian state with the second highest prevalence of HIV among pregnant women (0.76%).¹² Although several studies have been conducted that assess challenges to HAART adherence,¹⁴⁻¹⁷ and several interventions have been identified as efficacious towards promoting proper use of these medications,¹⁸⁻²⁰ there are no published data describing the prevalence of non-adherence or predicting factors associated with HAART non-adherence among HIV/AIDS patients in the high prevalence state of Andhra Pradesh. Our objective was to assess the barriers and facilitators to HAART adherence and determine their prevalence among HIV/AIDS patients in Hyderabad, Andhra Pradesh.

Methods

We conducted a cross-sectional study among HIV-infected persons prescribed HAART and receiving care from one of nine Hyderabad outpatient clinics located in various parts of the city:

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Diagnostics & Reference laboratories (P) Ltd., Medicity Institute of Medical Sciences (MIMS), Catholic Health Association of India (CHAI), Chaithanya Mahila Mandali (CMM), Darpan Foundation, HIV of Positive People Efficiency Society (HOPES), King Koti Hospital, Sivananda Rehabilitation Home, and Network of HIV Positive People clinics. This convenient sample of

outpatient facilities included one government hospital, two private clinics, two NGO clinics and four community-based organizations.

Informed consent, survey questionnaires and other study materials were translated into Telugu and Hindi, and then back translated into English to ensure fidelity of translation. The questionnaire was previously piloted in one of the clinics and was revised based on the piloting experience. The questionnaire included demographic information of the respondents, questions regarding the barriers and facilitators of HAART adherence, factors associated with adherence, screening for depression, and assessment of the feasibility of implementing a mobile telephone-based intervention to promote prescribed use of HAART medication. The Patient Health Questionnaire 9 (PHQ-9) was used as the depression screening instrument.²¹ The PHQ-9 is a validated instrument for depression screening in a South Indian population,²² and was previously translated into Telugu and Hindi by Pfizer, Inc.²³ We used an 11-item scale to assess facilitators of HIV medication adherence which yielded a total positive attitude to disease score. It included personal motivation, support systems, organizational skills, and a convenient and well-tolerated ARV medication regimen.²⁴ Responses ranged from 0 (totally disagree) to 4 (totally agree) and therefore a score of up to 44 points was possible.

A trained research assistant visited each of these centers twice every month and identified eligible patients available at that center on that day. Men and women 18 years or older who were willing

and able to provide informed written consent, had a previous diagnosis of HIV-infection, and were receiving HAART medication were eligible to participate in this study. A total 213 patients were enrolled in the study after providing their informed written consent in the language of their choosing (Telugu, Hindi, or English) and 211 completed the survey. The N for the study was based on limited resources and convenience as this was an exploratory study without major funding support. The research assistant administered the structured study questionnaire in the same language in which informed consent was obtained.

Due to the high level of adherence required for patients to derive any sustained clinical benefit from HAART medication, we defined a respondent as non-adherent if they reported missing more than a single dose of HIV medication in the previous two weeks. We interviewed the non-adherent respondents regarding their reasons for missing doses. Possible reasons for non-adherence were characterized as often, sometimes, rarely and never.

Data analysis

We calculated frequencies of demographic characteristics of the respondents. To be comparable with other studies on HIV medication adherence in different parts of India, we categorized age into three categories (≤ 30 years, 31 to 45 years, >45 years). We calculated the prevalence ratio (95% confidence interval) of non-adherence between different categories of potential risk factors. We used category of the risk factor with lowest prevalence rate as the reference category. To

identify statistically significant associations between categorical risk factors and medication adherence status of the respondents we performed χ^2 test and Fisher's exact tests. We categorized household income of the respondents based on the urban income quartiles for India.²⁵ For descriptive analysis, we categorized PHQ-9 scores to five categories of depression [Minimal or no depression (0-4), mild depression (5-9), moderate depression (10-14), moderately severe depression (15-19) and severe depression (20-27)] following the PHQ-9 scoring and interpretation guide.²¹ During bivariate analysis we dichotomized depression categories into major depression (moderate/moderately severe/severe depression) and no major depression (minimal/mild depression) using the recommended cutoff value of PHQ-9 score of 10 or greater²¹. We performed the t test to compare mean "facilitators to adherence" scores between the adherent and non-adherent population. Factors that were significantly associated with non-adherence at $p < 0.1$ in bivariate analysis were included in a multivariable log binomial regression model to identify the independent risk factors. In addition, demographic factors which were reported in published literature as associated with non-adherence were included into the initial model irrespective of whether those were statistically significant in bivariate analysis. As combined facilitators to adherence score was correlated with depression score, we did not include the "facilitators to adherence" score in the multivariate model. Since the log binomial regression model failed to converge, we used SAS PROC GENMOD's Poisson regression with the robust variance to estimate

multivariate adjusted prevalence ratios.²⁶ While analyzing the reasons for non-adherence we calculated frequencies by category of response for each of the reasons listed.

Ethical issues

The study design and methods were approved by University of Illinois at Chicago Institutional Review Board (Protocol number: 2012-0505). Informed consent was obtained from all participants in the study.

Results

Among the 211 respondents, nearly 54 percent were male and the median age was 34 years (range 19 years to 62 years) (Table 1). The educational level was generally low with more than 1/3 having either never attended or not reached higher than primary school (Table 1). Approximately 80% had some form of employment including 58 percent employed full-time. Although more than half had some level of depression, approximately 8 percent had either moderately severe or severe depression. The mean score for combined facilitators to medication adherence was 33.35 (± 7.88) (Table 2). Low scores were observed for having once daily dosing (only 14% had such a regimen) and using reminder tools. More than 80 percent of the patients owned a cell phone and nearly 20% were non-adherent. Phone ownership was not associated with adherence. Out of 175 respondents who answered to the question regarding use of their phone's alarm function, 35 (25%) of 141 adherents used the alarm function compared to 6 (18%) of 34 nonadherents ($p=0.38$)

Factors significantly associated with non-adherence included older age, female sex worker, moderate to severe depression, and the combined facilitators to medication adherence score (Table 3). Among these facilitators, having less of a strong sense of self-worth, less acceptance of their HIV diagnosis, and having less of an understanding of the need to adhere to their HIV medication were associated with non-adherence. Younger age had an elevated prevalence ratio and approached statistical significance. Among non-adherent respondents, the most frequent reason for missing doses was that they forgot or were traveling away from home (Table 4). Among the other reasons that accounted for at least 10% total for often or sometimes responses were being busy doing other things, transportation problems and running out of pills. The most frequent reasons varied somewhat by group. For female sex workers, they were travel (often for 3 [17%], forgot (often for 3 [17%]), and avoid side effects (often for 1 [5.6%]). For persons who were older age, they were busy (Sometimes for 3 [22%]), to avoid side effect (Often for 2 [11%]), and travel (Often for 2 [11%]). For those with moderate to severe depression (n=47), they were forgot (Often for 5 [10%] and Sometimes for 2 [4%]), avoid side effect (often for 4 [8%] and rarely for 2 [4%] and travel (Often for 4 [8%] and Sometimes for 1 [2%]).

Discussion

Information about non-adherence to ART is essential to planning interventions that may impact on the HIV epidemic. These data from a broad range of clinical settings in Hyderabad reveal that key

groups to focus on for adherence intervention are female sex workers, older persons and those with depression. The overall level of non-adherence was nearly 20 percent. It is difficult to compare studies of adherence as the measured outcome (e.g., the time interval assessed [4 days, 2 weeks, 4 weeks]), the method of collection (self-report or pill count) and the population demographics may vary. The level of non-adherence we observed is higher than that reported from a tertiary care hospital in West Bengal (13.4%) for whom the measurement was the number of doses missed over the last 4 days.¹⁴ However, it is lower than that observed at a tertiary care center in Chandigarh (26.5%) where the measurement was the number of doses missed over the past 4 weeks.²⁷ Pooled results from seven cross-sectional studies and one retrospective study in India revealed ART non-adherence was 30%.²⁸ None of these studies were derived from populations in Andhra Pradesh.

Among the population subgroups in our study, the highest level of non-adherence and the strongest association was observed in female sex workers (50%). Although this subgroup comprised only 8.53% of the total subjects of our study, they represent a very important population for control of the HIV epidemic. Unlike most other HIV-infected persons, HIV-infected female sex workers may be engaged in sexual intercourse daily and multiple times per day. They may lack the power in their relationships to insist their partners use condoms and they may fear disclosure of their status to partners due to stigma and loss of income.²⁹ They often have children who may be infected or at risk from infection (as from breast feeding) and for whom the mother's

health is critical so they do not become orphaned.³⁰ In addition, they have a high incidence of ulcerative sexually transmitted diseases which may promote spread of HIV and acquisition of other (possibly drug-resistant) strains of HIV to themselves.^{31,32} For example, a study of female sex workers in Karnataka state reported that 28.3% and 3.6% of female sex workers had herpes simplex virus type 2 and syphilis infection, respectively.³³ Due to their high number of partners, risk for sex without barrier protection, and the high level of non-adherence identified in our study, this population of HIV-infected persons should be a priority for HIV adherence intervention. To our knowledge, this is the first study to report HIV medication non-adherence among female sex workers in India.

Our finding that younger age was nearly associated with non-adherence is consistent with other reports. As an example from India, in the West Bengal study, 32.6 percent of persons 18 to 30 years reported non-adherence, somewhat higher than our result of 25.71 percent.¹⁴ Other data concerning this age group in India are scarce. Reasons for non-adherence in young persons could be related to denial, lower emotional tolerance to side effects, heightened concern for stigma, or perhaps higher levels of mobility. The area is in need of research. A stronger association was observed for older persons. These results are contradictory to Indian studies from Bangalore and Mumbai which each found favorable associations with older age and with a study from Chennai which did not find an association with age.^{34,35,36} However, the age ranges used in these other studies were quite different; ≥ 50 years in Bangalore, >40 years in Mumbai, and ≥ 30 years in

Chennai. Also, in studies such as those from West Bengal, Mumbai, and Chennai, age was analyzed as a dichotomous variable whereas we compared the extremes of age with a middle age group.^{14,34,36} Therefore, the role of age is not a generalizable finding in India and would benefit from additional and consistent research methodology.

Depression is another important factor that was associated with non-adherence in our study. This finding is consistent with another Indian study from Pune and Delhi which showed a significant association with severe depression.¹⁶ The inclusion of a depression score is a particular strength of our study as not many adherence studies from India have examined this condition. However, future studies of adherence should consider this factor not only because of its association but because it is a potentially treatable factor. In addition to the importance of treating depression because of its complications, treatment of depression might impact adherence. A retrospective observational study revealed that treatment of depression was borderline associated with a rise of CD4 count at follow-up.³⁷ Although in other studies, this effect was not observed including one among homeless and minimally housed HIV-infected person in San Francisco.³⁸ However, none of these studies are considered conclusive. None of these studies were performed in an Indian population.

Among the facilitators that were associated with adherence, the one which might be most feasible to modify may be improving patient understanding of the need to adhere to their HIV medication.

Understanding of the need to adhere to HIV medication has not been studied in Indian female sex workers. Theoretically, if basic understanding of the health benefits of adherence and consequences of non-adherence are not present in persons who are non-adherent, there may be room for improvement. In addition, if there are indigenous leaders among these women who might provide such information to others, the effect of such information might be augmented. Reductions in HIV and sexually transmitted infection prevalence and high rates of condom use have been observed following interventions among female sex workers in Karnataka that included a peer educator.³¹ Similarly, the prevalence of sexually transmitted infections and condom use were reduced among female sex workers in Mysore following an intervention including peer-mediated outreach.³²

Study limitations included that we did not collect duration on antiretroviral therapy. Adherence may change over time as might reasons for non-adherence. We also did not collect information on active substance abuse which could affect adherence. Our sample size was based on available personnel time for the study and therefore the study may have been underpowered, especially for subgroup analysis. However, despite its size, we did identify several important and biologically plausible associations. And while subjects were not randomly selected, multivariable regression analysis was performed which may minimize confounding. Finally, representativeness is another potential limitation. We included many HIV outpatient sites in Hyderabad. However, they were based on convenience and not systematically sampled. Therefore, they offer a good preliminary

look at a population of HIV-infected patients in this high incidence area but additional systematic investigation is needed to validate our findings.

Our study reveals important groups for whom HIV medication adherence intervention may be especially beneficial. HIV-positive female sex workers are a vulnerable and marginalized group with a clear relationship to transmission of HIV to other adults and their own children. Given that adherence and its consequent reduction in viral load is associated with substantial reduction in HIV infection risk to others as well as personal health benefit and their potential for sexual contact with a relatively large number of person, female sex workers in Hyderabad and possibly elsewhere in India should be given priority for study of effective adherence intervention. Future research in a larger number of female sex workers may validate the association identified in this study, specifically examine and elucidate the issue of to what extent they understand the need to adhere and further explore what barriers and facilitators might most inform the design of an effective intervention. As in other parts of the world, studies and interventions to assist older patients and involving screening for and treatment of depression may also be worthwhile in an effort to maximize the benefit of treatment as prevention.

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Declaration of conflict of interests

The authors declare that there is no conflict of interest.

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