

Adherence to Antiretroviral Therapy and Its Related Factors among HIV-Infected Patients: A Mixed-Methods Study

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ARTICLE INFO	ABSTRACT
Article type: Original article	Background & aim: High levels of adherence to treatment among HIV patients as one of the sexually transmitted diseases (STD) are essential for promoting viral suppression and preventing drug resistance, but little is known about the factors that contribute to antiretroviral adherence. This study aimed to evaluate adherence to therapy and its related factors among HIV-infected patients.
Article History: Received: 28-Oct-2022 Accepted: 05-Aug-2023	Methods: This mixed-methods study was carried out at the Behavioural Diseases Center in Tabriz, Iran in 2021. In a cross-sectional study phase, 137 HIV-infected patients were selected through census sampling method. Then, 21 in-depth interviews were conducted during the qualitative phase using a content analysis approach. Quantitative and qualitative data analysis was performed by SPSS (version 24) and MAXQDA (Version 10), respectively.
Key words: Adherence Human immunodeficiency virus Medication Promoters inhibitors	Results: The mean score of Adherence was 8.96 ± 2.36 and the majority of participants had moderate to high adherence to treatment. The analyses of regression, predictors of adherence included marital status ($\beta = 0.219$, $SE = 0.090$, $P = 0.016$), income level ($\beta = 0.206$, $SE = 0.201$, $P = 0.030$), and education ($\beta = 0.226$, $SE = 0.063$, $P = 0.021$). Also, two themes of "perceived barriers" and "perceived facilitators" emerged which included six main categories at the individual, socio-environmental and organizational as well as drug and treatment levels.
	Conclusion: Despite moderate to high adherence, antiretroviral treatment is a challenging issue. Based on the results, various factors play a role as obstacles and facilitators factors of adherence to treatment among HIV patients. So, intervention programs can be aimed at removing barriers and strengthening facilitators based on based on the factors involved.

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Introduction

Human Immunodeficiency Virus-related infection is one of the most important pandemics infectious diseases that has an impressive influence on the rate of mortality, quality of life, and increases the burden of medical services (1- 2). The prevalence of this illness is different all over the world (1, 3) and it has a very higher prevalence in some parts such as Sub-Saharan Africa (4). Since the detection of

HIV in Iran, about 44,000 infected people have been identified, of which 23,000 are alive until 2022, and due to a recent increase in occurrences, this issue has emerged as a significant public health concern (5-6). Controlling HIV/AIDS as one of the sexually transmitted diseases (STD) in any country needs to design and apply a cohesive caring system (7- 8); Interest in sexually transmitted infections

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(STIs) was further fuelled in the early 1980s by the advent of the HIV/AIDS epidemic and recognition of the role of STI in facilitating the sexual transmission of HIV2 (9) and people with high-risk behaviors are more likely to be infected with HIV/STI transmission (10). Iran is one of the countries for which applied the HIV/AIDS care and control program years ago (11). However, the world still is in danger of HIV expansion (1).

Providing anti-retroviral treatment has made an impressive decrease in appearing diseases and mortalities related to HIV (12-14). The purpose of this treatment is to prevent the development of illness and improve the quality and length of life (15). Treatment adherence is a vital part of AIDS disease and is the most important factor in recovery and medicinal resistance (16). Since providing medication is completely free of charge in Iran, the expectation for complete coverage of anti-retroviral treatment is not impossible (17). The desire and willingness of HIV-positive patients to adhere the anti-retroviral diets are the most important success factor (18). However, different factors affect the access of patients to treatment and non-adherence to therapy (17, 19-20).

Studies show that the factors such as alcoholism and pessimism about illness disclosure are effective in decreasing the application of treatment (19, 21-22). Cultural issues also can be effective in adherence and inaccessibility to treatment (18). Unfortunately, the rate of adherence is lower among Iranian patients (11). Since treatment adherence is very important to achieve appropriate therapeutic results, it is necessary to explain the important factors of treatment adherence in society's cultural situations (18, 20). There is no doubt that being informed about the status of treatment adherence, as one of the most effective factors in HIV controlling, can be an important key. Also, finding the reasons for non-adherence to treatment based on the patient's own experiences can give us the solving point. So, this mixed-method study was conducted to evaluate the adherence to antiretroviral therapy and its related factors among HIV infected patients.

Materials and Methods

This mixed-method study with an explanatory sequential approach was conducted from May to October 2021 in the "Behavioural Diseases Center" which is the only referral center for HIV patients in Tabriz, Iran. The qualitative findings were used as supplement of the quantitative results.

Phase I: The quantitative study

In phase one, a cross-sectional study was conducted to evaluate adherence to therapy in individuals living with HIV in 2021. Inclusion criteria were HIV-positive status, age over 18 (in self-care theories, this age range is considered as an independence mental and physical level), and taking ART drugs for at least 30 days. The exclusion criteria were the inability to provide consent.

Based on the study by Sarna et al. (23), taking into account a 90% adherence to therapy, a (d) of 0.05, $\alpha = 0.05$, and a power of 80% as indicated by the formula, a sample size of 138 was determined.

$$n = \frac{(Z_1 - \frac{\alpha}{2})^2 \times p(1 - p)}{d^2}$$

During the study, 140 patients were identified and a census sampling method was used. We could not contact six of patients. So, a total of 134 patients were included in the study. The socio-demographic characteristics questionnaire included age, gender, marital status, educational levels, and socioeconomic status.

The Persian version of Morisky Medication Adherence Scale (MMAS-8), which was validated by Moharamzad et al. in Iran (24). The MMAS-8, developed by Morisky and Wood, assesses medication-related behaviors which can be either unintentional (e.g., forgetfulness) or intentional (e.g., avoiding medications due to side-effects) (25). Other researchers have provided evidence of good psychometric properties of the scale (26-27). This questionnaire consists of seven questions with two options (with yes=0 or no=1), and a five-point response format is used to rate the final item (e.g. 'How often do you have difficulty remembering to take all your medication' with a range of 0-4). The overall scores range from zero to eleven, and were dichotomized into high (≥ 8), moderate (6-7), and low adherence (<6) (25). The reliability and validity of the 8-item

MMAS-8 have been assessed by Moharamzad et al., in Iran. Internal consistency was acceptable with an overall Cronbach's coefficient of 0.697 and test-retest reliability showed good reproducibility ($r = 0.940$); $P < 0.001$ (24).

The researcher was present at the center on a daily basis, distributing questionnaires to individuals with HIV for completion in a private setting. In case of any questions, the researcher offered necessary explanations. It took approximately 5 to 10 minutes to complete the questionnaire. Participants were chosen based on eligibility criteria, and informed consent was obtained from those who agreed to take part in the study.

Data were analyzed with SPSS statistical software (version 22). The normality of data was measured based on Kolmogorov-Smirnov test, and because the data were not normally distributed, Mann-Whitney and Kruskal-Wallis tests were used to evaluate the association between demographic characteristics and adherence to therapy. Then, independent variables, with $P \leq 0.05$ on bivariate tests inserted into the multivariate linear regression model (enter method). Since the total score of treatment adherence was not normally distributed, this value was first converted by using a natural logarithm (Ln) transformation.

Phase II: The qualitative phase

A qualitative study adopting conventional content analysis approach based on the Graneheim and Landman method was conducted (28). The study recruited HIV-positive patients with the inclination and capacity to articulate and convey ideas, employing purposive sampling to ensure maximum diversity in the factors like education, age, and socioeconomic status. Patients who withdrew or did not will to participate in the study, were excluded. Data were collected through semi-structured interviews. The interviews were done by the main author of the study who had the experience of several qualitative studies. The interview began with a key question, "How much do you know and act about treatment adherence?", and continued with other questions, such as "frequency of missed medication doses and reasons for missing"; "probes regarding adherence promoters and inhibitors". The interview

continued with more in-depth items, such as "what do you mean? Can you explain further?" All interviews were carried out in a quiet room in health center and lasted as 20-35 min. The interviews were recorded and field notes were used as much as possible and then transcribed at the right time. Data saturation was achieved after the 19th interview. However, an additional two interviews were also conducted to ensure thorough completion. Analysis was performed by MAXQDA (Version 10). The five Guba and Lincoln criteria (including credibility, dependability, transferability, conformability, and authenticity) were applied to ensure the trustworthiness of data (29). In order to validate the results, the corresponding author thoroughly reviewed the interviews and shared them with colleagues, incorporating their feedback. Additionally, the researcher's prolonged involvement in the study was acknowledged. Moreover, to enhance the credibility of the data, a process of actively seeking contradictory evidence was undertaken, extracting data which challenged the conceptualization and descriptive theory derived from the data. Therefore, it was tried to select participants with maximum diversity of experiences.

Written informed consent was obtained from the participants before data collection. This study has been approved by the Ethics Committee of the Islamic Azad Medical Sciences University, Tabriz, Iran (code number: IR.IAU.TABRIZ.REC.1398.013).

Results

Quantitative results (Phase 1): The mean age of participants was 40.39 years old. Based on the results, 63% cause of infection was sexual. The Mean of MMAS-8 score was 8.96 ± 2.36 , and 89(66.4%), 31(23.1%), and 14(10.4%) of participants had high, moderate, and low levels of adherence to treatment (Table1).

There was a correlation (median) between marital status, income level, education level, type and duration of infection with treatment adherence. The model could predict the 11.8 percent of the treatment adherence variations ($P=0.006$) and based on the model, education level, marital status and income level are significantly effective on treatment adherence,

so, by increasing one unit in standard deviation of these variables, the treatment adherence will increase 0.226, 0.219 and 0.206 unit, respectively (Table 2).

Qualitative results (Phase 2): A total of 21 patients participated in the interviews (age range 19-58, mean (SD) = 38.24 (9.65)). Most participants (n=11, 52.4%) were sexually infected (Table 3). Table 4 showed the examples of content analysis, coding, and categorization. Six main categories and two themes of “perceived barriers” and “perceived facilitators” were derived (Table 5).

Perceived Barriers

The barriers were classified into three main categories of Individual inhibitors, Socio-environmental, and organizational inhibitors, and Drug and treatment related inhibitors.

1. Individual inhibitors

1.1. Psychological inhibitors

Some participants described the negative points that come with HIV eventually leading to a sense of hopelessness, fear of disclosure, and having a mental problem such as depression.

“I experienced a love failure and wanted to suicide. I was very sad when I realized that the girl was married. I didn’t want to take my medication” (Man, 48 years old).

“When I realized I am infected to HIV, I hated myself and there was nothing important to me. I lost my hope over the time” (Man, 38 years old).

“Anywhere that I go, I remove the name of drugs that I take that no one would understand about my illness. Because in this way they will ask the reason on my illness and it’s unpleasant for me” (Woman, 58 years old).

“Sometimes that I go to our garden I forget to take my drugs”. (Man, 36 years old, infected by syringe).

“My family don’t know about my illness. I always hide my drugs and in parties or ceremonies I take them secretly or I don’t go such places” (Man, 32 years old).

1.2. Disabilities and bad habits

According to the reports by participants, fatigue, laziness, and drug addiction can be the reason for not taking the drug properly and following medical treatment.

“Formerly that I was addicted, I didn’t want to take my medications and I even didn’t think of taking them” (Man, 39 years old).

“Sometimes I’m out of energy. Especially when I’m tired I don’t take my drugs” (Woman, 51 years old).

“Sometimes I felt weakness and pain in my body in I thought I can’t take my drugs” (Man, 42 years old).

2. Socio-environmental and organizational inhibitors

2.1. Negative social effects

Many participants noted that the stigma of HIV infection causes being abused by other people and their own families. It makes feeling of shame and self-hatred that resulted in confidential use of antiretroviral drugs. Also, some of them believed that lack of knowledge about HIV among patients and people was another major cause of no adherence. Other negative effects of the environment are loneliness and lack of the family, friends and the community support.

“What could I do? Formerly I didn’t know much about it and treatment. Also, many people don’t know about the infection ways. As they knew you are infected, they repulse you” (Man, 39 years old).

“Unfortunately, I don’t receive any support from my family (“Man, 42 years old).

“Some people take fun of you and someone harass. They say you are the scourge of society. This make me unpleasant. I don’t want to be alive so that why should I take my drugs” (Man, 42 years old).

2.2. Financial pressures

One of the factors involved in non-adherence to treatment is the high cost of living and the financial pressures. This factor makes it difficult to obtain medicines and decreases motivation to take drugs. Some of them have lost their jobs due to illness.

“I was a barber, but I left it because of my illness and now I am unemployed. I am dependent to my family. I sometimes think of not taking the drugs, so that I will get worse and will die” (Man, 36 years old).

“The costs of life are very high. It is about 5 months that I am unemployed. If the drugs

weren't free, I couldn't take them" (Man, 24 years old).

2.3. Problems related to the health system

A number of participants reported that some factors related to the provision of health services can make it difficult to provide medication. One of these factors can be the provision of care services only in a specific center in the city, and this causes not only patients have to travel long distances to access care, but also from the patients' point of view, giving a specific name to the care center as "special disease center" can make it difficult to refer to the center and cause social stigma.

"I come from a small town and I should spend some money for transportation. Although there is a center for HIV infected patients, but I can't go there because the town is small and everyone would be aware of my illness." (Man, 32 years old).

3. Drug and treatment related inhibitors

3.1. Intolerance of medication

Side effects of medication were discussed as nonadherence to treatment, including physical symptoms such as nausea and drowsiness, which cause discomfort and problems in taking the drug. Also, the large size of the drug is a disturbing factor in taking the drug.

"Formerly, I experienced headache and vertigo that even I could not go to work, because I felt sleepy there. Also, I couldn't eat enough food" (Woman, 46 years old).

"The drugs have some side effects especially when you start to take them for first time. I myself had nausea" (Man, 42 years old).

3.2. Interaction effects with other drugs

According to the reports of some participants, the number of drugs and the presence of other diseases, especially addiction and concomitant use of methadone are the barriers to ART adherence.

"I should have taken 3 pills per day. I removed one of them by myself, but I lost" (Woman, 46 years old woman).

"I have hypertension. So that I should take several drugs. Doctors say I must take all of them, otherwise I will face several problems" (Man, 40 years old).

Perceived Facilitators

A wide variety of meaning units were extracted about facilitators which were classified into three main categories: individual promoters, socio-environmental and organizational, drug and treatment related promoters.

1. Individual promoters

1.1. Psychological promoters

Most participants believed that one of the key elements for improving treatment adherence is having positive perceptions and values inside. Having a positive outlook and inner motivation such as desire to survive, benefiting the community, and awareness of the importance of taking medication are the factors that help improve ART adherence.

"I have to take all of my drugs because of my children. My illness has important effect on them. Now that I come here regularly and receive treatment, I have got better" (Woman, 33 years old).

"If you want to live, you must take all the drugs. I think I should take my medications so that I can get married and keep the society safe" (Man, 39 years old).

"If you don't take this illness's drugs, be sure that you will die. I mean taking the drugs is the only and necessary way" (Man, 36 years old).

1.2. Abilities and good habits

Some participants believed that it depends upon individuals to manage the consumption of antiviral drugs. In addition, engaging in daily activities and performing appropriate activities such as exercise are effective to control the disease and treatment adherence.

"My own efforts are important to correctly use the drugs. First of all, I myself should want to take the drugs to keep my body without any virus" (Man, 42 years old).

"Formerly I didn't want to take drugs. But now I am better and I think it's like a food and I must take them" (Man, 39 years old).

"I was 95 kilos but now I am thinner. I refuse methadone. If I give it up I will get better, restart physical exercise and I will defeat this illness" (Man, 36 years old).

2. Socio-environmental and organizational promoters

2.1. Positive environmental effects

The other important facilitator factors briefly discussed by the participants included: support from family and friends, having social welfare, and existence of supporting organizations. Patients believed that getting support can really play an important role in achieving adherence to therapy and dealing with the issue of noncompliance.

"I am supported and covered by social welfare organization (one of the governmental supportive organizations) and receive financial supports" (Woman, 32 years old).

"I help my husband and always remind him to take his drugs. My daughter reminds me and every night asks me to take my drugs then go to sleep" (Woman, 39 years old).

2.2. Promoters related to the health system

According to the reports by participants, the most important contributing factor in treatment adherence is the proper behaviour of employees, having good communication and trusting them. In addition, psychological counselling helps them to visit the health center regularly and motivates them to receive medication.

"All the clerks in this center help me. I love and appreciate them" (Woman, 45 years old).

"The doctor said if you take your drugs regularly you can live in a normal way. He is so kind of me always. He spends time to talk with me and answers to any question that I ask" (Man, 49 years old).

3. Drug and treatment-related promoters

Another factor influencing the regular use of medication is free access to the drugs. Also, having a regular treatment plan is important.

"I know that these drugs are very expensive. But here I get them completely free. Otherwise I never could afford them" (Woman, 43 years old).

"Thanks the God that these drugs are free. Any time that I need them, I come here and get" (Man, 32 years old).

Formerly I didn't want to take my drugs but after following me up from this center I was forced to take the drugs (Man, 49 years old).

Integration of quantitative and qualitative findings

The integration of findings reveals a comprehensive understanding of adherence to HIV treatment. While quantitative data highlighted demographic predictors and adherence levels, qualitative insights provided depth by uncovering individual experiences, socio-environmental factors, and perceived barriers and facilitators. The combined approach enriches the study, offering a holistic view of the complexities surrounding treatment adherence among the participants.

Discussion

Although treatment adherence was fairly good among patients in the present study, there were multifaceted promoters and inhibitors to ART adherence. Demographic and personal characteristics, environmental and social factors, and factors related to the treatment and medication can affect ART adherence.

The majority of participants had moderate to high level of treatment adherence and it is lower than the findings of a study conducted in Uganda (93%) (30) and other studies with $\geq 95\%$ adherence (19, 31-32). However, some publications reported the same rate as the present study (33-35). According to researchers, across the United States, a majority of patients had suboptimal adherence, but, adherence to ART was assessed in patients during the 12-month follow-up period (36). Also, differences observed can be due to the use of different adherence measurement scales. The results of the present study showed that marital, educational, and income status were predictors of treatment adherence. These findings are similar to other studies conducted in Brazil (2) and Vientiane (20). But Pinheiro et al. (2) found no association between income level and treatment adherence. Yu et al. reported (35) that single patients had a higher level of treatment adherence than married patients, which is contrary to the findings of the current study.

According to the results of the present study, multiple barriers were identified. The three main categories formed perceived barriers which included individual inhibitors (e.g., fear of disclosure, hopelessness, forgetfulness, depression, fatigue, and substance abuse), Socio-environmental and organizational inhibitors (e.g., stigma, lack of social support, jobless,

financial pressures, fear of not being confidential), and drug and treatment related inhibitors (e.g., side effects, negative effects of methadone treatment and the number of drugs use). These results are similar to other studies (8, 37-39). Brigido et al. also reported (39) that forgetfulness and intolerance were the most frequent factors affecting non-adherence. Weiser and colleagues showed that the main barriers to HIV adherence were financial constraints, stigma, travel/migration, and side effects of drugs (40). In addition, Shumi et al. reported that receiving support from the spouse can play an important role in receiving care in pregnant women (8). Social stigma as negative environmental effect and drug side effect as treatment-related inhibitors were mentioned by the participants in the present study, but migration was not a barrier, however being away from home was one of the inhibitors in the current study which can be due to forgetting to take drug or fear of disclosing. The researchers indicated that the most frequently encountered inhibitor was a shortage of drugs caused by insufficient funds (41). As it was found in quantitative phase in the current study, income level was one of the predictors of treatment adherence. Also, in the qualitative part, participants emphasized the impact of economic pressures as an important barrier. In a study in Uganda, forgetfulness, drug inaccessibility, adverse effects of the medication, travelling away from home, unclear instructions by the health provider, and being too busy were reported as barriers of adherence (41). However, in the present study, fatigue, forgetfulness and lethargy were mentioned instead of being busy. Similarly, in a qualitative study (42), the common barriers to non-adherence included experiencing depression or overwhelm, accidental forgetfulness, and challenges with timing.

Another barrier mentioned in the current study was the long distance to the center. In addition, the concern about the non-confidentiality of the disease status is due to the name of the center, which is called the Special Patient Counselling center, and this concern is a kind of fear of disclosure and escape from social stigma. This obstacle must be considered in the interventional programs.

According to the findings of the current study, multiple promoters affecting ART adherence were identified, including individual inhibitors (e.g., having a positive perception, positive values, ability to manage a medication schedule, choose the appropriate lifestyle), socio-environmental and organizational inhibitors (e.g., social and familial support, having social welfare, health workers support, providing free consulting services), and drug and treatment related inhibitors (e.g., free medication, continuous follow-up). When patients had positive perception (e.g., understanding the good effects of treatment and awareness on the importance of taking medication) and positive values (e.g., desire to survive, tendency to be useful to society, and having a goal), they were more careful in taking their medications. These findings are consistent with the study conducted in Saudi Arabia (18). Finding ways to use drug correctly and according to the plan is another effective factor in improving the status of taking medication. Patients sometimes use adherence strategies including having daily schedules (38) and use of alarm clock as reminder (38, 43).

Other factors were social support, free counselling services, and an adequate supply of ART medications. Partner and family support positively impacted participants, especially in reminding to take medications. Conversely, providing free counselling and good relationship with health care staff were facilitator factors. It is unsurprising to find that healthcare workers play a central role in various strategies for utilizing health services. According to the literature, patients need to be encouraged by health care workers (4, 44-45). Appropriate and gentle manner of health care providers causes trust in patients which can lead to patients' returning for routine care.

Conclusion

In general, achieving >90% adherence to therapy among all HIV patients is still a challenge in Iran. The findings of the present study generated important insights to develop effective interventions which address the barriers and facilitators of ART adherence in Iran. By emphasizing the positive health outcomes resulting from ART treatment regimens in patients, there is a focus on

developing efficient reminder tools and educational programs, especially at the community level, promoting trust in treatment, self-management, and taking supportive measures to have a suitable job for patients.

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Conflicts of interest

Authors declared no conflicts of interest.

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