


BMJ Open Magnitude of optimal adherence and predictors for a low level of adherence among HIV/AIDS-infected adults in South Gondar zone, Northwest Ethiopia: a multifacility cross-sectional study

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ABSTRACT

Objectives This study aims to identify levels of adherence to antiretroviral therapy (ART) drugs and factors associated with them in Northwest Ethiopia. We hypothesise that in the era of COVID-19, there would be suboptimal adherence to ART drugs.

Design An observational cross-sectional study was conducted. Factors associated with the level of adherence were selected for multiple logistic regressions at a p value of less than 0.2 in the analysis. Statistically significant associated factors were identified at a p value less than 0.05 and adjusted OR with a 95% CI.

Setting The study was conducted in one specialised hospital and three district hospitals found in the South Gondar zone, Northwest Ethiopia.

Participants About 432 people living with HIV/AIDS receiving highly active ART in South Gondar zone public hospitals and who have been on treatment for more than a 3-month period participated in the study.

Primary and secondary outcome measures Levels of adherence to ART drugs and their associated factors.

Results Among 432 study participants, 81.5% (95% CI: 78% to 85.2%) of participants were optimally adherent to ART drugs. Determinants of a low level of adherence: stigma or discrimination (OR=0.4, p=0.016), missed scheduled clinical visit (OR=0.45, p=0.034), being on tuberculosis treatment (OR=0.45, p=0.01), recent CD4 cell count less than 500 cells/mm³ (OR=0.3, p=0.023) and patients who had been on WHO clinical stage III at the time of ART initiation (OR=0.24, p=0.027) were factors significantly associated with adherence to ART drugs.

Conclusions Level of adherence was relatively low compared with some local studies. The intervention targeted to reduce discrimination, counselling before initiation of treatment and awareness regarding compliance is advised to improve adherence to antiretroviral regimens.

INTRODUCTION

HIV/AIDS is one of the pandemic public health problems still affecting many people.

Strengths and limitations of this study

- There is a possibility of recall bias and social desirability bias.
- Findings are also generalisable only for patients treated as outpatients.
- Being a cross-sectional survey, causality cannot be inferred from those findings.
- Adherence level is a snapshot of adherence behaviour during COVID-19 infection.
- The present study has a strength due to the use of robust data collection tools that ensured the quality of the study.

At the end of 2020, 37.7 million people globally were living with HIV. In the same year, 1.5 million people were newly infected by the virus and 680 000 people died from AIDS-related illnesses.¹ Countries are taking different actions to tackle the HIV/AIDS epidemic as well as to improve the quality of life among people infected by the virus; one of these was the treatment of patients with antiretroviral therapy (ART).²

In Ethiopia, achieving optimal adherence and sustainable follow-up in care and treatment are the most difficult in HIV/AIDS management. A 5-year retrospective medical record review of 3012 adult patients who were enrolled in therapy at Gondar University Hospital ART clinic demonstrated that 31.4% of patients had been lost to follow-up.³

Highly active ART (HAART) involves sophisticated regimens that necessitate careful adherence to intricate treatment schedules owing to the high risk of developing treatment-resistant forms of HIV as a result of missing, underdosing and irregular use of antiretroviral drugs.⁴

Adherence to multidrug antiretroviral regimens has been a focus of attention since ART drugs' introduction owing to their complexity, frequent adverse effects and chronic nature.^{5,6}

To get optimal viral suppression and prevent treatment failure, individuals should take more than 95% of prescribed drugs. If once the individual fails to take more than 95% of prescribed drugs, the virological failure rate will be more than 50%.^{7,8}

Antiretroviral medication non-compliance can result in negative clinical, immunological and virological effects. In the absence of good adherence, the immune system continues to be distracted, resulting in lower CD4 cell levels and the establishment of resistant virus strains.^{9,10} According to a WHO survey study in developing countries, the HIV/AIDS drug resistance rate among people starting ART ranged from 4.8% in 2007 to 6.8% in 2010.¹¹

A considerable number of ART patients struggle to maintain a high level of adherence. According to previous studies, 12%–50% of HIV-positive patients do not attain adequate adherence.¹² A study conducted in rural Tanzania showed that 70% of the participants achieved the desired level of adherence.¹³ In Soweto, South Africa, 88% of patients report more than 95% adherence rate, and the main reasons given for missing doses were being away from home (30%), difficulty with the daily routine (23%) and running out of pills (12%).¹⁴

A study done in Addis Ababa city describes that among patients on ART drugs, 73.3% of participants had an optimal level of adherence. Stigma, discrimination and poor relationship with healthcare providers were predictors for a suboptimal level of adherence.¹⁵

Social and economic difficulties, the healthcare policies, disease traits, disease therapies and patient-related factors are all potential impediments to patients complying with treatment plans.¹⁶

Fear of disclosure, concurrent substance abuse, forgetfulness, suspicions of treatment, overly complicated regimens, number of pills required, decreased quality of life, work and family responsibilities, falling asleep and access to medication were all identified as obstacles to adherence in a systematic review study.¹⁷

Now, countries devised a comprehensive plan to address HIV/AIDS prevention and care. This is in line with the three 90s target set by United Nations Programme on HIV/AIDS (UNAIDS) to help end the AIDS epidemic by 2030.¹⁸ The target states that 90% of all people receiving ART will have viral suppression. The plan and strategic objectives are fruitless if adherence to HAART is not well recognised.

Currently, our world, including Ethiopia, has been struggling to prevent and control a new pandemic disease called SARS-CoV-2; thus, chronic diseases like HIV/AIDS were put aside especially in developing countries. We hypothesise that there may be suboptimal adherence to ART drugs among people living with HIV (PLHIV). Having a strategy to sustain an optimal level of adherence among PLHIV is an essential step towards ensuring

treatment success. The knowledge would help to evaluate the clinical management strategies and define relevant, efficient, acceptable adherence support measures for patients within the health system. So the main purpose of this study was to determine the level of adherence and its predictors among PLHIV who have been using HAART.

Therefore, this observational study hypothesises that in the era of COVID-19, there would be suboptimal adherence to ART drugs among PLHIV/AIDS.

MATERIALS AND METHODS

Study setting, design and periods

A multicentre facility-based observational cross-sectional study was conducted from August to January 2021 in the South Gondar zone, Amhara region. South Gondar zone is divided into 19 woredas and structured with 1 general hospital and 7 primary hospitals. All of them are providing ART care and treatment for its consumer. In the zone, there are 6870 HIV/AIDS-infected patients enrolled in ART care and treatment. In this study, four public hospitals were selected randomly which provide ART care and treatment for HIV/AIDS-infected people.

PLHIV/AIDS (≥18 years old) receiving HAART in South Gondar zone public hospitals were the study population and the study participants were adult PLHIV/AIDS (≥18 years old) treated as outpatients in selected public hospitals and who have been on treatment for more than a 3-month period.

Eligibility criteria

HIV/AIDS-infected people greater than or equal to 18 years of age, and PLHIV who have been on treatment for more than a 3-month period and continuing their ART during the study period were eligible for this study.

Sampling technique and procedure

The study was conducted in four randomly selected hospitals. Then, the possible number of participants in each of the hospitals of the study area was allocated proportionally based on their order of arrival. Using the eligibility criteria, each study participant was included in the study and a systematic random sampling technique (every fifth interval) was applied based on their order of arrival in the ART clinics.

Explanatory variables

Sociodemographic (age, educational status, residence, marital status), personal and family-related (disclosure of serostatus, stigma and discrimination, use of complementary medicine), medication-related (drug other than antiretroviral, patients on ART, missed scheduled clinical visit), clinical (patients on tuberculosis (TB) treatment) and immunological factors (recent CD4 count, WHO clinical stage) were included in the regression analysis.

Data collection instruments

The data collection tool was adapted from two main sources. First was a questionnaire from AIDS Clinical Trial Groups¹²

adherence instrument which measured level of adherence based on patient self-report. Second was a questionnaire from the Community Programs for Clinical Research on AIDS¹⁹ that was used to collect other information including the clinical aspect of the patient. Taking all ARTs at a right time in the week before the study was a cut-off value to consider optimal adherence to the ART medication. Otherwise, it is categorised as non-adherent. If they report missed doses during the last 7 days, the questionnaire asks a range of multiple-choice questions about why they miss their daily dose. Patients' clinical data such as WHO clinical stage and the CD4 counts were extracted from their medical records at the ART clinic by using a checklist which was adapted from different literature. Data collection was performed by five diploma nurses (supervised by three BSc nurses). A 2-day comprehensive training was given for data collectors and supervisors.

The questionnaire was compiled in English and evaluated by experts who had expertise in AIDS care and treatment situations in our country. Five AIDS experts were invited to review the Amharic version (local language) of the questionnaire for face validity and readability. The questionnaire was pilot tested on 30 (5% of the sample) HIV-infected people. It was reported reliable and valid with Cronbach's $\alpha=0.83$, shows high level of internal consistency, 85% general interobserver agreement, 78% sensitivity and 95% specificity, so it had been appropriate and easy to understand by participants. Data collectors were trained to have a common understanding of the objective and the methodology of the research. The investigators closely supervised the performance of the data collectors daily.

Operational definition

Good (optimal) adherence

Good (optimal) adherence means taking all ARTs in a correctly prescribed dose in the 1 week before the study.²⁰

Sample size calculation

The sample size in this cross-sectional study was determined using a single proportion formula: $n = (Z^2)^2 pq / d^2$. The minimum sample size required for the study was estimated to be 432 using the above formula where n is the sample size, Z is the standard normal deviate set at 1.96 (for 95% confidence level), d margin of error acceptable or measure of precision (taken as 0.035) and $p=85.3\%$ taken from the previous study²¹ and sample size adjusted by 10% non-response.

Statistical analysis

Data entry and analysis were done by using Epi Info V.7.1 and SPSS V.23, respectively. We have computed the frequencies and percentages of different variables for description as appropriate. Using X^2 test, bivariate analysis of variables was completed with OR at 95% CI to assess the presence and degree of association between the dependent and independent variables. We hypothesise that there would be suboptimal adherence to ART drugs among PLHIV so a one-tailed p value was applied.

Table 1 Demographic and economic characteristics of the study participants in South Gondar zone, 1 August 2020–31 January 2021 (n=432)

Variables	Frequency (n=432)	Percentage
Sex		
Male	172	39.8
Female	260	60.2
Place of residence		
Urban	335	77.5
Rural	97	22.5
Age		
18–24	103	23.8
25–34	217	50.2
35–45	70	16.3
>45	42	9.7
Monthly income		
<1000	79	18.3
≥1000	353	81.7
Educational status		
Primary level of education	55	12.7
Secondary level of education	314	72.7
College and above	63	14.6

To control possible confounding variables, explanatory variables associated with outcome variables with $p < 0.2$ were entered into multivariable logistic regression analysis. Statistically significant associated factors were identified based on a p value of < 0.05 .

Patient and public involvement

Members of the public were not involved in the study concept or design.

RESULTS

Demographic and economic characteristics

A total of 432 HIV/AIDS-infected patients who reported using ART were interviewed about adherence to their medication, giving a response rate of 100%. The population consists of 172 (39.8%) male and 260 female (60.2%) patients, and 335 (77.5%) were urban residents. Out of the total population, 217 (50.2%) were in the age group between 25 and 34 years, and the mean age of study participants was 30.6 ± 8 years. The majority of participants (322, 74.5%) were married. From the total population, 211 (48.8%) participants were government employees and the majority of patients' monthly income was more than or equal to 1000 Ethiopian birr (table 1).

Family and clinical-related characteristics

Out of the total population, 255 (59%) patients disclose their serostatus. From the overall population, 45 (10.4%) participants were stigmatised and/or discriminated by

Table 2 Family and clinical-related characteristics of the study participants in South Gondar zone, 1 August 2020–31 January 2021 (n=432)

Variables	Frequency (n=432)	Percentage
Serostatus of sexual partner		
Positive	226	52.3
Negative	17	3.9
Unknown	189	43.7
Disclosure status		
Not disclosed	177	41
Disclosed	255	59
To whom serostatus disclosed		
Family	79	31
Sexual partner	173	68.2
Friend	3	0.8
Stigma and discrimination		
No	387	89.6
Yes	45	10.4
Do you use complementary medicine?		
No	351	81.3
Yes	81	18.8
Do you use a reminder?		
No	40	9.3
Yes	392	90.7
Baseline CD4 count		
≤500 cells/mm ³	51	13.2
>500 cells/mm ³	336	86.8
Treatment regimens		
TDF+3TC+EFV	259	60.0
AZT+3TC+EFV	143	33.1
AZT+3TC+NVP	30	6.9
TDF+3TC+EFV	259	60.0
WHO clinical disease stage during initiation of ART		
Stage I	50	11.6
Stage II	352	81.5
Stage III	30	6.9
Recent CD4 count		
≤500 cells/mm ³	87	20.1
>500 cells/mm ³	341	78.9

ART, antiretroviral therapy; AZT, Zidovudine; EFV, Efavirenz; NVP, Nevirapine; 3TC, Lamivudine; TDF, Tenofovir.

their family, friends or community. Again, 81 (18.8%) were using traditional medicine in addition to their ART drugs. Regular mealtimes (193, 44.7%) was the most common reminder (table 2).

Adherence and healthcare service characteristics

Based on the patient's self-report, 81.5% (95% CI: 78% to 85.2%) of participants had optimal adherence level (take

Table 3 Adherence and healthcare service-related characteristics of the study participants in South Gondar zone, 1 August 2020–31 January 2021 (n=432)

Variables	Frequency (n=432)	Percentage
Do you miss your dose in the last 7 days?		
No	352	81.5
Yes	80	18.5
Number of missed doses		
1–2	57	13.2
3–4	23	5.3
Reason for missing taking ART medication		
Away from home	19	23.75
Forgot about it	31	38.75
Busy with other things	12	15
Sickness	18	22.5
Missed scheduled clinical visit		
No	386	89.4
Yes	46	10.6
Do you take drugs other than ARV?		
No	328	75.9
Yes	104	24.1

ART, antiretroviral therapy; ARV, antiretroviral.

their entire daily dose) 1 week before the interview. The reasons given for missing their treatment were forgetting about it (31, 7.1%) and being away from home (19, 4.4%). Only 46 (10.6%) of study participants missed the scheduled clinical visit and 104 (24.1%) patients were taking drugs other than their ART medicine (table 3).

Factors associated with adherence to ART

Stigmatised or discriminated patients were 60% less likely to adhere to ART compared with non-stigmatised and non-discriminated patients (adjusted OR (AOR)=0.4, 95% CI (0.2 to 0.84)). Patients who missed scheduled clinical visits were 55% less likely to adhere to their ART compared with patients who did not miss scheduled clinical visits, 55% (AOR=0.45 (0.21 to 0.94)). Patients who had been on TB treatment have been 55% less likely to adhere to ART compared with patients who had not been on TB treatment (AOR=0.45 (0.24 to 0.83)). Respondents whose recent CD4 cell count was less than 500 cells/mm³ were 70% less likely to adhere to treatment compared with respondents whose CD4 count was greater than 500 cells/mm³ (AOR=0.3 (0.14 to 0.73)). Patients in WHO clinical stage III at the time of ART initiation were 76% less adherent to ART compared with their counterpart (AOR=0.24 (0.098 to 0.57)) (table 4).

Table 4 Factors associated with ART adherence among adult patients on ART in public health institutions in South Gondar zone, 1 August 2020–31 January 2021

	Adherence to ARV		COR (95% CI)	AOR (95% CI)	P value
	Adherent	Non-adherent			
Drug other than ARV					
No	275	53	1	1	
Yes	77	27	0.55 (0.3 to 0.9)	1.14 (0.53 to 2.45)	
Stigmatised and discriminated patients on ART					
No	326	61	1	1	
Yes	26	16	0.26 (0.13 to 0.5)	0.4 (0.2 to 0.84)	0.016
Missed scheduled clinical visit					
No	325	61	1	1	
Yes	27	19	0.27 (0.14 to 0.51)	0.45 (0.21 to 0.94)	0.034
Patients on TB treatment					
No	297	50	1	1	
Yes	55	30	0.41 (0.18 to 0.53)	0.45 (0.24 to 0.83)	0.01
Recent CD4 count					
≥500 cells/mm ³	328	65	1	1	0.023
<500 cells/mm ³	27	17	0.23 (0.12 to 0.56)	0.3 (0.14 to 0.73)	0.007
WHO clinical stage at the time of ART initiation					
Stage I	42	8	1		
Stage II	291	61	0.208 (0.68 to 0.633)		
Stage III	12	11	0.23 (0.1 to 0.55)	0.24 (0.098 to 0.57)	0.027

AOR, adjusted OR; ART, antiretroviral therapy; ARV, antiretroviral; TB, tuberculosis.

DISCUSSION

This study was focused on the magnitude of optimal ART drug adherence and associated factors for a low level of adherence among HIV/AIDS-infected patients at public hospitals in the South Gondar zone. The study found that 81.5% of participants were having an optimal adherence based on a 1-week recall before the actual interview. This is far less than the finding in Southwest Ethiopia where 95% of patients had optimal adherence to their prescribed doses²² and similarly, in Northeast Ethiopia, 95% of patients also had optimal adherence to their medication.²³ However, our findings were comparably higher than those found in Tanzania, where only 70% of the participants achieved the desired level of adherence.¹³ Another study conducted in Northeastern Ethiopia explains that the level of optimal adherence was found to be 71.8% in the past 7 days of recall of their daily doses.²⁴ But it is almost consistent with a study finding in Addis Ababa reporting 82.8% of patients had optimal adherence.²⁵

Stigmatised or discriminated patients were 60% (AOR=0.4, 95% CI (0.2 to 0.84)) less likely to adhere to ART compared with their counterparts. Stigma and discrimination, especially in sub-Saharan Africa, play the main role for poor patient follow-up in treatment care and extensive contribution for inadequate HIV/AIDS prevention.²⁶ Patients frequently skipped doses

due to fear of being identified as HIV positive. A systematic review of 26 715 HIV-positive people in 32 countries discovered that HIV-related stigma hampered adherence to ART, principally through impairing social support and adaptive measures taken to manage stigma during medication. The study highlights the relevance of social relationships in improving adherence, particularly in resource-constrained contexts, and highlights the importance of social integration in HIV-positive people's treatment experiences.²⁷

Patients who had been on TB treatment are 55% less likely to adhere to ART compared with patients who did not have TB treatment (AOR=0.45 (0.24 to 0.83)). A cross-sectional study found that individuals who had been on TB treatment in addition to ART drugs have a high level of ART non-adherence.²⁸ Patients more frequently adhered to TB treatment compared with ART. This might be due to the shorter duration of TB treatment compared with life-long ART medication. Another possible reason was that patients prioritise TB treatment and would have less attention to life-long ART medication to avoid the burden of medications.²⁹

Respondents whose recent CD4 count less than 500 cells/mm³ were 70% less likely to adhere to treatment compared with respondents whose CD4 count was greater than 500 cells/mm³ (AOR=0.3 (0.14 to 0.73)). A study finding shows that optimal level of adherence was

found to be a key factor in virological and immunological results. A CD4 cell count was increased by 179, 159, and 53 cells/mm³ in the groups who had 100%, 80%–99%, and 0%–79% level of adherence, respectively.³⁰ A study conducted in a developing nation found that patients with CD4 counts below 200 cells/mm³ had nearly five times higher chance of treatment failure than those with CD4 counts above 200 cells/mm³.³¹ Viral replication reduces when CD4 cell count rises, implying that viral burden is inversely proportional to CD4 cell count. When compared with immune-competent patients with HIV infection, patients with deteriorated immune status had raised viral load. Furthermore, individuals with weakened immunity are more vulnerable to a variety of opportunistic illnesses, which make them suffer from the vicious cycle of immune depletion and viral replication.³²

Patients who had been on WHO clinical stage III at the time of ART initiation were 76% less adherent to ART compared with their counterparts. It has been proven that HAART is effective in suppressing HIV replication, decreasing morbidity and mortality associated with HIV, suppressing development and spread of ART drug-resistant HIV, and improving quality of life in adults as well as children infected with HIV. However, drugs do not work in patients who do not take them properly so optimal adherence to HAART is a crucial step towards the successful outcome of therapy.⁷⁸

Poor adherence has several effects on patients' health. Some of them severely compromise the effectiveness of treatment, making this a critical issue in the population health from the perspective of quality of health and health economics. So there should be an intervention aimed at improving adherence because it has a significant positive return on patients' health through primary prevention and control of adverse outcomes.³³

Using the health belief model, further exploration is important to identify the possible trigger that enforces adherence behaviour. The health belief model helps to have deep insight on the consequences of non-adherence to ART, the personal risk of problems about medication non-adherence, the value of adhering to ART drugs and the obstacles for not taking ART medication.

The limitation of this study was the measurement of adherence is based on PLHIV self-reports of missed doses which may be subject to social desirability and recall biases. Findings are also generalisable only for patients treated as outpatients; it excludes patients treated at the inpatient level. This condition may limit to conclude inpatient treated PLHIV/AIDS. Since the study was conducted during the COVID-19 pandemic, the actual magnitude of optimal adherence may not be similar to our finding. As this is a cross-sectional study, cause–effect relation could not be analysed. Despite these limitations, our study demonstrates strengths. One of the strengths was it was conducted using two standardised and sounded adherence measurement tools which helped in ensuring the quality of the study.

CONCLUSIONS

Stigma or discrimination, missing scheduled clinical visits, being on anti-TB treatment, recent CD4 cell count less than 500 cells/mm³ and patients in WHO clinical stage III at the time of ART initiation were factors associated with a low level of adherence to ART drugs. The establishment of a monitoring and evaluation system during clinical visits helps to achieve optimal adherence. Maintaining relatively high CD4 cell counts during HAART encourages patients on ART to have optimal adherence; again, this reduces disease severity. The intervention targeted to reduce discrimination, counselling before initiation of treatment and educational therapy during follow-up is advised to have maximum effect on improving ART adherence.

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Contributors SBZ conceived the research project, supervised the data collection process, conducts the analysis, write-up and review of literature. TMA collected the data, helped with the analysis of data and statistics. All authors agreed the final version to be published and are responsible for all aspects of the work.

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Patient consent for publication Not required.

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