

Assessment of Adherence to Antiretroviral Therapy among Adult People Living with HIV/AIDS in North East, Ethiopia

Almaz Mengistie^{1*}
Adugnaw Birhane¹
Esubalew Tesfahun²

¹Department of Public Health, Medicine and Health Science Institute, College of Health Science, Debre Berhan University, Ethiopia

²School of Public Health, College of Health Science, Addis Ababa University, Ethiopia

Abstract

Back ground: The scale-up of anti-retroviral treatment is among the greatest successes of the global Acquired Immunodeficiency Syndromes (AIDS) response to date and it is on a Fast-Track- approach. To contribute to the global and local target of HIV /AIDS response as well as to obtain full benefits of ART medication, strong adherence of $\geq 95\%$ to Anti-Retroviral Therapy (ART) is needed.

Methods: A cross-sectional study among 352 and 20 study participants for quantitative and for in-depth interview respectively. Data was collected using semi-structured questionnaire with a face-to-face interview for quantitative and interview guide for the in-depth interview. Bivariate and Multivariable logistic analysis was applied to examine the association between the dependent and independent variables. Additionally, thematic analysis, interpretation and triangulation of the finding were done for in-depth-interview.

Results: A total of 352 people living with HIV/AIDS were responded to the study with 90% response rate. Of the total 352 respondents 87.2 % were adherent and the overall adherence level was found to be 95%. The study revealed factors associated to adherence to ART were marital status(AOR:4.4;95%CI:1.3-14.7), use of memory aids (AOR:6.5;95%CI:2.6-16.2) Living condition (AOR: 2.9;95%CI: 1.1-7.6), Experienced side effect (AOR: 4.6;95%CI;1.9-11.3),drug regimen (AOR: 5.5; 95%CI: 1.4-22.3) and distance in km (AOR:2.7;95% CI; 1.11-6.4).

Conclusion: Patient counselling, health education and health system strengthening are very important for improvement of ART drug adherence.

Keywords: Adherence, Acquire, Immunodeficiency, Retroviral, Syndromes, Treatment.

Introduction

Adherence to an ARV treatment regimen involves taking all pills in the correctly prescribed doses, at the right time, and in the right way. To achieve the global and local target of HIV/AIDS response, strong adherence to Anti-Retroviral Therapy (ART) is needed to obtain full benefits of ART medication. The global Acquired Immunodeficiency Syndromes (AIDS) response to date and it is on a Fast-Track-Strategy scale-up of anti-retroviral treatment is among the greatest successes. Its goal is to achieve and sustain viral suppression. Even though its roll-out has led to a massive reduction in AIDS-related deaths, viral suppression rates are still too low to realize the prevention role of treatment. In some

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*Corresponding author: Almaz Mengistie, Department of Public Health, Medicine and Health Science Institute, College of Health Science, Debre Berhan University, P. O. Box: 445, Debre Berhan City, Ethiopia. Tel: +251 911386536; Email: [almazesub2121\(at\)gmail.com](mailto:almazesub2121(at)gmail.com)

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settings, the early initiation of ART may place demands on the health system that could increase the risk of drug resistance, drug stock-outs, insufficient patient preparation and suboptimal adherence [1-3].

Long-term adherence to treatment is critical for the success of ART and presents new challenges. Adherence to ART is a primary determinant of viral suppression and transmission risk, disease progression and death. In all regions suboptimal adherence is a major challenge, at all stages of HIV disease, and is associated with a diversity of patient- and program-related challenges. Study has suggested that when adherence rates are between 50% and 85%, drug resistance is more likely to develop [2-5].

The evidence in different countries and settings has shown that sub optimal level of adherence and non-adherence to ART are the most common reasons for treatment failure and call for additional assessment and intervention.

The reasons for poor health outcomes and increased health care costs may be as a result of poor adherence to long-term therapies. It severely compromises the effectiveness of treatment making this a critical issue in public health both from the perspective of quality of life and of health economics [6]. It is the most common cause of treatment failure. Due to cross-resistance, the virus can become resistant to an entire class of ARVs thereby rendering that class ineffective not just for the individual but also for the society. This can lead to change of treatment regimen to more expensive second-line drug [7-9]. Adherence is increasingly understood as a dynamic behaviour influenced by a matrix of interrelated factors that change over time and periodic assessment is recommended. Additionally, the rapid scale up and current early initiation of ART may be associated with an increase in HIV drug resistance in the population, if appropriate assessment and prevention measures are not taken. Because this early initiation leads people to start before they are ready, with adverse consequences for adherence and treatment outcomes. Because of these, evaluation of adherence was recommended in the literature in order to develop appropriate adherence interventions [2].

In order to implement appropriate intervention aimed to improve adherence, the discovery of factors for non-adherence to ART could help guide new public health policies and aid in developing more effective prevention strategies. In spite of the high non-adherence rate, there is very little information on the factors for these non-adherences. Thus, this study was conducted with an aim to assess the recent level of adherence to ART and investigate determinant factors. This study was conducted with an aim to assess the recent level of adherence to ART and investigate factors associated with adherence to ART medication using mixed method approach. Therefore, the result of this research project will have a paramount importance for the improvement of ART drug adherence intervention.

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Methods

Study area and period

The study was conducted from February to April, 2018 at ART units in Debre Berhan Kebele Health Centre and Debre Berhan Referral Hospital. These two health institutions are the only public health facilities in the town currently giving ART service. According to the data from the two health facilities, there were a total of 2,644 adult patients actively following ART therapy in both health facilities (1,864 at the hospital and 780 at the health centre).

Study design and data collection

An institutional based cross-sectional quantitative study supported by qualitative approach was conducted. The data was collected using a standardized semi-structured questionnaire adopted from the World Health Organization (WHO) by directly interviewing study participants and gathering relevant information from their records. In addition, unstructured one-on-one in-depth interviews using interview guide were conducted at the study facilities with ART patients and healthcare workers and case managers administering ART services. The method used to measure adherence level was patient self-report on the number of doses skipped or missed on the past four days recall. The sample sizes for this study are 276 and 115 from the hospital and health centre respectively.

Analysis

Self-reported adherence was classified as being "adherent" when not even a single dose is missed corresponds to dose adherence. If the patient admitted having missed at least one dose corresponds to non-adherence. Adherence measurement of 95% or more is classified as adherent and less than 95% is classified as having non-adherence.

Therefore, self-report of four-day recall adherence rates measured as proportion using the formula:

$$\text{Adherence rate} = \frac{\text{Number of pills (doses) taken}}{\text{(doses prescribed or supposed to be taken)} \times 100} \text{ for each respondents.}$$

Descriptive statistics such as percentages, means, and standard deviations were calculated to describe and the data was also summarized in tables and graphs. To examine the relationship between levels of adherence and the independent variables, the bivariate and multivariable logistic regression analysis was carried out. The outcome ART adherence variable is dichotomized and defined as 0= none adherents to ART: 1= adherents to ART. Each independent variable was tested with the adherence status for the association. Thematic analysis was used for qualitative data. Interpreted and triangulation of the finding with quantitative finding was done and presented in text.

Results

Socio demographic characteristics

A total of 352 adult patients living with HIV/AIDS on first line ART were included in the study with the response rate of 90%. More than two third 249 (70.7%) of the respondents were females and the mean age of the respondents was 36.9 ± 10.6 years.

Information regarding psycho social conditions

When the respondents asked about their living condition 242(68.8%) of them were living with their families (spouse or children). Regarding their disclosure status, 307(87.2%) were disclosed their sero status to their families, but only 134(38.1%) of the total respondents were disclosed their HIV status to the communities. About half 85(52.6%) of respondents reported they have discomfort of taking medication in front of others.

Information regarding the clinical condition of the patient

About half of the patients 166(51%) had base line CD4 count less than 200 but; 210 (68%) of the participants had current CD4 count greater than 350. The initial WHO clinical

stage was stage III for 131(37.3%) patients and the current WHO stage, for more than three fourth 336(95.5%) of the respondents one was T1 (Table 1).

Drug related

Of respondents on medication 194(55%) were taking one pill of ART once daily and the rest were taking twice during the study period. About 273 (77.9%) of them reported that the schedule was convenient and easy to fit to their daily routine, but the rests found it was inconvenient and difficult to fit to their daily routine (Table, 2).

ART adherence level and reasons for missing their treatment

Regarding the adherence assessment to ARV therapy using missed dose self-report medication adherence

Table 1: The clinical condition and clinical marker of respondents in Debre Berhan Health Centre and Debrebrahan Referral Hospital, North East Ethiopia, 2018.

Variables	N (%)	Variables	N (%)
Duration of infection	(n=352)	Current CD4 count	(n=310)
37+month	272(77.3)	<200	35(11.3)
25-36month	23(6.5)	200-350	65(21)
13-24month	31(8.8)	>350	210 (67.7)
6-12months	26(7.4)	Initial WHO stage	(n=351)
How health described	(n=352)	Stage I	124(35.3)
Better	268(76.1)	Stage II	91(25.9)
Same	73(20.7)	Stage III	131(37.30)
Worse	11(3.1)	Stage IV	5(1.4)
Initial viral load	(n=13)	Current WHO clinical stage	(n=352)
<1000	1(7.7)	Stage T1	336(95.5)
>1000	12(92.3)	Stage T2	10(2.8)
Current viral load	(n=243)	Stage T3	6(1.7)
<1000	217(89.3)		
>1000	26(10.7)		
Initial CD4	(n=327)		
<200	166(50.8)		
200--350	92(28.1)		
>350	69(21.1)		

Table 2: Drug related information of respondents in Debrebrahan Health Centre and Debrebrahan Referral Hospital, North East Ethiopia, 2018.

Variables	N (%)	Variables	N (%)
ART drug regimen	(n=352)	Experience the side effects of ART	(n=352)
AZT-3TC-NVP	79(22.4)	Yes	96(27.3)
AZT-3TC-EFV	33(9.4)	No	256(72.70)
TDF-3TC-NVP	46(13.1)	Symptoms experienced	(n=96)
2. TDF-3TC-EFV	194(55.1)	Nausea & vomiting	11(11.5)
Number of pills used each time	(n=352)	Skin rash	8(8.3)
One	273(77.6)	Pain and numbness	5(5.2)
two	0	Head ache	43(44.8)
one or two	79(22.4)	Fatigue	8(8.3)
Frequency used per day	(n=352)	Depression	4(4.2)
Once	194(55.1)	Abdominal pain	10(10.4)
Twice	158(44.9)	Others	7(6.2)
Duration on art in months	(n=352)	Schedule fitting daily life	(n=352)
6-12 months	51(14.5)	Yes	273(77.6)
13-24months	33(9.4)	No	79(22.4)
23-36months	53(15.1)	Special instructions given?	(n=352)
>37+months	215(61.1)	Yes	344(97.7)
Adherence to the given adherence instructions	(n=344)	No	8(2.3)
Yes	336(97.7)		
No	8(2.3)		

Table 3: Bivariate and multivariate analysis of adherence and socio demographic variables of respondents in Debrebrahan Health Centre and Debrebrahan Referral Hospital, North East Ethiopia, 2018.

Variable	Non adherent	Adherent	COR(95%CI)	AOR(95%CI)
Age	36(12.7%)	247(87.3%)	1(0.47- 2.25)	
<45years	9(13%)	60(87%)	Ref	
>45years				
Residence of participant				
Urban	29(9.8%)	266(90.1%)	3.6(1.8-7.2)*	1.8(0.717-4.6)
Rural	16(28.1%)	41(71.9%)	3.6(1.8-7.2)*	
Marital status				
Married	16(8.9%)	163(91.1%)	3.2(1.4-7.5)*	3.2(1.06-9.9)*
Divorced	8(10.8%)	66(89.2%)	2.6(0.96-7.04)	3.6(0.923-14.1)
Widowed	6(13.3%)	39(86.7%)	2(0.68-6.10)	1.6(0.33-7.44)
Separate	4(50. %)	4(50%)	0.3(0.07-1.47)	1.1(0.089-13.1)
Single	11(23.9%)	35(76.1%)	Ref	
Occupational status				
House Servant	1 (20%)	4(80%)	0.44(0.36-4.7)	3.6(0.154-84.6)
Daily Laborer	14(11.6%)	107(88.4%)	0.8(0.51-8.3)	2.1(0.51-8.3)
Students	5(41.7%)	7(58.3%)	0.16(0.04-0.65)*	0.22(0.024-2)
Farmer	9(15%)	51(85%)	0.6(0.209-1.9)	8.8(0.905-86.3)
House wife	4(13.3%)	26(86.7%)	0.7(0.187-2.8)	1(0.14-7.4)
Merchant	6(9.4%)	58(58%)	0.7(0.187-2.8)	1.7(0.36-8.11)
Govt employee	6(10%)	54(90%)	Ref	
Educational status				
Educated	20(9.7%)	186(90.3%)	1.9(1.02-3.6)*	
Not educated	25(17.1%)	121(82.9%)	Ref	

measurement, 307(87.2%) of all participants interviewed were adherent to the dose, and the rests 45(12.8%) were missed at least one dose in the last four days prior to the survey. The overall mean adherent level was 95%±14 in this study area. Of non-adherents, 37(82.2%) of the study participant missed two doses (Table 3). The primary reasons reported by participants for treatment non-adherence were 15(33.3%) due to simply forgotten, 12(26.7%) being away from home, being busy 7(15.6%).

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Findings from in-depth interview also indicated that forgetfulness was mentioned by participants as barrier to adherence.

During the in-depth interview some patients forget their appointment dates and the dose of medication when they go to holy water and think of other spiritual and religious practice.

Factors associated with medication adherence

The association of factors to medication adherence is reported in the tables (Table 3). Variables like age, gender, monthly income, active substance use, WHO clinical staging, CD4 count drug regimen and others variables were not associated with medication adherence.

Patients whose current viral load <1000 copies/μL were 11 times more (COR:10.9; CI: 4.5-26.6; P<0.0001), those who had side effects of ART drug 0.2 times less (COR: 0.193; CI: 0.01-0.37; P<0.0001) likely were adherence to ART than their counter parts using bivariate analysis.

The association of health system related factor also indicated patients who came from nearby places (<5km or less) were 2.5 times more (COR: 2.5; CI: 1.3-5; P=0.006) in bivariate analysis.

Selective variables were entered simultaneously into multivariate logistic regression to identify the most independent predictor variables of ART adherence.

Accordingly, the result showed that, married patients on ART were 3 times more (AOR: 3.2; CI: 1.06-9.9; P=0.039) adherent than singles (Table 3).

Similarly, the in-depth interview indicated that, married people and patients who use memory aids were adherent due to the support and encouragement given from the spouse and family members as reported below.

"I never miss my medication because I use mobile alarm as a reminder. In addition to that, even though my husband's sero status is negative, he supports and encourages me to stick to my medication schedule." (A 28 years old house wife female Patient from the Hospital).

Responses from the in-depth interviews with patients however indicated different findings. Some of them indicated that, alcohol consumption and being busy with social events were the reasons of forgetfulness to take their medication properly and influence adherence.

According to the in-depth interview of patient from the Hospital other patient related factors like, staying healthy and the desire to live longer motivate some people on ART to adhere to their treatment.

Example A 45 year old male government employee said:-

"I want to stay healthy for my kids. I want to see them grow up, graduate from university and start their own family. That is why I take my medication properly. The medication has done wonders in improving my health and even if people heard that I am infected, they would not believe it. Since I look healthy and strong, people do not treat me any differently than uninfected people." (Male participant from hospital).

Discussion

In this study we tried to assess the level of adherence and factors associated with HAART adherence in Debre Berhan Health Centre and Debre Berhan Referral Hospital, from February to April 2018.

Of the total respondents 87.2% of individuals has adherence level of $> 95\%$ to their ART drugs while 12.7% of them were non-adherent ($<95\%$) and this finding is consistent with (61.8%,62.8%,75.4%,74.2%,63.8%,83.1%,86%,95.5%) studies done in Tawan Mai, an outpatient clinic, Taksin Hospital, Bangkok in Thailand, in Keffi, Nigeria, in Ibadan, Nigeria, Yirgalem hospital, Jimma University, in Bale Robe and Ambo [10-16]. However it is lower than the finding (97.9%, 90%) of study conducted in South Eastern Nigeria, and Lagos Islan Nigeria [17,18]. And higher than (62.3%, 69%, 43.2%, 48.2%, 86%, 85.3%) Review study done in Africa 2014, studies done in Thailand (2010), Eldorate Kenya, Emu Kenya, Ghana and South Gondar $\geq 95\%$ adherence rate respectively [18-24]. This variation observed in different location may have different reasons, for example, It could be related to the heterogeneity in measurement methods since there is no consensus exists about the gold standard measurement of adherence

Regarding psychosocial findings using bivariate analysis this study found that patients who disclosed their sero status to the family and community were 4.6 times higher likely adhered than not. On the other hand, patients who felt discomfort of taking medication in front of others were 0.5 times less likely to adhere than their counter parts in bivariate analysis. This finding is in line with the study conducted in Nigeria kefi, Ambo, Emmu Kenya and Bale Robe [11,15,16,22].

In bivariate logistic regression analysis disclosure of HIV status to the family member shown 3.5 times more adherent than their counter parts similar other finding in which Respondent who disclosed their sero status to at least one person were 3.5 times more likely to be HAART adherent than those respondent who did not disclose their sero status [16]. This is the same as finding in qualitative study. However, in the multivariate analysis no association was found which is similar with study in Mekele [25].

Using bivariate analysis and from in-depth interview Patients who got family support were more likely adhered than their counterparts which is consistent with studies in Diredawa and Harer [26]. In this study the individuals who had support from the family was found to be 3.2 times likely to adhere in bivariate analysis. Similarly, findings in, Bale Robe, Gana, Jimma, North west Ethiopia and Diredawa also are in agreement with our finding [14,15,24,26]. But in current study support was not significantly associated

with adherence in the multivariate analysis and similar with study in Yirgalem, Bale robe, Gana and Diredawa [15,23,26,27]. This disappearance might be due to the effect of confounders.

This study also found that, patients who use memory aids like mobile, watch or other means of reminders were 6 times more likely to adherent than those who did not in bivariate and multivariate analysis but the odd of adherent in multivariate was decreased to 5. Our finding is not consistent with the finding from Nigeria which has shown the use of memory aids was not associated with medication adherence [11]. But it was in agreement with the study that revealed the use of reminder tools are factors that influence adherence to ART and with current in-depth interview [28].

In this study current study there was association of current viral load with adherence, but no association was found between adherence and duration of infection, WHO clinical stage, base line CD4, current CD4 and baseline viral load. In contrary to this, baseline CD4 count of <350 cells/ml were significantly associated predictors of ART adherence as shown in Oromia [29]. Longer time between HIV infection and AIDS had an important problem within the first six months of HAART adherence [30].

Generally, in the current study we identified that memory aids, marital status, side effect of medication and frequency of adherence to instruction were the main predictors of adherent to medication.

Conclusion

Adherence level and certain important factors affecting adherence of patients have been explored and identified in this study.

The level of adherence to ART was relatively higher when compared to other studies done in Ethiopia and other developing countries but it is below the recommended level ($\geq 95\%$) and multiple determinants of adherence were identified which needs to be addressed. The most frequently reported reason for non-adherence were forgetting, went away from home, being busy with other things and do not want others to notice. The use of memory aids and being marred were found to be independent positive predictors for drug adherence whereas medication side effect and adherence instruction were the negative predictors for medication adherence. Additionally, ART dug stock out, long waiting time, use of alternative and traditional medicines, desire to live longer and fear of stigma and discrimination, were the findings reported as barriers to adherence

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Authors' Contribution

All authors involved in preparing the proposal, analyses of the results and writing the final manuscript.

Availability of Data and Material

The data set used for this study are available from the corresponding author at reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Ethics Approval and Consent to Participate

Written consent was obtained from the Debre Berhan University (DBU) Health Science College and Debre Berhan town city admiration. Verbal consent obtained from each respondent. The confidentiality of the respondent respected throughout the procedures.

Acronyms and List of Abbreviations

3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
D4T	Stavudine
DOT	Directly Observed Treatment
EFV	Efavirenz
LPV/r	Lopinavir/Ritonavir
MEMS	Medication Event Monitoring System
NNRTI Inhibitor	Non-Nucleoside Reverse-Transcriptase Inhibitor
NRTIs Inhibitors	Nucleoside Reverse Transcriptase Inhibitors
NVP	Neverapine
PI	Protease Inhibitors
PIT	Pill Identification Test
TDF	Tenofovir Disproxil Fumarate
TDM	Therapeutic Drug Monitoring
VAS	Visual Analogue Scale
ZDV	Zidovudine

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