Original Research

Rate and Predictors of Adherence to Antiretroviral Therapy among Clients on Antiretroviral Therapy at Tepi Health Center, South-west Ethiopia

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Abstract	Article Information
Highly Active Antiretroviral Therapy (HAART) has resulted reduction of mortality and improved quality of life of peoples living with HIV/AIDS. Maximum benefits can only be achieved through maximum adherence. We designed this study to assess rate and predictors of adherence to antiretroviral therapy at Tepi health center. A facility based cross-sectional study was conducted through patient's self report using structured pre-tested questionnaires and medical record of the clients in a total of 341 samples using systematic random sampling technique. The data were collected from January1, 2012 to February15, 2012 in Tepi health centre. The data was analyzed using SPSS version 16. Multiple logistic regression model was constructed to determine predictors of adherence. Self-reported dose adherence in the study area was 78.6% and that of combined indicator was 43.4%. Positive predictors of adherence includes alcohol drinking (AOR=4.36, 95% CI =2.03, 9.35), and a belief of ART cures HIV (AOR = 1.95, 95% CI = 1.21, 3.13) while long-duration on HAART (≥49 months) (AOR=0.29, 95%CI=0.11, 0.75) was negative predictor. The adherence rate in this study was much less than studies in many parts of Ethiopia. Interventions should target on reduction of alcohol use and on imparting appropriate knowledge of HAART that will address false beliefs of "ART cures HIV".	
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INTRODUCTION

Highly active antiretroviral therapy (HAART) is a breakthrough and celebrated in the reduction of mortality and in the improvement of quality of life of PLWHA. Since the introduction of HAART in 1995, important reduction in HIV progression to both AIDS and death is observed (Cooke, Lee *et al.* 2014; Dewing, Mathews *et al.*, 2014). Antiretroviral therapy (ART) is designed to suppress viral replication and thus reduce the likelihood of development of drug resistant viral strain and also prevents further viral destruction of the cellular immune system (Edison Hughes *et al.*, 2014).

Adherence to HAART is one of potentially alterable factors determining outcomes for patients with HIV (Lee Rand *et al.*, 2014). However non-adherence to HAART is common in all groups of treated individuals (Tiyou Belachew *et al.*, 2010; Maqutu Zewotir *et al.*, 2011; Mirkuzie Hinderaker *et al.*, 2011; Kebede and Wabe, 2012; Mengistu and Chere, 2012; Biressaw Abegaz *et al.*, 2013; Arage Tessema *et al.*, 2014; Mulu Liebert *et al.*, 2014).To achieve goal of HAART maximal and durable viral suppression and successful HIV therapy requires adherence of ≥ 95% (Hassan, Nabwera *et al.*, 2014). Failure rates increase sharply as adherence decrease (Edison Hughes *et al.*, 2014).

Literature survey shows that, there are no studies conducted at health center level in Ethiopia where as a large segment of population is treated at health center. This study was therefore designed to determine the adherence rate and determinates of adherence to HAART among clients on ART in Tepi health center.

MATERIALS AND METHODS

Study Area and Design

Data was collected from January 1, 2012 to February 15, 2012 in Tepi health centre. Tepi health centre is located in Tepi town Sheka zone, SNNPR. Tepi town is 565 kilometers away from Addis Ababa (capital of Ethiopia) ART had been commenced in Tepi health center in 2005.

A facility based cross-sectional observational study was conducted through patient's self report using structured questionnaires and medical record of the clients. The study population was all PLWHA on HAART for at least three months and following their treatment follow-up from January 1, 2012 to February 15, 2012. Clients on treatment for less than 3 months, under the age of 18 years and with severe acute illness were excluded from the study.

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Sample Size and Sampling Technique

A sample size was calculated using a similar study from Jimma University Specialized Hospital which has a combined self reported adherence rate of 72.4 9. Single population proportion formula with 95% confidence interval was used and the sample size was calculated to be 341. The sampled population was selected using simple random sampling technique.

Data Collection Tool

Data were collected on structured pre-tested questionnaire by interviewing clients and transferring clinical information such as CD4 cells, WHO Stage, duration on treatment and regimen from medical records. The questionnaire was adapted from studies from other Ethiopian studies (Tadios and Davey, 2006; Amberbir Woldemichael et al., 2008; Tiyou and Belachew et al., 2010; Emiru and Wakgari, 2014). The questionnaire was developed in English and translated to Amharic. The clients were interviewed for variables. Data collection was conducted at ART clinic of Tepi health center by trained health professionals. The questionnaire was pre-tested on 5% of study population and the data was not included in actual study.

Adherence status is a dependent variable while independent variables includes Socio-demographic and economic characteristics (age, sex, ethnic group, residence, distance from service facility, religion, education, employment, marital status, monthly income and having cell/public phone), clinical characteristics of the disease (WHO staging, CD4 count), duration on treatment and regimen type. Disclosure status, psychosocial support and substance and alcohol use, adherence to treatment information, attitudinal factors contributing for non-adherence was also assessed.

Data Quality and Analysis

The data was collected using structured pre-tested questionnaire under control of the investigator through trained data collectors five clinical nurses and a senior nurse supervising them. The completeness and logical consistency of the data was checked and corrected at the spot during data collection.

The collected data was edited, cleaned, coded and entered into Epi Info version 7 and then exported to SPSS version 16 for analysis. Finally data was summarized using descriptive statistics to assess basic client characteristics such as socio-demographic status and for the calculation of adherence rate. Predictors of adherence were determined using logistic regression. In bivariate analysis each independent variable was tested for the presence of association with the dependent variable. After bivariate analysis, final multivariate analysis was conducted.

Self reported dose adherence to all antiretroviral agents could be summarized as the ratio of the average daily number of antiretroviral medications adhered to total number of antiretroviral medication prescribed (Tadios and Davey, 2006). These can be written in the following way:

Adherence rate =
$$= \frac{(\text{Number of doses prescribed-Number of doses missed})}{\text{Number of doses prescribed}} \times 100$$

Ethical Consideration

The study proposal was approved by institutional ethical review committee of Hawassa University and Addis Continental Institute of Public Health. Permission obtained from Sheka zone health department and Tepi town administration health office to conduct the study. Informed consent obtained from every respondent before proceeding to the interview and the information is kept confidential.

RESULT

Socio-demographic and Economic Characteristics

A total of 341 study subjects were included in this study. The majority of the study participants were between the age group of 25-34 about 146 (42.8%) with mean (SD) of 35±9.6 and a range of 50. The rural population comprise 211 (61.9%) of the study participants. 175 (51.3%) of the study participants have less than 1km distance from the health service facility. 209 (61.3%) of the study subjects were Orthodox Christian, while the 14.7% Protestant and 24.0% Muslim. The whole socio-demographic data of the study participants were summarized in table 1.

Table 1: Socio-demographic & Economic characteristics of ART clients in Tepi HC, (n=341), Tepi 2012

Variable	Number	Percent (%)
Age		
18-24	28	8.2
25-34	146	42.8
35-44	111	32.6
45+	56	16.4
Sex		
Male	151	44.3
Female	190	55.7
Residence		
Urban	130	38.1
Rural	211	61.9
Distance		
<1Km	175	51.3
1-5Km	44	12.9
6-10Km	62	18.2
>10Km	60	17.6
Educational level		
No formal education	96	28.2
1-8	189	55.4
9-12	37	10.9
12+	19	5.6
Marital status		
Single	42	12.3
Married	161	47.2
Divorced	86	25.2
Widowed	47	13.8
Cohabitating	5	1.5
Employment		
Employed	42	12.3
Unemployed	299	87.7
Monthly Income		
No source	35	10.3
<400	189	55.4
401 – 1000	81	23.8
1001 – 2000	30	8.8
>2000	6	1.8
Cell/public phone		
Yes	182	53.4
No	159	46.6

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216(63.3%) of the study participants believe taking ART reminds their HIV sero-status and 53(15.5%) believe that taking ART continuously could harm them. About half of the study participants 51.3% believe "ART cures HIV/AIDS".

Majority 269(78.9%) of the study subjects were in WHO stage III during initiation while 2(0.6%) were on asymptomatic stage (stage I). Baseline CD4 cell count <200cells/m^3 contributes for 137(40.2%) and a CD4 range 350–500 cells/m^3 about 16(4.7%), nearly 30% of the clients have no recorded baseline CD4 count. More than half 188(55.1%) of clients has no recorded recent CD4 count either because of failure to record or were not totally measured. 60(17.6%) clients have a range of CD4 cell 200-350 cells/m^3. 91(26.7%) have been on HAART for 3-12 months, while 45(13.2%) for more than 49 months. Predominantly, 113(33.1%) of study participants were on regimen containing D4T+3TC+NVP, whereas 19(5.6%) were on TDF+ 3TC+NVP.

Rate of Adherence and Reasons for Non-adherence

Missed doses were assessed for "the day before", "past three days" (three days recall) and "past seven days" (seven days recall). 11.7% of clients missed at least a single dose of drug the day before, 17.9% missed at least a dose in three days recall, while 22.3 missed at least a dose in seven days recall as shown in table 2.

Table3 summarizes that 268(78.6%) of the participants were dose adherent, while 207(60.7%) were time/schedule adherent and 221(70.8%) were food adherent (follow the food restriction). The overall adherence (dose, time and food) calculated by using participants who were adherent in all (dose, time/schedule and food) was 148(43.4%).

Forgetting and being away from home are the major reasons for dose non-adherence as indicated in figure 1.

Table 2: No. of Clients missed at least a tablet by self-report in Tepi HC (n = 341)

No. of days	Number	Percent (%)
The day before		
Yes	40	11.7
No	301	88.3
Past three days		
Yes	61	17.9
No	280	82.1
Past seven days		
Yes	76	22.3
No	265	77.7

Table 3: Self reported (dose, time, food and overall) adherence among ART clients in Tepi health center (n=341), Tepi 2012.

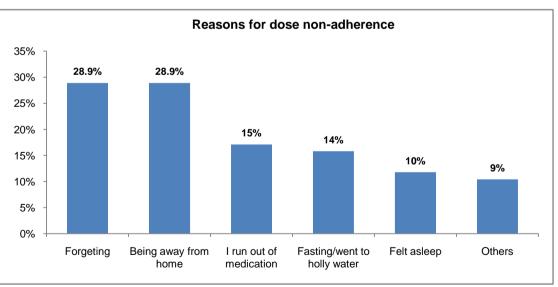| Variables	Number	Percent (%)
Self reported 7-day recall dose adherence		
Adherent	268	78.6
Non-Adherent	73	21.4
Time(schedule) adherence		
Adherent	207	60.7
Non-Adherent	134	39.3
Is there food restriction in your regimen?		
No	312	91.5
Yes	29	8.5
Food adherence (following restrictions)		
Adherent	221	70.8
Non-Adherent	91	29.2
Over all adherence (dose, time and food)		
Adherent	148	43.4
Non-Adherent	193	56.6

Figure 1: Reasons for dose non-adherence

Predictors of Adherence

In bivarate analysis each independent variables were tested with the overall adherence for association. Variables such as family support, alcohol use and a belief that "ART cures HIV/AIDS" were found to be significantly associated with the adherence. Family support was likely to increase adherence by odds of 1.8 times (COR=1.8, 95% CI=1.07, 3.01). Not using alcohol was likely to increase adherence by odds of 3.7 times (COR=3.69, 95% CI=1.83, 7.41). Not having belief of "ART cures HIV/AIDS" was likely to increase adherence by odds of 1.7 times (COR=1.69, CI=1.10, 2.61).

Table 4: Predictors of ART adherence in Tepi health center (n=341)

Variable	Adherent No. (%)	Non-adherent No. (%)	COR(95%CI)	AOR(95% CI)
Age				
18-24	61(41.8)	85(58.2)	1.78(0.713, 4.457)	1.37(0.49, 3.79)
25-34	50(45.0)	61(55.0)	1.11(0.591, 2.081)	0.83(0.41, 1.69)
35-44	22(39.3)	34(60.7)	1.27(0.659, 2.436)	1.04(0.50, 2.16)
44[+]	15(53.6)	13(46.4)	1.00	1.00
Disclosure status				
Yes	136(44.7)	168(55.3)	1.69(0.82, 3.48)	0.94(0.36, 2.46)
No	12(32.4)	25(67.6)	1.00	1.00
Family support				
Yes	28(32.9)	57(67.1)	**1.80(1.07, 3.01)**	1.92(0.96, 3.83)
No	120(46.9)	136(53.1)	1.00	1.00
Alcohol use				
Yes	11(20.0)	44(80.0)	1.00	1.00
No	137(47.9)	149(52.1)	**3.69(1.83, 7.41)**	**4.36(2.03, 9.35)**
"ART cure HIV"				
Yes	65(37.1)	110(82.9)	1.00	1.00
No	83(50.0)	83(50.0)	**1.69(1.10, 2.61)**	**1.95(1.21, 3.13)**
WHO stage				
Stage 1	1(50.0)	1(50.0)	1.00	1.00
Stage 2	19(32.2)	40(67.8)	0.46(0.03, 8.01)	0.45(0.23, 8.71)
Stage 3	122(45.4)	147(54.6)	0.83(0.51, 13.41)	0.98(0.05, 18.0)
Stage 4	6(54.5)	5(45.5)	1.20(0.59, 24.47)	1.85(0.08, 45.0)
Recent CD$_4$ C.				
No Data	70(37.2)	118(62.8)	0.70(0.29, 1.65)	0.49(0.19, 1.32)
>500 cells/mm^3	20(58.8)	14(41.2)	1.69(0.59, 4.65)	1.76(0.49, 6.23)
350- 500 "	18(51.4)	17(48.6)	1.25(0.44, 3.55)	0.85(0.26, 2.80)
200- 350 "	29(48.3)	31(51.7)	1.11(0.43, 2.86)	0.78(0.27, 2.27)
<200 "	11(45.8)	13(54.2)	1.00	1.00
Duration on HAART				
3-12 mo.	46(50.5)	45(49.5)	1.00	1.00
13-24mo.	34(44.2)	43(55.8)	0.77(0.42, 1.42)	0.90(0.45, 1.82)
25-36mo.	28(41.2)	40(58.8)	0.69(0.36, 1.29)	0.53(0.25, 1.13)
37-48mo.	23(38.3)	37(61.7)	0.61(0.31, 1.18)	0.58(0.26, 1.29)
49mo.	17(37.8)	28(62.2)	0.59(0.29, 1.23)	**0.29(0.11, 0.75)**
Regimen				
TDF+3TC+NVP	12(63.2)	7(36.8)	1.00	1.00
TDF+3TC+EFV	25(41.0)	36(59.0)	0.41(0.14, 1.17)	0.44(0.14, 1.33)
AZT+3TC+NVP	32(50.8)	31(49.2)	0.60(0.21, 1.73)	0.69(0.22, 2.19)
AZT+3TC+EFV	12(41.4)	17(58.6)	0.41(0.13, 1.35)	0.45(0.12, 1.66)
D4T+3TC+NVP	45(39.8)	68(60.2)	0.39(0.14, 1.11)	0.58(0.19, 1.77)
D4T+3TC+EFV	22(39.3)	34(60.7)	0.38(0.13, 1.11)	0.45(0.14, 1.44)

Multivariate Analysis Result of Combined (Dose, Time and Food) Adherence

Variables which were associated with the dependent variable *P*<0.25 and others that had been significant in the previous other studies were included in the model. All variables which were significant in bivariate analysis were also significant in multivariate model except family support. Duration on HAART was significant predictor in multivariate model. Not using alcohol was likely to increase adherence by odds of 4.36 (AOR= 4.36, 95% CI =2.03, 9.35), not having belief of "ART cures from HIV/AIDS" was likely to increase adherence by odds of 2 (AOR = 1.95, 95% CI = 1.21, 3.13) and long-duration on HAART (≥49 months) decrease the odds of adherence by 70% (AOR=0.29, 95%CI=0.11, 0.75).

DISCUSSION

The adherence status of clients to ART was assessed using patient self-report in this study; due to its simplicity, relatively inexpensive, and easy to implement in the patient's follow-up. It can also provide information about the reasons why a patient did or did not take the medication properly. This type of adherence measurement was used in many studies in Ethiopia independently without other supplementary methods (Tadios and Davey, 2006; Amberbir Woldemichael *et al.*, 2008). This method has been shown to overestimate adherence both in the HIV setting and non-HIV setting and non-consistent results were found when compared to more objective measures (Michel Lionel *et al.*, 2001). Self-reported non-adherence is suggestive of worse virologic control (Miller and Hays, 2000; Michel Lionel *et al.*, 2001).

The adherence rate in this study was also presented using a combined (dose, time and food). Some studies use only dose adherence as a measurement 13, 14. Best adherence measurement has to assess whether or not dose is skipped, maintaining the scheduled time and food or dietary instructions agreed with the health provider to get the overall adherence rate. Recent studies prefer to use the combined measurement (Amberbir Woldemichael *et al.*, 2008; Tiyou Belachew *et al.*, 2010).

In this study the dose and food adherence were higher than the time adherence; unlike a study by Amberbir, Woldemichael *et al.* (2008). The rate of dose adherence in the study area was 78.6%; which was lower than reported in Southwest Ethiopia (Deribe Hailekiros *et al.*, 2008; Tiyou Belachew *et al.*, 2010) and nearer to studies from Northwest Ethiopia (Tessema Biadglegne *et al.*, 2010).

The overall rate of self reported adherence in this study area based on the combined indicators of the three adherence rates; dose, time and food was 43.4%. There are few studies in Ethiopia used the three adherence errors (dose, time and food) to obtain the combined adherence rates (Amberbir Woldemichael *et al.*, 2008; Markos Worku *et al.*, 2008 and Tiyou Belachew *et al.*, 2010). The overall adherence rate found in this study was much lesser than studies conducted in several parts of Ethiopia, which ranges from 72.4 to 79.3 (Amberbir Woldemichael *et al.*, 2008; Tiyou Belachew *et al.*, 2010). This may be partly attributed lowest level of the health facility in which the service is rendered. Health center in Ethiopian health care system is operated by low level health professional.

Alcohol non-users were 4 times more likely to adhere than alcohol users (AOR=4.36, 95% CI = 2.03, 9.35). Alcohol use was significant predictor of non- adherence in many other studies. A prospective study conducted in USA revealed dose adherence rate for alcohol drinkers and non-drinkers were 66% and 74% respectively and adherence decreased by 8% among drinkers (Gardner Hullsiek *et al.*, 2010). Alcohol use was a negative predictor of adherence in study conducted in south-west Ethiopia (Tessema Biadglegne *et al.*, 2010). Alcohol use negative association with adherence is mostly referred to impaired judgment and forgetfulness.

Unlike to this finding, alcohol and substance use were not a significant negative predictor for adherence in cross sectional studies in Ethiopia (Amberbir Woldemichael *et al.*, 2008; Markos Worku *et al.*, 2008; Tiyou Belachew *et al.*, 2010). This inconsistent finding may be partly attributed to missing the target groups (alcohol users) among study subjects.

Believing "ART cures HIV/AIDS" decreases the odds of adherence 2 (AOR=1.95, 95% CI, 1.21, 3.13). The false belief may encourage the patients cease taking medication after improved quality of life. A study conducted in a general population in Kisumu, Kenya a belief of "ART cures HIV/AIDS" were associated with an increased HIV sero-prevalence (Talam Gatongi *et al.*, 2009). However we have not found studies used this variable to show its association with adherence in ART users.

Duration on HAART is another significant predictor observed in this study, duration greater than or equal to 49 months on treatment reduce the adherence by the odds of 70% (OR=0.29, 95% CI=0.11, 0.75). As duration on treatment prolongs quality of life improve, clients' attention will be diverted to their daily routines than dosing their medication. Many studies reveal interest or motivation to adhere to medication will decrease when they have no symptom (Mathes Pieper *et al.*, 2013; Nelsen Gupta *et al.*, 2013; Rai Mahapatra *et al.*, 2013). A study conducted in south-west Ethiopia, clients on WHO stage I are less likely to adhere to their treatment than

advanced stages (COR=0.26, 95% CI= 0.07, 0.960) (Tiyou Belachew *et al.*, 2010). Having good quality of life is therefore associated with impaired adherence because of the false perception of complete cure. TB co-infection and its treatment have negative impact on adherence to antiretroviral therapy (Eyasu Mengistu *et al.*, 2012). How such condition was not considered in this study.

Social support may enhance adherence through encouragement, reassurance, reinforcement, systematic cues, bolstering of competence, and motivation, or by masking the effect of stress, anxiety, and depression (Tadios and Davey, 2006; Eyasu Mengistu *et al.*, 2012). Family support was associated with adherence in the bivariate model of this study (COR=1.80, 95% CI = 1.07, 3.01). However there was no significant association with adherence in the multivariate model. This might be due to the effect of confounders and smaller sample size. Other studies conducted in Ethiopia witnessed clients with family support were more likely to adhere than those who didn't get family support (Amberbir Woldemichael *et al.*, 2008; Tiyou Belachew *et al.*, 2010).

CONCLUSIONS

Overall adherence rate in this study is lower than many other studies conducted in Ethiopia. Alcohol use, a longer duration on treatment and false belief "ART cures HIV" were negative predictors of adherence while social support was positive predictor in this study. Proper and uninterrupted counseling during initiation of therapy and follow-up visits are highly needed. Interventions should target on reduction of alcohol use and on imparting appropriate knowledge of ART that will address false beliefs of "ART cures HIV".

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