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Factors Affecting Levels of Antiretroviral Drug Adherence among Adult Patient Living with HIV in Public Health Facilities of Arba Minch Town, Southern Ethiopia: Using Cumulative Logit Model

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Authors' contributions

This work was carried out in collaboration among all authors. Authors SHH and KTG conceived and designed the study, developed data collection instruments and supervised data collection. They participated in the testing and finalization of the data collection instruments and coordinated the study progress. Authors SHH, KTG and MAE performed the statistical analysis and wrote all versions of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Adherence to antiretroviral therapy is essential to reduce the multiplication of the virus and improve disease outcomes. The studies have reported a range of factors influencing antiretroviral therapy adherence at various levels. Almost all studies were modeling the factors based on binary categorization of the adherence.
Objective: This study intended to determine the adherence level and its associated factors to antiretroviral therapy among adult people living with human immunodeficiency virus.

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Methods: This study was a cross-sectional study that employed among 391 adult patients that were selected by simple random sampling. The cumulative Logit model was used to examine the associations between the outcome of antiretroviral therapy adherence and independent variables.
Results: The study participants with good level of antiretroviral therapy adherence (67.77%) were approximately four times higher than study participants with fair (17.39%) and good (14.83%) adherence levels. As the duration on ART changed from ≤12 months to >12 months, the odds of high adherence/less adherence increased with approximately 61% *(p = 0.0347)* across the full scale of adherence levels. The estimated odds of patients with a CD4 ≥ 200cells/mm^3 was 1.65 *(p = 0.0279)* times toward poor level of antiretroviral therapy adherence than the estimated odds of patients with CD4 < 200cells/mm^3. Study participants who have single marital status tending to have more poor level of adherence to antiretroviral therapy than patients with married marital status *(p = 0.0003)*.
Conclusion: Levels of adherence to the antiretroviral therapy is significantly determined by the duration on antiretroviral therapy, the number of CD4 counts, the types of initial antiretroviral therapy regimens and the marital status of adult people living with HIV/AIDS.

Keywords: Human immune-deficiency virus; level of ART adherence; cumulative logit model.

ABBREVIATIONS

ARV: Antiretroviral; ART: Antiretroviral therapy; CPT: Cotrimoxazole preventive therapy; HIV: Human immunodeficiency virus; IPT: ISONIAZID preventive therapy; PLWHIV: People living with HIV.

1. INTRODUCTION

The burden of human immunodeficiency virus (HIV) infection persists as a public health problem throughout the globe [1,2]. In 2016, around 36.7 million individuals were identified as people living with HIV (PLWHIV) and more than half (54%) of adults received antiretroviral therapy (ART) in the world. In Ethiopia, more than 718, 500 individuals were depicted as PLWHIV at the end of 2016 [3]. Among these individuals, an estimated adult HIV prevalence in Ethiopia was 1.1% (5).

In response to HIV/AIDS burden, the world has been strived to increase the access to ART, especially for low income countries [3]. For instance, Ethiopia shows good success of ART services scaling up since 2005 [4].

In addition, the United Nations (UN) Joint Programs on HIV/AIDS aspired to curb HIV infection by 2020 under the 90-90-90 target platform [5,6]. To achieve one of these targets, the viral load suppression, improving the patients level of ART adherence is vital [7,8]. Adherence is abided to follow and take the treatments based on the health professional prescriptions and recommendations in terms of right doses, right times and right dietary recommendations [9].

According to different studies, improving the levels of patients adherence to ART significantly reduce the HIV multiplication and improves the HIV/AIDS treatment outcomes [10,11]. Thus, to achieve the whole benefits of ART, patients with HIV/AIDS should be adhered by > 95% to the therapeutic schemes [12,13].

However, achieving the patients ART adherence to the standard has been challenging throughout the world. For example, a synthesis of meta-analysis from 84 studies shows less than 62% of PLWHIV reached the recommended levels of adherence to ART (> 90% to the therapeutic schemes). In Ethiopia, patients in Yirgalem hospital have an adherence rate of 88.3% and 81.2% in other hospitals of Addis Ababa [14,15].

Ensuring adherence to ART regimens remain major challenges in Ethiopia [16,17]. The studies have reported a range of factors influencing ART adherence at various levels and varying depending on the contexts of the studies. In addition, almost all studies were modeling the factors based on categorizing the adherence level in to good and poor levels. Thus, this study intended to observe the adherence level to ART based on the three standard categorization (fair, poor and good) using Cumulative Logit Model approach. Evidences recommended the Cumulative Logit model is appropriate for ordinal response data [18,19].

2. MATERIALS AND METHODS

2.1 Study Area and Design

The study was conducted in Arba Minch General Hospital and Arba Minch health center, Arba Minch town, Gamo zone, Southern Ethiopia. The cross-sectional study was conducted from February to March 2018 among adult enrolled on ART between January 01, 2013 and December 30, 2017 in public health facilities of Arba Minch town, Ethiopia.

2.2 Study Population

In Ethiopia, the convenient regimens as fixed-dose combinations that are used as a first-line ART for adult patients includes: TDF + 3TC + EFV (FDC) which is the preferred regimen. The alternative first line ART regimens are AZT + 3TC + EFV or AZT + 3TC + NVP or TDF + 3TC + NVP. Thus, all adult PLWHIV who were taking first line antiretroviral therapy at Arba Minch public health facilities during January 2013 to December 2017 were used as a source population. The study included adult patients who were registered for ART clinic and had been taking their medicines for at least six months.

2.3 Sample Size Determination and Sampling Technique

Sample size was calculated by Open-Epi Version 3.01 statistical software based on the following assumptions: The study done in Jimma University Teaching Hospital, Southern Ethiopia reported that the study participants 36.19% had poor adherence and 63.8% had good adherence to their ART treatment [20]. In addition, 95% Confidence interval and 5% level of significance. Therefore, the calculated sample size was 355 participants. With an assumed non-response rate of 10%, the sample size needed for this study was 391 participants.

There are only two public health facilities that have ART clinic in Arba Minch town (Arba Minch General Hospital and Arba Minch Health Centre). Thus, both health facilities were used as a study sites for this study to have sufficient number of source population. From both institutions, adult HIV patients on ART for ≥ 6 months and enrolled between January 01, 2013 and December 30, 2017 was selected using simple random sampling technique.

Then patients with complete record of baseline data for the study were identified and given identification number to have a sampling frame. Finally, the study participants were proportionally allocated to each selected health facility and study participant was selected using lottery methods.

2.4 Data Collection Tools and Procedures

The standard data extraction tool was developed for recording information from patients' cards based on the revised 2017 Federal Ministry of Health patient card, ART intake forms and HIV care follow-up.

The outcome variable used in tools for this study was the level of ART adherence. The level of adherence was measured as ordinal scale (good, fair and poor) adheres to ART. Adherence was categorized based on the definition stated on the ART follow up card. A patient was categorized as having good adherence if pill count or self-reported adherence was greater than or equal to 95%. Fair adherence: if pill count or self-reported adherence was between 85%-95% while poor adherence: if pill count or self-reported adherence was less than <85%. The socio-demographic, clinical and chemo prophylaxis characteristic variables which are assumed to influence the adherence to ART treatment were considered in this study.

2.5 Data Processing and Analysis

The statistical software used for this study was the Statistical Analysis Software (SAS) version 9.4. Descriptive statistics was conducted in order to get details that may help to make decisions in the subsequent steps of the analysis. Frequencies distributions tables were used to provide an overall baseline characteristic of patients. Bivariate analysis was done to find associations between independent variables and the outcome. The independent variables that were found to be associated to the outcome at bivariate analyses up to 25% significance level were used in the cumulative Logit model to examine the magnitude and associations between the outcome of ART adherence and independent variables. Statistical significance was set at p-value <0.05.

3. RESULTS

3.1 Socio-demographic Characteristics

In this study, the study participants with the good level of ART adherence (67.77%) were

approximately four times higher than the study participants with fair (17.39%) and good (14.83%) adherence levels. From 391 study participants, 120 (45.28%) and 145 (54.72%) of male and female had good adherence to ART treatment. In addition, female 25(43.10%) had experienced lower poor adherence to treatment when compared with male. From the total study participants, 121 (45.66%), 31(45.59%) and 26(44.83%) were between 25-34 age group for good, fair, and poor adherence level to ART respectively (Table 1).

3.2 Baseline Clinical Characteristic

In this study 143 (53.96%), 27(39.71%), and 29(50.00%) had initial CD4 count greater than equal 200cells/mm3 for good, fair and poor level of adherence respectively. Out of the total respondents, 96(36.23%) of the participants were found on WHO stage III and the number of participants were few on WHO stage IV (Table 2).

3.3 Baseline Chemoprophylaxis Characteristic

About 162(61.13%) of the study participants were taking Cotrimoxazole preventive therapy and 184(69.43%) were taken Isoniazid preventive therapy at the time of enrollment. The majority of the respondents, 195 (75.58%), 47(69.12%) and 32(55.17%) were on TDF/3TC/NVP or EFV based regimen at baseline for good, fair and poor adherence respectively and followed by AZT/3TC/NVP or EFV regimen at baseline (Table 3).

Table 1. Baseline socio demographic characteristics of adult enrolled on first line ART at public health facilities of Arba Minch town, Gamo Zone, Southern, Ethiopia, 2013 to 2017

Variable	Category	Adherence level		
		Good (n=265(67.77))	Fair (n=68(17.39))	Poor (n=58(14.83))
Sex	Male	120(45.28)	30(44.12)	33(56.90)
	Female	145(54.72)	38(55.88)	25(43.10)
Age (Years)	15-24	37(13.96)	12(17.65)	4(6.90)
	25-34	121(45.66)	31(45.59)	26(44.83)
	35-44	72(27.17)	17(25.00)	21(36.21)
	45+	35(13.21)	8(11.76)	7(12.07)
Marital Status	Single	88(33.21)	18(26.47)	15(25.86)
	Married	140(52.83)	41(60.29)	31(53.45)
	Divorced	30(11.32)	6(8.82)	3(5.17)
	Windowed	7(2.64)	3(4.41)	9(15.52)
Educational Status	No education	27(10.19)	6(8.82)	9(15.52)
	Primary	94(35.47)	28(41.18)	17(29.31)
	Secondary	122(46.04)	26(38.24)	25(43.10)
	Tertiary	22(8.30)	8(11.76)	7(12.07)
Residence	Rural	55(20.75)	14(20.59)	39(32.76)
	Urban	210(79.25)	54(79.41)	39(67.24)
Religion	Orthodox	164(61.89)	41(60.29)	32(55.17)
	Muslim	7(2.64)	3(4.41)	1(1.72)
	Protestant	75(28.30)	22(32.35)	16(27.59)
	Other	19(7.17)	2(2.94)	9(15.52)
History of Substance Use	Yes	176(66.12)	37(54.41)	34(58.62)
	No	89(33.58)	31(45.59)	24(41.38)
Disclosure Status	Yes	113(42.64)	27(39.71)	20(34.48)
	No	152(57.36)	41(60.29)	38(65.52)
Time since HIV Diagnosis	<3 years	200(75.47)	51(75)	39(67.24)
	>= 3 years	65(24.53)	17(25.00)	19(32.76)
ART duration	<= 12 months	120(45.28)	36(52.94)	33(56.90)
	>12 months	145(54.72)	32(47.06)	25(43.10)
Health Facilities	Hospital	195(73.58)	57(83.82)	40(68.97)
	Health center	70(26.42)	11(16.18)	18(31.03)

Table 2. Baseline clinical characteristics of adult enrolled on first line ART at public health facilities of Arba Minch Town, Gamo Zone, Southern, Ethiopia, 2013 to 2017

Variable	Category	Adherence level		
		Good (n=265(67.77))	Fair (n=68(17.39))	Poor (n=58(14.83))
CD4 at Baseline	>= 200cells/mm^3	143(53.96)	27(39.71)	29(50.00)
	<200cells/mm^3	122(46.04)	41(60.29)	29(50.00)
	Working	207(78.11)	57(83.82)	38(65.52)
Functional Status at	Ambulatory	33(12.45)	5(7.35)	13(22.41)
Start ART	Bed ridden	25(9.43)	6(8.82)	7(12.07)
	<18.5	73(27.55)	27(39.71)	12(20.69)
BMI	18.5- 24.9	162(61.13)	34(50.00)	43(74.14)
	>= 25	30(11.32)	7(10.29)	3(5.17)
History of OI at	Yes	65(24.53)	13(19.12)	16(27.59)
Baseline	No	200(75.47)	55(80.88)	42(72.41)
	Stage I	92(34.72)	34(50.00)	19(32.76)
WHO clinical stage at	Stage II	59(22.26)	9(13.24)	10(17.24)
start ART	Stage III	96(36.23)	21(30.88)	24(41.38)
	Stage IV	18(6.79)	4(5.88)	5(8.62)

Table 3. Baseline chemo prophylaxis characteristics of adult enrolled on first line ART at public health facilities of Arba Minch Town, Gamo Zone, Southern, Ethiopia, 2013 to 2017

Variable	Category	Adherence level		
		Good (n=265(67.77))	Fair (n=68(17.39))	Poor (n=58(14.83))
CPT	Yes	162(61.13)	38(55.88)	37(63.79)
	No	103(38.87)	30(44.12)	21(36.21)
INH Therapy	Yes	184(69.43)	45(66.18)	33(56.90)
	No	81(30.57)	23(33.82)	25(43.10)
Initial Regimen	ABC/3TC/NVP or EFV	14(5.28)	5(7.35)	8(13.79)
	AZT/3TC/NVP or EFV	56(21.13)	16(23.53)	18(31.03)
	TDF/3TC/NVP or EFV	195(73.58)	47(69.12)	32(55.17)

3.4 Factors Affecting Levels Adherence to ART

A bivariate analysis result depicted that factors like ART duration, history of substance duration, CD4 at baseline, INH therapy, initial ART regimen and marital status had significant association with the level of adherence to ART (at α= 25%) (Table 4).

Table 5 shows the association between factors and level of ART adherence. Thus, ART duration, CD4 count at baseline of the study, initial regimen and marital status had significance association with level of adherence to ART. However, history of substance use, INH therapy, and place of residence were not associated with adherence level.

Estimated slope of ART duration is $\hat{\beta}$ = 0.4783 (SE=0.2265), so as HIV patients duration on ART changed from ≤12 months to > 12 months, the probability to be in the higher adherence-category (high adhere) as compared to the probability to be in the lower adherence-category (less adhere) increased. OR= exp(0.4783) = 1.6133: with ART duration changed from ≤12 months to > 12 months the odds P(high adhere)/P(less adhere) increases with approximately 61% across the full scale of adherence (when keeping the other factors fixed).

The estimated effect of history of CD4 at baseline is $\hat{\beta}$ = 0.5007 (SE = 0.2277). The estimated odds of patients with a CD4 ≥ 200cells/mm3 was 1.65 times toward poor level of ART adherence than the estimated odds of patients with CD4 < 200cells/mm3. Patients with CD4 count >= 200cells/mm3 tending to have more poor level of adherence than patients with CD4 count <200cells/mm3.

Table 4. Result of binary analysis of adult enrolled on first line ART at public health facilities of Arba Minch Town, Gamo Zone, Southern, Ethiopia, 2013 to 2017 data

LR statistics for type 3 analysis			
Source	**DF**	**Chi-Square**	**P-value**
Sex	1	1.28	0.2575
Educational Status	3	2.09	0.5548
Time since HIV Diagnosis	1	1.05	0.3049
ART duration	1	3.26	0.0709
Disclosure Status	1	1.21	0.2707
History of Substance Use	1	3.18	0.0744
Functional Status at Start ART	2	1.25	0.5339
History of Opportunistic Illness at Baseline	1	0.01	0.9125
CD4 at Baseline	1	2.27	0.1317
CPT therapy	1	0.02	0.9008
INH Therapy	1	2.75	0.0974
BMI	2	1.46	0.4815
Initial Regimen	2	7.31	0.0258
Marital Status	3	14.47	0.0023
Age	3	1.04	0.7926
Place of Residence	1	2.23	0.1357
WHO clinical stage at start ART	3	2.66	0.4465
Religion	3	1.41	0.7020
Occupation	5	3.42	0.6356
Health Facilities	1	0.12	0.7264

Table 5. Result of multivariable analysis: Parameter estimate, standard errors, OR and p-values

Analysis of maximum likelihood parameter estimates					
Parameter		**Estimate**	**St. error**	**AOR**	**P-value**
Intercept1		0.3823	0.2888		0.1855
Intercept2		1.4769	0.3023		<.0001
ART Duration	>12 months	0.4783	0.2265	1.6133	0.0347
	<= 12 months (Ref.)				
History of Substance Use	Yes	0.4066	0.2279	1.5017	0.0744
	No (Ref.)				
CD4 at Baseline	>= 200	0.5007	0.2277	1.6499	0.0279
	<200 (Ref.)				
INH Therapy	No	-0.3030	0.2369	0.7386	0.2008
	Yes (Ref.)				
Initial Regimen	ABC/3TC/NVP or EFV	-1.0811	0.4108	0.3392	0.0085
	AZT/3TC/NVP or EFV	-0.5828	0.2624	0.5583	0.0264
	TDF/3TC/NVP or EFV (Ref.)				
Marital Status	Single	0.2242	0.2563	1.2513	0.3817
	Divorced	0.4294	0.4174	1.5363	0.3036
	Widowed	-1.7575	0.4860	0.1725	0.0003
	Married (Ref.)				
Place of Residence	Rural	-0.2815	0.2617	0.7547	0.2821
	Urban (Ref.)				

LR statistics for type 3 analysis			
Source	**DF**	**Chi-square**	**P-value**
ART Duration	1	4.50	0.0339
History of Substance use	1	3.17	0.0751
CD4 at Baseline	1	4.90	0.0268
INH Therapy	1	1.62	0.2026
Initial Regimen	2	9.74	0.0077
Marital Status	3	16.27	0.0010
Place of Residence	1	1.14	0.2857

As initial regimen changed from TDF/3TC/NVP or EFV to ABC/3TC/NVP or EFV, the probability to be in the higher adherence-category (high adhere) as compared to the probability to be in the lower adherence-category (less adhere) decreases. OR= exp (-1.0811) = 0.3392: with initial regimen changed from TDF/3TC/NVP or EFV to ABC/3TC/NVP or EFV the odds P(high adhere)/P(less adhere) reduces with approximately 66% across the full scale of adherence (when keeping the other factors fixed). Similarly, OR= exp (-0.5828) = 0.5583 as initial regimen changed from TDF/3TC/NVP or EFV to AZT/3TC/NVP or EFV. So, the odds P(high adhere)/P(less adhere) reduces with approximately 44% across the full scale of adherence (when keeping the other factors fixed).

4. DISCUSSION

This study aimed to identify the factors affecting the level of ART adherence level among PLWHIV in Arba Minch public health facilities using cumulative logit model. The good adherence level to ART among PLWHIV in this study is suboptimal (67.77%) while 17.39% and 14.83% of PLWHIV are also adhered fairly and poorly to the ART. The logit model showed that the adherence level is significantly affected by duration of ART, CD4 count at baseline, the type of initial ART regimen and marital status.

The duration of PLWHIV on ART is one of the factors significantly affecting the adherence level to ART among PLWHIV. As the stay in ART changed from <= 12 months to > 12 months, the probability to be in the higher adherence level (high adhere) as compared to the probability to be in the lower adherence-level (less adhere) increases. Similar trend was observed in the studies done in Harar, Yirgalem and Axum of Ethiopia, and Nigeria [21-24]. This trend might be due to the fact that the longer patients are on treatment thereby they become complacent and find it less hard to follow the strict regimen.

The study also identified that, the tendency of the patients toward poorly adhering to ART regimens is higher among patients who had CD4 count ≥ 200 than their counter parts at baseline. The higher the patients CD4 count at the beginning of HIV/AIDS treatment the higher the probability toward poor adherence of the ART regimens. This might be due to patients who have higher level of CD4 count in their blood less likely to have serious illness. It is known that individuals are usually seeking more care and give attention to their treatment while they have faced more serious illnesses.

The level of adherence to ART drugs is also significantly affected by the patient's marital status. The results of the study depicts that patients who were single tending to have more poor level of adherence than married patients while the divorced patients tending to have more poor level of adherence than married patients. Thus, patients with the support of their husband have better probability of good adherence than single and divorced patients. This could be due to the contribution of the partner by remembering the time of ART drug schedule and emotional support.

5. CONCLUSION

The level of HIV/AIDS patients' adherence to the ART regimen is significantly determined by the time duration of the treatment, the level of CD4 counts, the types of initial antiretroviral drugs and the patients' marital status. Therefore, the healthcare professionals and adherent supporter should intimately follow up patients and stepped up the targeted adherence support for those patients with high baseline CD4 counts, with alternative first line ART regimens and patients without partners.

6. LIMITATIONS

The findings of this study should be viewed under the following limitations. The conclusion of this study was done based on the data from two public health institutions in the town and thus findings may not be generalizable to other similar settings. This study used secondary data that was quantified based on patients self-reports of missed doses which may be subject to biases.

CONSENT AND ETHICAL APPROVAL

Ethical clearance was obtained from ethical review board (IRB) of Arba Minch University, College of Medicine and Health Sciences before conducting the study. Personal identifier was excluded during data extraction; rather code was used. Since it is secondary data obtaining informed consents from the participants is not possible, but the confidentiality of information was maintained by not recording their name from the chart.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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