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Level of non-adherence and its associated factors among adults on first-line antiretroviral therapy in Amhara Regional State, Ethiopia

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Abstract

Background

In Ethiopia, nearly one-third of people living with human immunodeficiency viruses do not adhere to antiretroviral therapy. Moreover, information regarding non-adherence and its associated factors among adults on first-line antiretroviral therapy in Northeast Ethiopia is limited. Therefore, this study aimed to assess the level of non-adherence and its associated factors among adults on first-line antiretroviral therapy in North Shewa Zone, Amhara Regional State, Ethiopia.

Methods

A facility-based cross-sectional study was conducted on 326 participants selected by systematic random sampling technique from the five randomly selected public health facilities. Data were collected using the questionnaire adapted from the studies conducted previously and the collected data were entered into Epi data version 3.1 and exported to Stata version 14 for further analysis. Multivariable logistic regression analysis was done and an adjusted odds ratio with its corresponding 95% confidence interval was used to declare a statistical significance.

Results

The overall prevalence of non-adherence was 17.4% [95% CI: (12.8%, 21.2%)]. Patients with no formal education [AOR (95% CI) = 5.57 (1.97, 15.88)], those who did not use memory aids to take their medications [AOR (95% CI) = 3.01 (1.27, 7.11)], travel more than 10

kilometers to visit the nearby antiretroviral therapy clinics [AOR (95% CI) = 2.42 (1.22, 25.86)], those who used substance [AOR (95% CI) = 3.57 (1.86, 28.69)], and patients whose medication time interfered with their daily routine activities [AOR (95% CI) = 15.46 (4.41, 54.28) had higher odds of having non-adherence to first-line antiretroviral therapy compared to their counter groups.

Conclusion

The level of non-adherence to first-line antiretroviral therapy was 17.4%, higher compared to WHO's recommendation. Hence, patients counseling focused on avoiding substance use, use memory aids, and adjusting working time with medication schedule are very crucial. Furthermore, the ministry of health and the regional health bureau with other stakeholders should expand antiretroviral therapy service delivery at health facilities that are close to the community to address distance barriers.

Background

According to the 2019 global estimate, about 36.2 million adults were living with the human immunodeficiency virus (HIV), of these, 20.6 million were found in Sub-Saharan countries [1–3]. In Ethiopia, more than half a million (722,248) people are living with HIV, of these, one-third (30%) were from Amhara Regional State [4, 5].

The adult HIV prevalence in Ethiopia is 0.9% [6], with 2.9% in urban and 0.4% in rural settings [4, 7, 8]. The incidence of a new infection is also at a steady state [7, 9], below three-fourth of People Living With HIV(PLWHIV) ever enrolled on antiretroviral therapy (ART) in the country [3, 8, 10].

Recent data showed that above 95% adherence to the ART regimen is required for HIV infected patients to reach full viral suppression[11–13], but sustaining its adherence level requires accurate and consistent monitoring activities, and this is a major challenge for sub-Saharan African countries like Ethiopia [14]

In Ethiopia, 5% to 35% of PLWHIV did not adhere to the prescribed ART regimens [15–20] which is far away from the national target of HIV prevention programs [4]. Studies conducted in different settings identified socio-demographic, behavioral, disease characteristics, medication, and health systems-related factors as the common factors affecting adherence to ART regimens [15, 21–26].

In Ethiopia, different strategies like a transformation of a fee-based ART program in 2003 to a free ART program in 2005, decentralization of services to lower-level public health facilities and private hospitals, and capacity building for a service provider on counseling aspect have been tried to improve adherence to ART [27, 28]. However, still maintaining adherence to ART regimens has been one of the challenges of ART programs in the country [17, 29, 30].

Studies conducted previously were focused on clinical determinants of non-adherence rather than looking at the clients' behavioral aspects. Besides, little is known about the level of non-adherence and its associated factors in the study area. Therefore, this study aimed to determine the level of non-adherence and its associated factors among adults on first-line ART in North Shewa Zone, Amhara Regional State, Ethiopia.

Methods and materials

Study setting, design, period, and population

A facility-based cross-sectional study was conducted from 15th March to 15th April 2019 in North Shewa Zone, Amhara Regional State, Ethiopia, which is located 120 kilometers away from Addis Ababa, the capital of Ethiopia. In this Zone, there are thirteen health centers and five public hospitals. In all of the health facilities, the patients have a regular visit to the ART clinic on a monthly follow-up basis.

In this study, out of the ART providing public health facilities in the study area, one referral hospital (Debre Birhan Referral Hospital) and four health centers (Chacha, Debresina, Shewa-Robit, and Debre Brihan Health Centers) were randomly selected. All of the five health facilities are located in urban areas and are providing ART services for people coming from both urban and rural dwellers.

All adults on ART who were at least 18 years of age, able to hear, mentally fit, and being on follow-up for at least 3 months before the data collection period were eligible for this study. While those who were seriously ill during the data collection period were excluded.

Sample size determination and sampling techniques

For the first specific objective (i.e. to determine the level of non-adherence to first-line antiretroviral therapy among Adults in North Shewa Zone, Amhara Regional State, Ethiopia), the sample size was estimated using a single population proportion formula by considering a 95% confidence level, 5% margin of error, and non-adherence level of 25.8%, taken from the study conducted in Southwest Ethiopia [31].

$$n = \left[\frac{\left(z\frac{\alpha}{2}\right)^2 p(1-p)}{d^2}\right]$$

Where, n = required sample size, Zα/2 = critical value for normal distribution at 95% confidence level (1.96), p = expected level of non-adherence, and d = margin of error). Based on the above assumptions, the final sample size for the study was 296.

For the second specific objective (i.e. to identify the factors associated with non-adherence to first-line antiretroviral therapy among adults in North Shewa Zone, Amhara Regional State, Ethiopia), the sample size (118) was estimated using Epi-info version 7.2.1 by considering different variables that have a statistically significant association with non-adherence [20], the ratio of exposed to unexposed to be 1:1, 95% confidence level, and power of 80%. Finally, from the sample sizes estimated for both specific objectives, the minimum largest sample size was 296 (i.e. the sample size of the first objective). Then, with a 10% non-response rate, the final sample size was 326 adults on first-line ART.

Finally, the sample size was proportionally allocated to each health facility based on their preceding one-year adult ART case flow. Then, the sampling fraction was determined by dividing the total number of the eligible population getting services in each facility by the allocated sample size (N/n), which is approximately equal to six for all facilities. Accordingly, every 6th participant was selected using a systematic random sampling technique from the patients' registration book.

Study variables

Dependent variable. Adherence status to first-line ART that was dichotomized into "non-adhered" and "adhered" was measured by using the patient's self-reported percentage of missed doses during the last month. Thus, participants who missed more than 5% of the

prescribed ART doses based on self-report were considered to have non-adhered to the treatment and otherwise considered to have adhered to the treatment [32, 33]

Independent variables. Sociodemographic characteristics (educational level, monthly income, marital status, residence), use of memory aids to take ART drugs, get social support, type of substance used, medication time interfere with daily activities, and distance from ART clinics.

Definition of terms

Social support. A participant was considered as getting social support if he/she gets economic, psychological, and social support from his relative's/family's members.

Emotional life. The emotional life of the participants was assessed using five (yes/no) questions. Participants who responded correctly to three or more questions were categorized as having a stable emotional life and those who provided a correct response for less than three questions were categorized as having unstable emotional life.

Substance use. Participants who reported using at least one substance (alcohol, cigarette, and khat) 7 days before the data collection period were considered as "using a substance" and otherwise considered as "not using a substance".

Data collection tools and procedure

The questionnaire was adapted from studies conducted in developing countries [6, 34–37]. The questionnaire consists of sociodemographic, social support, behavioral factors, level of adherence, use of memory aids to take the ART drugs, and history of other medical illnesses. It was initially developed in the English language and translated to the local language (Amharic) and translated back to English to confirm its consistency. The tool was pretested on 5% (16 participants) of sample size other than selected health facilities and some amendments were made based on the pretest findings. Data were collected by trained health professionals who were not working in the ART clinic in the selected health facilities.

Data management and statistical analysis

The data were cleaned, coded, and entered into Epi data version 3.1 and exported to Stata version 14 for analysis. To assess the association between the dependent variable with each independent variable, bivariable logistic regression analysis was done and those independent variables with a p-value less than 0.25 were considered in the final multivariable logistic regression model. The eligible covariates were socio-demographic characteristics, use of memory aids, distance to ART clinics, social supports, substance use (alcohol, chat chewing, or cigarette smoking), and time of medication taking. The correlation between independent variables was checked using variance inflation factor (VIF) and its value for all variables was less than 5. The model fitness was assessed using the Hosmer-Lemeshow model fitness test (p-value of 0.32). Adjusted odds ratio with its corresponding 95% confidence interval was used to declare a statistical significance.

Ethical consideration and consent to participate

Ethical clearance was obtained from Research Ethics Review Committee, Dream Science and Technology College (DSTC) with an ethical letter of DSTC/0123/2019. Confidentiality of the information was secured by excluding respondents' identifiers, such as names, from the data collection format. Finally, written and verbal informed consent was obtained from those who were willing to participate in the study.

Results

Participants' socio-demographic characteristics

In this study, 310 participants were included with a response rate of 95.1%. The mean age of the respondents was 40.3±1.32 years. The median duration on ART was 39 [interquartile range (24–72)] months. Of the total respondents, 193 (62.3%) were residing in rural areas, 60 (19.4%) did not attend formal education. Regarding occupation and religious status, 137 (44.2%) were merchants, and nearly half (48.1%) were orthodox religious followers (**Table 1**).

HIV/AIDS and ART service-related information

Two hundred twenty- six participants (72.9%) heard about HIV/AIDS before their first contact with health care providers, and 199 (64.2%) participants got information about ART from health care providers. Nearly two-thirds (69.7%) of the participants were aware of the benefits of ART before they started treatment and 226 (72.9%) reported as they were benefited from their ART (**Table 2**).

Behavioral, psycho-social, health service, and ART drug-related information

The main reasons for missed ART doses were living far away from the health facilities (11.9%), forgetting (7.4%), drug side effects (6.8%), and being busy (6.1%). Moreover, 61.0% of the participants reported as they had ART-related side effects predominantly vomiting (24.8%) and diarrhea (18.7%). The study revealed that 60.3% of respondents had a history of substance use (**Table 3**).

Table 1. Socio-demographic characteristics of participants on first-line ART at public health facilities of North Shewa Zone, Amhara Regional State, Ethiopia, 2019.

Variable	Category	Frequency	Percent
Educational level	No formal education	60	19.4
	Elementary	79	25.5
	Secondary	117	37.7
	Tertiary	54	17.4
Occupational status	Farmers	93	30.0
	Government employees	31	10.0
	Merchants	137	44.2
	Others*	49	15.8
Monthly income (in ETB)	<1500	100	32.2
	≥1500	210	67.8
Religion	Orthodox	149	48.1
	Protestant	121	39.0
	Others**	40	12.9
Marital status	Single	70	22.6
	Married	90	29.0
	Divorced	14	4.5
	Widowed	136	43.9
Residence	Urban	117	37.7
	Rural	193	62.3

Others*(daily labor[20], Non-governmental organization(NGO) employee[14], student[15]), Others** (catholic[10], Muslim[17], Jehovah witness[6], and Waka Feta[7])

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Table 2. HIV/AIDS and ART service-related information of adults on first-line ART at public health facilities of North Shewa Zone, Amhara Regional State, Ethiopia, 2019.

Variable	Category	Frequency	Percent
Heard about HIV infection before illness	Yes	226	72.9
	No	84	27.1
Heard about the availability of ART	Before diagnosis	99	31.9
	During diagnosis	149	48.1
	After diagnosis	62	20.0
Source of information for ART	Health care providers	199	64.2
	Radio	38	12.3
	Television	61	19.7
	Others*	12	3.8
Aware of the benefit of ART when initiated	Yes	216	69.7
	No	94	30.3
Place where ART initiated	Health center	140	45.2
	Hospital	151	48.7
	Others**	19	6.1
Aware of adherence before starting ART	Yes	234	75.5
	No	76	24.5
Adherence in patients understanding	Taking all prescribed drugs	70	22.6
	Not missing more than 2 doses	56	18.1
	Not missing more than 3 doses	65	21.0
	Not missing more than 4 doses	43	13.9
Know the current CD4 count	Yes	264	85.2
	No	46	14.8
Benefited from ART	Yes	226	72.9
	No	84	27.1

Others* (peers[5], religious leaders[3], and family members[4]), Others** (NGO clinics[11], and private clinics[8])

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Non-adherence level

Of the total respondents, 54 (17.4%) [95% CI: 12.8% to 21.2%] were non-adherent to their prescribed ART drugs.

Factors associated with non-adherence level

After Adjusting for selected covariates, patients with no formal education had more than five times higher odds of non-adherence compared to those who attended at least secondary education [AOR (95% CI) = 5.57 (1.97, 15.88)]. In this study, patients who did not use memory aids to take their medications were three times more likely to be non-adhered compared to their counterparts [AOR (: 95% CI) = 3.01 (1.27, 7.11)]. The likelihood of non-adherence was 3.57 times higher among adults who used the substance compared to those who were not users [AOR (95% CI) = 3.57 (1.86, 28.69)]. This study revealed that the odds of non-adherence among adults living at a distance greater than 10 km and above from ART clinic was more than two times higher compared to those residing near the ART-providing clinic [AOR (95% CI) = 2.42 (1.22, 25.86)]. Finally, patients whose medication time interfered with their daily routines were fifteen times more likely to be non-adherent compared to their counterparts [AOR (95% CI) = 15.46 (4.41, 54.28)] (**Table 4**).

Table 3. Behavioral, psycho-social, health service, and ART drug-related information among adults on ART at public health facilities of North Shew Zone, Amhara Regional State, Ethiopia, 2019.

Variable	Category	Frequency	Percent
Experienced ART related side effects	Yes	189	61.0
	No	121	39.0
Type of side effects	Skin rash	52	16.8
	Vomiting	77	24.8
	Diarrhea	58	18.7
	Others*	2	0.7
Decision made by patients during side-effects	Discontinue ART till next Appointment	72	23.2
	Continue ART till next Appointment	42	13.5
	Immediately call for health care providers	43	13.9
	Others**	32	10.3
Pills taken by patients per day	1–3 pills	247	79.7
	Above 3 pills	63	20.3
Use memory aids to take ARV drugs	Yes	169	54.5
	No	141	45.5
Type of memory aids commonly used	Pill box	42	13.5
	Written schedule	38	12.3
	Watch alarm	75	24.2
	Family members	11	3.5
	Others***	3	1.0
Feels Comfortable when taking ARV drugs in front of others	Yes	78	25.2
	No	232	74.8
Reasons for not feeling comfortable	Fear of stigma	138	44.5
	Fear of insult from partner	66	21.3
	Others****	28	9.0
Get social support	Yes	121	39.0
	No	189	61.0
Pattern of emotional life	Unstable	110	35.5
	Stable	200	64.5
Medication schedule interfere with daily activity	Yes	168	54.2
	No	142	45.8
Use any substance in the last seven days	Yes	182	58.7
	No	128	41.3
Type of substance used in the last seven days	Alcohol	102	56.0
	Cigarette	39	21.4
	Khat	41	22.5
Missed prescribed doses in the last month	Yes	100	32.3
	No	210	67.7
Number of doses missed in the last one month	0 doses	210	67.7
	1–2 doses	35	11.3
	3 doses	11	3.6
	4 and more doses	54	17.4
Reasons for a missed dose	Being busy	19	6.1
	Due to ART side effects	21	6.8
	Forgetting	23	7.4
	Living far away	37	11.9

(*Continued*)

Table 3. (Continued)

Variable	Category	Frequency	Percent
Distance from ART clinic	< 10killometers	119	38.4
	10killometers and above	191	61.6

Others* (sever headach[1], and nausea[1]), Others** (take pain killers[12], visit private clinic[9], visit health facility[11]), Others*** (calendar[2], and partner[8]), Others**** (lack of confidence[16], and fear of insult from parents[12])

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Discussion

Non-adherence to ART led to HIV-related morbidity and mortality [38, 39]. Our study revealed that ART non-adherence level based on self-report at the time of follow up was 17.4% (95% CI: 12.8%, 21.2%), higher than the findings of the studies in Southwest Ethiopia [17], northwest Ethiopia [20, 40], Eastern Ethiopia [22], Tanzania [41], South Africa [42], and Uganda [33]. The discrepancy could be due to differences in the study setting and the existence of socio-cultural differences of the participants.

However, the level of non-adherence in this study is lower than the findings of the studies in Southwest Ethiopia [19], Northeast Ethiopia [43], Southern Ethiopia [31], Papua New Guinea [44], and Nigeria [35]. The discrepancy might be explained by differences in the access to ART service, interventions taken [22], and awareness about the benefits of ART in the study areas.

In this study, the odds of non-adherence among adults who had no formal education was more than five times higher compared to those who attended secondary education and above. This finding is consistent with the result of the studies in Togo [45] and Guangzhou-China

Table 4. Factors associated with non-adherence among adult on first-line ART follow up at public health facilities of North Shewa Zone, Amhara Regional State, Ethiopia, 2019.

Variable	Category	Adherence Status		COR (95%CI)	AOR (95% CI)
		Non-adhered	Adhered		
Educational level	No education	26 (48.2)	34 (13.3)	8.57 (4.06, 18.12)	5.57 (1.97, 15.68)*
	Primary	14 (25.9)	65 (25.4)	2.42 (1.09, 5.35)	2.19 (0.83, 5.76)
	Secondary and above	14 (25.9)	157 (61.3)	1.00	1.00
Monthly income	< 1500	24 (44.4)	76 (29.7)	1.00	1.00
	≥ 1500	30 (55.6)	180 (70.3)	052 (0.28, 0.96)	0.95 (0.37, 2.40)
Marital status	Married	14 (25.9)	76 (29.7)	1.00	1.00
	Unmarried	40 (74.1)	180 (70.3)	1.21 (0.62, 2.34)	0.52 (0.21, 1.26)
Residence	Urban	9 (16.7)	108 (42.2)	1.00	1.00
	Rural	45 (83.3)	148 (57.8)	3.65 (1.71, 7.78)	1.41 (0.13, 5.98)
Use memory aids to take ART drugs	Yes	14 (25.9)	155 (60.6)	1.00	1.00
	No	40 (74.1)	101 (39.4	4.38 (2.27, 8.46)	3.01 (1.27, 7.11)*
Get social support	Yes	11 (20.4)	110 (42.9)	1.00	1.00
	No	43 (79.6)	146 (57.1)	2.95(1.45, 5.97)	2.11 (0.84, 7.11)
Substance used in the last 7days	Yes	46 (85.2)	136 (53.1)	5.10 (2.30, 11.17)	3.57(1.86, 28.69)*
	No	8 (14.8)	120 (46.9)	1.00	1.00
Medication time interfere with daily activities	Yes	51 (16.5)	117 (37.7)	20.20(6.14,66.39)	15.46 (4.41,54.28)*
	No	3 (1.0)	139 (44.8)	1.00	1.00
Distance from ART clinic	<10killometer	10 (18.5)	109 (42.6)	1.00	1.00
	10killometrs and above	44 (81.5)	147 (57.6)	2.26 (1.57, 6.77)	2.42 (1.22, 25.86)*

* = statistically significant variables at 95%CI, COR = Crude Odds Ratio, AOR = Adjusted Odds Ratio, CI = Confidence Interval

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[24]. Higher education level has been one of the independent predictors to have adherence to ART [21, 22, 24, 42].

This study revealed that the odds of non-adherence among adults who used substances were more than three times higher compared to counterparts. This finding is supported by the studies conducted in Uganda [33], Vietnam [46], Togo [45], United States [47], Atlanta [48, 49], Amana Hospital, Tanzania [37], and Yaounde, Cameroon [50]. This will be can be explained by the fact that the use of substances like alcohol associated with memory impairment, subsequently failing patients to take the drugs as per schedule [34, 46, 49, 51–53]. It has also the potential to disrupt self-organizing skills and sleeping time patterns.

The odds of non-adherence among adults who did not use memory aids to take their ART drugs were three times higher compared to those who were using memory aids. This finding is in line with the study conducted in Jimma, Ethiopia [25], Vietnam [54], and Chicago [15]. The use of memory aid methods like peer counselors, mobile phone text messages, reminder devices, cognitive-behavioral therapy, and behavioral skills or medication adherence training [1, 5, 25, 55] have a great role in improving adherence. Thus, people using different reminders had a better level of adherence to the ART treatment [3, 56].

In this study, adults whose medication-taking time interfered with their daily routines had more than fifteen times higher odds of non-adherence compared to those whose medication schedules did not interfere with their daily activities. This finding is consistent with the findings of other studies [35, 56]. Hence, the people whose medication-taking time interfere with their working time are more likely to miss their ARV drugs which results in non-adherence [23, 31, 41].

In this study, the odds of non-adherence among adults living at a distance greater than 10 km and above from the ART clinic were more than two times higher compared to those residing nearer to the clinic. This finding is similar to the study conducted in Harari, Ethiopia [15], southwest Ethiopia [18], Indonesia [57], and the Democratic Republic [58]. This might be related to the availability of transportation and its costs. Thus, patients who live far away from the ART-providing clinics may not afford the transportation cost which leads to defaulting from the follow-up treatment.

As a limitation of the study, there might be recall bias since adherence was assessed based on data taken one month before the study period. Besides, the findings may not be generalized to patients who get ART services in private health facilities. However, to minimize recall bias we used triangulation of information from a medical record for some of the variables. In addition, due attention was given to all the study procedures throughout the field activities.

Conclusions

In this study, the level of non-adherence to first-line ART was higher than the WHO standard. patients with no formal education, those who did not use memory aids to take their medications, travel more than 10 kilometers to visit the nearby ART clinics, those who used substance and patients whose medication time interfered with their daily routine activities had higher odds of having non-adherence to first-line ART compared to their counter groups.

Therefore, patients counseling focused on avoiding substance use, use memory aids, and adjusting working time with medication schedule are very crucial. Furthermore, the ministry of health and the regional health bureau with other stakeholders should expand ART service delivery at health facilities that are close to the community to address distance barriers.

Supporting information

S1 Dataset. Minimal dataset.
(DTA)

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