Adherence to Combined Antiretroviral Therapy and Associated Factors Among People Living with HIV Attending Nekemte Specialized Hospital, Oromia, Ethiopia: A Cross-Sectional Study

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Background: For people living with HIV, to have sustainable viral suppression and better clinical outcomes, they should have a high level of adherence to antiretroviral therapy. In the treatment of human immune deficiency, antiretroviral therapy adherence became the major challenge in both developed and developing countries. The level of antiretroviral therapy differs across the settings. This study aimed to assess the level of combined ART adherence and associated factors among adult people living with HIV attending Nekemte Specialized Hospital, Ethiopia.

Methods: The institution-based cross-sectional quantitative study was conducted from August 2017 to September 2017. A total number of 284 clients participated in the study and a simple random sampling technique was used to allocate study participants. Data were entered into Excel and exported to SPSS version 20 for analysis. Bivariate analysis was conducted to identify candidate variables for multivariate analysis at p-value <0.2. Multiple logistic regression analysis was conducted to determine the predictors of non-adherence to ART. P-value <0.05 was considered to indicate statistical significance.

Results: About 81% of the study participants adhered to combined anti-retroviral therapy. Mentioned reasons for missing ART medications were simply forgot to take medication (44.4%), lack of transportation (21%), to avoid side effects (11.4%), do not want significant others to notice taking medication (11.4%) and felt sick (11.4%). Not using reminder (AOR=4.98 (1.65, 15.02)), poor knowledge on ART (AOR=2.79 (1.49, 5.25)), and engaging in unprotected sexual intercourse (AOR=2.16 (1.15, 4.05)) were significantly associated with non-adherence to combined ART.

Conclusion: About 81% of study participants adhered to combined ART, and poor knowledge about ART, engaging in unprotected sexual intercourse and not using the reminder were significantly associated with non-adherence to combined ART. Efforts to increase adherence levels should be encouraged.

Keywords: HIV patient, ART, combined ART adherence, Nekemte Specialized Hospital

Introduction
HIV becomes the major public health problem worldwide since its appearance, and the majority of infected people are living in Sub-Saharan Africa.1,2 ART is the base for comprehensive health sector response to Human Immunodeficiency Virus treatment, care, and support. Adherence of clients for their treatment plan near perfect is mandatory to keep the virus suppressed, as per World Health Organization guidelines.3
Successful ART program is when the patient adheres, and retained in care. It has been expected that for ART treatment to be effective; adherence should be at least 95%. High-level adherence is necessary for all HIV-infected people who are enrolled in chronic care services adhere to ART and OI medication and follow treatment plans.4

ART plays a pivotal role to maximize and sustain suppression of viral replication, restore immune function, minimize morbidity and mortality, improve quality of life and life expectancy.5

Globally, ART recommended for all HIV patients irrespective of CD4 count, WHO staging and clinical status. The focus of patient management has changed from identifying and managing early ARV related toxicities to test and treat strategy. To achieve sustained viral suppression over a lifetime, both long-term and short-term ART toxicities must be expected and overcome. The clinician must consider potential adverse effects when selecting an ARV regimen and a previous history of drug intolerances.6

Even though launching free accessibility of ART to several facilities in Ethiopia adherence is still challenging for ART programs, the test and start strategy has implemented in August 2016. ART should be initiated for all HIV (children, adolescents and adults) living with HIV immediately after HIV diagnosis, regardless of WHO clinical stage and CD4 cell count to improve quality of care, improve access to HIV care and treatment for all and to achieve the sustainable development goal global targets of 390s by 2020.7 Adequate adherence preparation and assuring patient willingness as per the national guideline (2014) are important for all individuals before initiating ART.8

Failure to adhere cause major impacts on patients, family, caregivers, community, and also a high burden for providers, health facilities, health care systems, health plans, industry, and society. Poor drug adherence among PLHIV leads to drug resistance and failure, and then increase morbidity and mortality. They may be more complex than the first-line regimen. Second and third-line regimens require optimal adherence to sustain viral suppression more than the first-line regimen.9,10

Various studies worldwide showed poor adherence is common. Literature reviews that the level of adherence to antiretroviral therapy in Ethiopia look like findings in most of the SSA countries. In yirgalem 72.8%, Gonder University and Felege Hiwot hospitals 82.7%, Gobba Hospital 90.8%, in Debre Markos Specialized hospital 88.6%, JUSH 72.4%.9,11–14

This study was focused on different independent indicators in addition to self-report; to avoid overestimation of adherence and fabrications caused by self-report. In addition to self-report, the studies focus on viral load, pharmacy refill, patient card (schedule for appointment plan, comparing baseline CD4 cell count with current CD4 cell count). Therefore, this study aimed to assess the level of combined ART adherence and associated factors among adult PLHIV attending Nekemte Specialized Hospital, Ethiopia.

Methods

Study Area

The study was conducted at Nekemte Specialized hospital located in Nekemte town, 328 km from Addis Ababa, the capital city of Ethiopia. Nekemte town has six sub-cities; Derge, Bake Jema, Cheleleki, Kessso, Burka Jato, and Bakanisa Kesse. Nekemte town has 2 Specialized hospital (Nekemte Specialized hospital and Wollega University Specialized hospital), and 2 health centers (Nekemte health center and Cheleleki health center). Nekemte Specialized hospital was established in 1939 G.C. by Sweden missionary. The Hospital gives service for Nekemte town, East Wollega zone, West Wollega zone, KellamWollega zone, Horo Guduru Wollega zone, West Shawa zone, Benishangul region, and nearby Amhara region with a total population of 934,860. The hospital has 178 beds for inpatient services. There is 294 clinical and administrative staff serving in the hospital (9 specialists, 23 MD, 42 BSc Nurses, 57 diploma Nurses, 58 other health professionals, and 24 administrative workers). The hospital gives all health services including ART for the community. ART was initiated in 2004 G.C. in the hospital. Currently, 2234 patients are receiving ART services in the hospital and 2051 of them were adults.

Study Design and Period

An institution-based cross-sectional study was used to assess ART adherence among HIV-infected adults on chronic care follow up in Nekemte Specialized hospital attendants. The study period was from August 2017 to September 2017.

Study Population

All PLHIV were the target group, and study populations were HIV-infected adults who were on chronic care follow up service in Nekemte Specialized hospital.
Sample Size and Sampling Techniques
The sample size was determined by using a single population proportion formula, taking P-value 80%, from the study conducted in Addis Ababa.\textsuperscript{15} The maximum sample size was calculated using marginal error =0.05, critical value =1.96 and 15% non-response rate which yielded a sample size of 284. A simple random sampling technique was used to draw study participants. First, the clients were given sequential order numbers; then, according to our inclusion criteria clients who were on ART for at least 6 months, age >18 years, and have an appointment during the data collection period were included. Then, by using a simple random sampling procedure, the participant’s card was selected from the appointment calendar logbook by the lottery method.

Data Collection
Structured questionnaire was used to collect the data, ART register, patient folder (follow up, laboratory results, intake form). Three trained data collectors were assigned and carried out the face-to-face interviews in a separate room to address the demographic, socioeconomic, disclosure status, health care providers and health care system variables. Available clinical (WHO stage) and immunological (CD4 count) and viral load data were collected. The questionnaire was prepared in English and translated to “Afan Oromo” which is a regional working language then translated back to English to check for consistency.

Ethics Approval and Consent to Participate
Ethical clearance was obtained from Wollega University’s research ethics review committee, and written informed consent was obtained from each study participant and the study was conducted in accordance with the Declaration of Helsinki. Permission from the town health office and Nekemte Specialized hospital was obtained. The privacy of participants was kept. Besides, the confidentiality of the results was ensured by assigning identification numbers during registration.

Operational Definitions
ART adherence: - is a patient’s ability to follow a treatment plan, take medication at a prescribed time and follow instructions and restrictions regarding food and other follow up schedules.

Non-adherence to ART: - is the condition of missing dose, not following a treatment plan, instruction and restriction regarding food and other follow up schedule.

Combined ART Adherence: - the ability of a patient to adhere for dose, for time, for diet, virally suppressed and attended pharmacy refill. A patient has a combined ART adherence if and only if it fulfills listed indicators. (Patients adhere to self-report, suppressed viral load and Pharmacy refill timely). Otherwise, if they miss one or more indicators they were said to be non-adherent to combined ART adherence. Because patients need to achieve 100% adherence (near perfect adherence) to ART dose, time, dietary, schedule, pharmacy refill, and viral load.

Combined non-ART Adherence: - the inability of a patient to adhere for dose, for time, for diet, virally suppression and does not attend pharmacy refill.

Baselines CD4 count: - the number of CD4 cells in the blood determines how the immune system is functioning at enrolment time.

Current CD4 count: - the number of CD4 cells in the blood determines how the immune system is functioning currently within 6 months.

Viral Load: - a blood test that counts the amount of HIV in the blood of HIV-infected people who are taking ART service for a minimum of 6 months.

A pharmacy refill record: - Pharmacy refill information can be used to calculate the drug-possession ratio, which represents the maximum possible adherence for a patient over a defined refill period that means if the client collects ART medication within 7 appointment days.

Self-report: - is when patient’s report about the adherence of dose, time and food orally

Duration on ART: - is time (duration) of the patient’s taking ART medication.

Disclosure status: - is time (duration) of the patient’s taking ART medication.

Unprotected sex: - sexual intercourse without a condom

Good knowledge: - Those who scored more than calculated mean

Poor knowledge: - Those who scored less than the calculated mean

Adherence level was assessed using a self-reported and patient folder as follows:

The number of doses missed: - follow medication time and dietary instructions and restrictions given by health
care provider. By using a structured questionnaire (self-report).

Adhere = if ≤2 doses/30 dose or ≤3 doses/60 dose, taking no more than 2 hrs before or after the time and follow dietary instructions and restrictions given by health care provider in the past 1 day, 3 days, 7 days, and 1 month properly as prescribed.

Non adhere = >2 doses/30 dose or >3 doses/60 dose, taking more than 2 hrs before or after the time and not follow dietary instructions and restrictions given by health care provider.

Viral load monitoring: - is one of the most reliable indicators of adherence and can be used as positive reinforcement to encourage continuous adherence. (Good if <1000 copies/mL (undetectable), poor if ≥1000 copies/mL (detectable))

A pharmacy refill: - it is another potential approach for routine adherence monitoring. Pharmacy refill information can be used to calculate the drug-possession ratio, which represents the maximum possible adherence for a patient that means if the Clint collects its ART medication on the appointment day or within 3 days after appointment day.

Data Quality Control
Data quality was ensured by giving training for data collectors and strict supervision during data collection. A pretest was conducted on 10% of the sample size in the Nekmeth health center before the actual data collection.

Data Processing and Analysis
Data were checked for completeness and consistency manually. Data entry and coding was done by using Excel and exported to SPSS version 20 for analysis. Descriptive summary using frequencies, proportions, graphs, and cross tabs were used to present results and then bivariate and multivariate logistic regression analysis was made to observe the relative effect of independent variables on the dependent variable by controlling the effect of other variables. P-value <0.2 as a cut-off point was taken as a reference to go to the multivariate analysis. Finally, to determine significant association at a 95% confidence interval and to predict association factors for combined ART level of adherence P-value less than 0.05 was used.

Results
Socio-Economic Characteristics of the Respondents
Two hundred eighty-four participants took part in this study with a 100% response rate. More than half, 159 (56%) were females. The majority of the respondents, 112 (39.4%) were between the age group of 25–34 years. The mean age of the respondents was 35.52 ± 10.1 years and the range extends from 18 years to 80 years. Regarding marital status, the majority of the respondents, 170 (59.9%) were married followed by widowed 42 (14.8%) and divorced 41 (14.4%). About 107 (37.7%) had attended secondary school (grades 9–12). Ninety-two (32.4%) were government employees with their occupation followed by housewives 46 (16.2%). Concerning religions, the majority of the respondents 131 (46.1%) were orthodoxly followed by protestant 129 (45.4%). Regarding ethnicity, the majority, 247 (87%) were Oromo followed by Amhara 35 (12.3%). More than half (52.8%) earned monthly income of less than 500 Ethiopian Birr (Table 1).

The Clinical Condition of Study Participants
Seventy percent of study participants have started ART 5 years ago. About 184 (64.8%) were at WHO stage 3 at ART initiation followed by WHO stage 2, 61 (21.5%). Regarding the recent treatment stage, almost all (97.9%) were at treatment stage 1. This is seen clinically by health care providers. Out of the total 284 participants, 180 (63.4%) had a baseline CD4 count of below 200 c/mm3, followed by CD4 count between 200 and 350 c/mm3 49 (17.3%) at the time of ART initiation. Regarding recent CD4 status of the participants who had been receiving ART for a minimum of 6 months and those CD4 count determination test done within the past 6 months were assessed, that 137 (48.2%) had a CD4 count of >500 c/mm3, followed by CD4 count between 200 and 350c/mm3 65 (22.9%).

Out of the total study participants, 224 (78.9%) had viral load <1000 copies/mL, 10 (3.5%) had ≥1000 copies/mL that means detectable viral load and 50 (17.7%) participants had Unknown result. However, no recent viral load was done for all participants except for those whose VL is >1000 copies/mL retest after 3-month adherence counseling. Regarding the schedule for the clinical appointment for the respondents, the majority, 222 (78.2%) was scheduled for their clinical appointment. Of the total 284 participants, 270 (95.1%) came for a pharmacy refill on their scheduled time within 7 days. About 35 (12.3%) were suffered from illness during the past 1 month. About 35 patients reported illness in the last month.

Among the 35 participants who were ill in the past month, about 62.9% reported mild, 22.8% moderate, and 14.3% severe illness (Table 2).
Types of Current ARV Regimen and Level of Adherence in Pts in NRH

Most of the patients, 157 were receiving (TDF + 3TC + NVP), 74 patients were receiving (AZT + 3TC + NVP) and 46 and seven (7) patients were receiving (AZT + 3TC and EVP) and (TDF + 3TC and NVP) respectively.

Knowledge About Antiretroviral Therapy

Concerning knowledge about ART therapy, more than half of the respondents 191 (67.3%) had good knowledge about ART therapy.

Social Support to the Respondents

Almost all of the study participants, 275 (96.8%) disclosed their status to their friends and/or family members. About 265 (93.3%) said that they had either a friend and/or a family member that supported them in taking their ARV medications. From 265 study participants who had friends and/or family member to support them, 139 (52.5%) always got help from them to remember to take HIV medications. Majority of them (94.7%) mentioned that they used reminder s to help them to remember taking their ARV medications properly at the right time (Table 3).

Perception of Patients’ on Their Relationship with Health Care Providers

Regarding the perception of patients’ on their relationship with health care providers almost all, 283 (99.6%) perceive as health care providers give them appropriate information about the medications. All of the respondents believe as discussing their health problems with health care providers is easy. All of the study participants respond as they are satisfied with the overall support they got from the health care providers.
Table 2 Clinical Condition Related Characteristics of HIV-Infected Adults on Chronic HIV Care Follow-Up at Nekemte Referral Hospital, Nekemte, Ethiopia, 2017

| Clinical Condition Characteristics          | Frequency | Percent (%) |
|---------------------------------------------|-----------|-------------|
| WHO Clinical Staging at ART Initiation      |           |             |
| WHO Stage 1                                 | 25        | 8.8         |
| WHO Stage 2                                 | 61        | 21.5        |
| WHO Stage 3                                 | 184       | 64.8        |
| WHO Stage 4                                 | 14        | 5           |
| Total                                       | 284       | 100.0       |
| Recent Treatment Stage                      |           |             |
| T1                                          | 278       | 97.9        |
| T2                                          | 3         | 1.1         |
| T3                                          | 2         | 0.7         |
| T4                                          | 1         | 0.4         |
| Total                                       | 284       | 100.0       |
| Baseline CD4                                |           |             |
| < 200 c/mm³                                  | 180       | 63.4        |
| 200–350 c/mm³                               | 49        | 17.3        |
| 350–500 c/mm³                               | 29        | 10.2        |
| >500 c/mm³                                  | 26        | 9.2         |
| Total                                       | 284       | 100.0       |
| Latest CD4(at least 6 month)                |           |             |
| < 200 c/mm³                                 | 34        | 12.0        |
| 200–350 c/mm³                               | 65        | 22.9        |
| 350–500 c/mm³                               | 48        | 16.9        |
| >500 c/mm³                                  | 137       | 48.2        |
| Total                                       | 284       | 100.0       |
| Duration of ART initiation                  |           |             |
| 6 month                                     | 9         | 3.2         |
| 7–12 month                                  | 1         | 0.4         |
| 1–2 years                                   | 23        | 8.1         |
| 2–5 years                                   | 52        | 18.3        |
| >5 years                                    | 199       | 70          |
| Total                                       | 284       | 100.0       |
| Baseline Viral Load                         |           |             |
| < 1000                                      | 224       | 78.5        |
| ≥ 1000                                      | 10        | 8.1         |
| Unknown                                     | 50        | 13.4        |
| Recent Viral Load                           |           |             |
| < 1000                                      | 8         | 2.8         |
| ≥ 1000                                      | 9         | 3.2         |
| Unknown                                     | 267       | 94.0        |
| Appointment Scheduled plan                  |           |             |
| Scheduled                                   | 222       | 78.2        |
| Un Scheduled                                | 62        | 21.8        |
| Total                                       | 284       | 100.0       |

(Continued)

Table 2 (Continued).

| Clinical Condition Characteristics          | Frequency | Percent (%) |
|---------------------------------------------|-----------|-------------|
| Pharmacy refill on Scheduled                |           |             |
| Yes                                         | 270       | 95.1        |
| No                                          | 14        | 4.9         |
| Total                                       | 284       | 100.0       |
| Sickness in the past one month              |           |             |
| Yes                                         | 35        | 12.3        |
| No                                          | 249       | 87.7        |
| Total                                       | 284       | 100.0       |

Table 3 Social Supports That the Study Participants Reported Among HIV-Infected Adults on Chronic HIV Care Follow-Up at Nekemte Referral Hospital, Nekemte, Ethiopia, 2017

| Social Supports                                   | Frequency | Percent (%) |
|--------------------------------------------------|-----------|-------------|
| Have you disclosed your HIV status to your friends &/or family members? |           |             |
| Yes                                               | 275       | 96.8        |
| No                                                | 9         | 3.2         |
| Do you have a family/friend that supports taking your medications? |           |             |
| Yes                                               | 265       | 93.3        |
| No                                                | 19        | 6.7         |
| Frequency of help from friend/family              |           |             |
| Some Times                                        | 10        | 3.8         |
| Most of the time                                  | 116       | 43.8        |
| Always                                            | 139       | 52.5        |
| Do you use any method to remind taking your ARV medication? |           |             |
| Yes                                               | 269       | 94.7        |
| No                                                | 15        | 5.3         |

Reasons for Missing ART Medications
Out of the 72 patients who missed ART medication, 44.4% of them pointed out their reason as they simply forgot taking the medication and 21% of the patients mentioned a lack of transportation as a reason for missing the medication (Figure 1).

Health Habits of the Patients
Majority of the respondents, 43 (15.1%) ever drunk alcohol from those, 10 (23.25%) drunk alcohol in the past
About 34.9% engaged in unprotected sexual intercourse (Table 4).

Level of Combined ART Adherence
From a total of 284 respondents, 230 (81%) of them adhered to combined ART and 54 (19%) of them were non-adhered to combined ART (Figure 2).

Factors Associated with Combined ART Adherence
In bivariate analysis literacy, recent CD4, baseline viral load, level of knowledge, using reminder and unprotected sexual intercourse were significant at P-value less than 0.2. They were considered as candidate variables for multivariate analysis. After adjustment for associated factors for non-adherence to combined ART, factors associated with adherence were level of knowledge on ART (AOR=2.79 (1.49, 5.25), using reminder (AOR=4.98 (1.65, 15.02) and unprotected sexual intercourse (AOR=2.16 (1.15, 4.05).

In this study, participants who have good knowledge were 2.8 times more likely to adhere to combined ART
compared to those who have poor knowledge. Patients who used a reminder to take medication were 5 times more likely to adhere to combined ART when compared to those who did not use a reminder. Respondents who had protected sexual intercourse were 2.16 times more likely to adhere to combined ART when compared to those who had unprotected sexual intercourse (Table 5).

### Discussion

This study assessed the level of Combined ART adherence and factors affecting ART adherence among HIV-infected adults on chronic HIV care follow up at Nekemte Specialized Hospital. Of the total 284 study participants, 230 (81%) have combined ART adherence. This result was similar to a study conducted in Addis Ababa (80%) and Gonder and Felege hiwot hospital (82.7%) and 83% in two hospitals of Oromia region.\(^{11,15,16}\) This finding is lower than the study conducted in Gobba (90.8%) DebreMarkos (88.8%) and Hiwot fana and Jugal hospitals (87%).\(^{12,13,17}\) The difference might be, this study contains combined ART adherence indicators while those studies used only self-report and dose adherence.

The socio-demographic variables such as age, religion, sex, occupation, ethnicity, educational status, marital status, and monthly income were not significantly associated with the level of combined ART adherence. But in a study conducted in Debre Markos monthly income was associated with ART adherence.\(^{15}\)

In this study, respondents who used a reminder to take medication were 5 times more likely to adhere to combined ART adherence compared to those did not use a reminder. This finding was similar to a study conducted in Nepal which showed the use of a reminder tool is positively associated with ART drug adherence.\(^{18}\) Also, a systematic review conducted in sub-Saharan Africa showed the use of memory aids is promoters of ART adherence.\(^{19}\) This showed that using the reminder helps them to memorize the time of taking the drug.

The patient’s knowledge of ART is important to maximize ART adherence. In this study, participants who had good knowledge about ART medication were 2.8 times more likely to adhere to combined ART adherence compared to those have poor knowledge.

In this study, respondents those had protected sex were 2.16 times more likely to adhere to combined ART when compared to...
compared to those had unprotected sex. This is in line with a study conducted in MACH14 sites which indicated an association between sexual risk behavior and adherence to ART. Patients who have difficulty in adhering to ART are also vulnerable to engage in risky sexual behaviour.

In this study, forgetting, lack of transportation, fear of side effects, avoiding the notice of others to take medication and illness were the major reasons for not taking ART medication. This is similar to a study conducted in different settings.12,21–23

**Limitation**
The first limitation comes from the nature of the study design, i.e. since the study design is a cross-sectional which collects data at a point in time it is difficult to identify existent factors that affect the study. The study was conducted only in the Nekemte Specialized hospital. Because of the single site, the findings may not be generalized to similar clinical settings. Recall bias and social desirability bias are also the possible bias which may encounter in this study. There is no gold standard for measuring adherence.

**Conclusion**
The level of Combined ART adherence was 81%. The major reasons for missing doses were simple forgetfulness, lack of transportation wanted to avoid side effects, felt sick or ill, being busy with other things, being away from home. The level of adherence was significantly associated with variables like knowledge on ART, used reminder and engaged in unprotected sexual intercourse.

**Data Sharing Statement**
All relevant data are within the manuscript.

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**Author Contributions**
All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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The authors declare that they have no competing interests.

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