

Cotrimoxazole prophylaxis therapy adherence and associated factors among adults on highly active antiretroviral therapy in Addis Ababa Ethiopia

Dagne Haile¹, Ararso Hordofa Guye², Elsabeth Legesse², Berhanu Senbeta², Daba Iticha², Eyob Ketema³, Tulu Tefera³, Duressa Mulatu Shiferaw⁴, Tadesse Nigussie^{2*}

¹Lemi Kura sub-city Health Office Addis Ababa, Ethiopia

²Salale University, College of Health Science, Fitcha, Ethiopia

³Bahir Dar University College of Medicine and Health Sciences, Bahir Dar, Ethiopia

⁴Menelik II Medical and Health Sciences College, Addis Ababa, Ethiopia

ABSTRACT

Background: Adherence to cotrimoxazole prophylactic medication is indispensable for adequately controlling viral load and lowering opportunistic infections linked to HIV/AIDS. However, the degree of adherence to cotrimoxazole prophylaxis among individuals with HIV in Ethiopia is not well recorded. Thus, the current study sought to determine adherence to cotrimoxazole prophylaxis therapy and associated factors among adults receiving highly active antiretroviral therapy (HAART) in Lemi Kura Sub-city, Addis Ababa, Ethiopia.

Methods: An institution-based cross-sectional study was conducted among 356 adults on HAART from May 20 to July 5, 2022. Participants were selected using a systematic random sampling technique. Data were collected using interviewer-administered structured questionnaires. The data were entered into EpiData version 3.1 and analyzed using SPSS version 25. Descriptive statistics were used to summarize the characteristics of participants, while a logistic regression model was performed to identify factors associated with the dependent variable. Variables with a p-value < 0.05 were considered significantly associated with adherence.

Results: The level of adherence to cotrimoxazole prophylaxis therapy (CPT) was 159 (46.1%). Being pregnant [AOR, 8.9, 95% CI; (4.1–16.5)], having a single marital status [AOR=2.8, 95% CI; (1.3–5.9)], initiating CPT concurrently with ART [AOR=4.9, 95% CI; (1.7–14.5)], and duration of CPT more than 3 months [AOR=3.8, 95% CI; (1.6–10.9)] were significantly associated with non-adherence.

Conclusion: The non-adherence level to CPT in the study area was found to be high, with 53.9% of individuals on HAART being non-adherent. Interventions targeting the timing and duration of CPT initiation, individuals with a single marital status, and those who have been on CPT for more than three months are crucial to reduce non-adherence.

Keywords: Cotrimoxazole prophylaxis therapy, Treatment adherence, Human immunodeficiency virus

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BACKGROUND

CPT is a life-saving, simple, and cost-effective intervention for adults living with human

immunodeficiency virus (HIV), which substantially improving health outcomes of infected individuals globally (1). HIV continues to pose a major public health challenge,

especially in sub-Saharan Africa, where it disproportionately impacts younger individuals, and 38% of new infections occur among those under the age of 25 (2,3). Beyond individual health, the disease has far-reaching consequences for families and communities through exacerbating existing socio-economic burdens (4).

According to the World Health Organization (WHO), approximately 38.4 million people were living with HIV by 2022 with a significant number of deaths attributed to tuberculosis (TB) and other opportunistic infections (5). Despite this, only around 24.5 million individuals were receiving antiretroviral therapy (ART) (6, 7). CPT remains a practical, cost-effective, and safe intervention to reduce HIV/AIDS-related morbidity and mortality, particularly by preventing opportunistic infections such as pneumocystis carinii pneumonia and other severe bacterial infections (8, 9).

Cotrimoxazole (CTX) prophylaxis is recommended for HIV-positive individuals with high viral loads and compromised immunity, despite concerns about increasing bacterial resistance associated with its widespread use in preventing opportunistic infections (10, 11). Studies have shown that nasopharyngeal colonization with pneumococci is common among patients receiving CTX prophylaxis, and prolonged use may contribute to the emergence of cotrimoxazole-resistant and multidrug-resistant strains of pneumococci (12). The World Health Organization (WHO) guidelines provide countries with flexibility in implementing CPT to reduce HIV-related morbidity and mortality. As a result, countries adopt varying recommendations regarding the CD4 count thresholds and WHO clinical stage criteria for initiating and discontinuing prophylaxis, reflecting differences in local epidemiology, healthcare infrastructure, and policy priorities (6).

Africa remains the region most heavily impacted by HIV/AIDS with an estimated 25.7 million people living with HIV in 2022, including approximately 1.68 million children under the age of 15 (2). Evidence from studies in the region has shown that cotrimoxazole prophylaxis

significantly reduces mortality among individuals living with HIV with one study reporting a 29% reduction in mortality among those receiving cotrimoxazole compared to a control group (13). CPT plays a crucial role in reducing opportunistic infections and the risk of severe bacterial infections in individuals living with HIV. Its benefits extend beyond the treatment of symptomatic conditions, offering prolonged protective effects against asymptomatic infections. This contributes to significant individual health improvements and broader public health gains (14). CPT has been shown to significantly reduce mortality and hospital admissions due to respiratory infections among HIV-positive individuals following the initiation of ART. Early initiation of CPT alongside ART is effective, which leads to lower mortality rates and is strongly recommended for individuals living with HIV in low- and middle-income countries. This approach represents a cost-effective and highly efficacious strategy for reducing both morbidity and mortality in HIV patients. Moreover, the implementation of CPT in developing countries serves as a key example of effective policy application in the management of HIV/AIDS (15, 16, 17).

An estimated 753,100 individuals are living with HIV with higher prevalence rates observed in urban areas compared to rural regions. Women are approximately twice as likely to be affected as men (18). CPT is implemented in alignment with national HIV treatment guidelines (19). A study reported revealed that 67.8% of individuals living with HIV are adherent to CPT based on self-reported measures (3). Adherence to CPT among adults living with HIV can be improved through factors such as higher educational status, proper counseling, the provision of group support services, and access to dedicated counseling rooms for HIV-positive clients (20).

However, adherence to CPT among adults living with HIV- remains insufficiently studied. Data available on adherence levels and the factors that influence adherence is limited. Therefore, this study aimed to assess the level of adherence to CPT and identify associated factors among

adults living with HIV who attending a selected health center in Lemi Kura Sub-city, Addis Ababa, Ethiopia.

METHODS

Study design, period, and setting

An institution-based cross-sectional study was conducted in Lemi Kura sub-city, Addis Ababa, from May 20, 2022, to July 5, 2022. Lemi Kura sub-city is located in the northeastern part of Addis Ababa and consists of 9 districts and 10 health centers. The sub-city has a total population of 366,922, comprising 177,362 males and 189,560 females. At the time of the study, 2,753 of individuals were on ART in the sub-city.

Source and study population

The source population comprised all adult individuals living with HIV who were on CPT and receiving ART follow-up in Lemi Kura Sub-city. The study population was all adults who were attending ART clinic of randomly selected health center within the sub-city.

Eligibility criteria

All adults living with HIV who were on CPT and attending ART follow-up at selected health centers in Lemi Kura Sub-city and residing within the catchment area during the data collection period were included in this study. However, adults living with HIV and younger than 18 years of age, critically ill, and unable to respond to study questionnaire were excluded.

Sample size determination and sampling technique

The sample size was determined using a single population proportion formula by assuming 69.8% prevalence of CPT adherence (20), 95% confidence interval, and 5% margin of error, and 10% contingency sample for non-response and registration errors. The final determined sample size was 356 participants.

Lemi Kura Sub-city consists of nine woredas and ten health centers. For this study, four health centers: Yeka, Abado, Woreda 2, and Goro health center were selected based on considerations of human resources, economic factors, and time

feasibility, representing 30% of the health facilities in the sub-city. Study participants were proportionally allocated to each health center according to their patient population size. From a total of 690 eligible patients in the selected health centers, 356 were selected using a systematic random sampling method with a sampling interval (k) of 2. The first participant was randomly chosen from the first two patients using the lottery method, and the following participants selected by interval of 2 using ART registration book as sampling frame.

Data collection tools

Data were collected through face-to-face interviews using a structured, interviewer-administered questionnaire. The study included adult people living with HIV on CPT for a minimum of two months. Adherence to CPT was assessed using the Morisky self-report adherence scale (3). To ensure data quality, the questionnaire was initially prepared in English, translated to the local language (Amharic), and then back-translated to English by language experts to maintain consistency and clarity. A one-day training session was conducted for data collectors and supervisors to familiarize them with the data collection procedures and overall study protocols. To ensure the reliability and validity of the data collection tools, a pretest was carried out on 5% of the sample size outside the study area. Based on the findings from the pretest, necessary modifications were made to refine the questionnaire and improve the data collection process.

Data Analysis

Data were entered using EpiData version 3.1 and subsequently exported to SPSS version 25 for analysis. Prior to conducting the analysis, the dataset was examined for outliers, missing values, and compliance with relevant statistical assumptions. Descriptive statistics such as frequencies, percentages, means with standard deviations were used to summarize the demographic and socioeconomic characteristics of the study population. Binary logistic regression was employed to identify factors associated with adherence to CPT. Variables with a p -value less than 0.20 in the bivariate

analysis were included in the multivariable logistic regression model. The multivariable logistic regression model was used to control for potential confounding factors and to determine independent predictors of CPT adherence. The goodness-of-fit of the logistic regression model was assessed using the Hosmer and Lemeshow test. Variables with a p-value < 0.05 in the multivariable analysis were considered statistically significant factors associated with CPT. Adjusted odds ratios (AORs) with 95% confidence intervals (CIs) were reported to quantify the strength and direction of associations between the independent variables and dependent variable.

RESULT

Socio-demographic characteristics

(Table 1), depict socio-demographic characteristics of the respondents. A total of 345 adults living with HIV participated in the study, yielding a response rate of 97.0%. Among the participants, 165 (47.8%) were between 30 and 39 years of age, while 21 (6.1%) were aged over 49 years. The majority (72.5%) of the study participants were female, of whom 38 (15.2%) were pregnant. The majority (50.7%) of the participants had completed primary school. About 136 (39.4%) of the participants were orthodox Christian followers and 198 (57.4%) of the participants were in marital union.

Table: 1 Socio-demographic characteristics of study participants Lemi Kura sub-city, Addis Ababa, Ethiopia, 2022

Variable	Category	Frequency	Percentage
Age	19-29	65	18.8
	30-39	165	47.8
	40-49	94	27.2
	>49	21	6.1
Sex	Male	95	27.5
	Female	250	72.5
Pregnancy status	No	212	84.8
	Yes	38	15.2
Educational status	Illiterate	26	7.5
	Primary	175	50.7
	Secondary	102	29.6
	Tertiary	42	12.2
Religion	Orthodox	136	39.4
	Muslim	74	21.4
	Catholic	36	10.4
	Protestant	99	28.8
Occupation	Housewife	54	15.7
	Government workers	83	24.1
	Private worker	65	18.8
	Daily labor	136	39.4
	Other (Merchant, NGO employee, unemployed)	7	2
Marital status	Single	119	34.5
	Marriage	198	57.4
	Widowed	20	5.8
	Divorced	8	2.3
Income	Less than 1501	167	48.4
	1501-4500	119	34.5
	More than 4500	59	17.1

Individual participant-related factors

Table 2 shows cotrimoxazole prophylaxis therapy score. A total of 339 (98.3%) participants were reported not forgetting to take CPT, while 176 (51%) occasionally missed for 3

days or fewer for reasons other than forgetfulness. Two hundred thirty (66.7%) participants were stopped taking Cotrimoxazole without consulting a physician, and 309 (89.6%) participants sometimes forgot to bring the tablets when they travel or leave home.

Most (61.4%) of the participants were taken Cotrimoxazole tablets the day before data collection, and 214 (62%) did not stop taking medication when they felt healthy. Of the total of the participants, 326(94.6%) had ever felt

hassled about adhering to their treatment plans. A total of 189 (54.8%) participants had sometimes difficulty in remembering cotrimoxazole tablets taking, while 102 (29.6%), miss the CPT usually (Table 2).

Table 2: Morisky's scale CPT adherence self-report scale assessment among adult people living with HIV clients Addis Ababa, Ethiopia, 2022

Variable		Frequency	Percent
Forgetting CPT sometimes	Yes	339	98.3
	No	6	1.7
Missing CPT sometimes	Yes	176	51.0
	No	169	49.0
Stopping CPT without consulting a physician	Yes	230	66.7
	No	115	33.3
Forgetting CPT ablate during travel	Yes	309	89.6
	No	36	10.4
Cotrimoxazole tablets taken day before data collection	Yes	232	67.2
	No	113	32.8
Cotrimoxazole tablet not stop taken when felt healthy	Yes	214	62.0
	No	131	30.0
Ever feel hassled about adhering plan	Yes	326	94.5
	No	19	5.5
Difficulty in remembering cotrimoxazole tablet taking	Yes	291	84.3
	No	54	15.7

Cotrimoxazole drug-related factors

Most of the study participants were actively receiving CPT during the data collection period (Table 3). Of the participants 161(46.7%) were initiated to CPT simultaneously with ART initiation, while 145(42.0%) initiated CPT before ART and 39(11.3%) after ART initiation (Table 3). Of the total of the study participants, 147(42.6%) took CPT for 4 to 6 months, and 104(30.1%) took CPT for 1 to 3 months, while 85(24.6%) for greater than 6 months (Table 3). A total of 67 (19.4%) participants discontinued medication within one week before the data

collection period due to they were in first-trimester pregnancy (53.1%), increased CD4 count (43.4%), and allergic reactions (3.5%) (Table 3).

Awareness regarding the use of CPT among the study participants was high (94.8%) about the importance of CPT for HIV patients. Moreover, 205(59.4%) participants were responded that CPT could support health to prevent opportunistic infections (Table 3). It was also noted that 245 (71%) participants were taking the CPT by reducing the dose (Table 3).

Table:3: Cotrimoxazole tablet drug-related factors among adult people living with HIV, Lemi Kura sub-city, Addis Ababa, Ethiopia, 2022

Variables	Category	Frequency	Percentage
Active patient on CPT	No	67	19.4
	Yes	278	80.6
CPT initiation time	Before ART	39	11.3
	Simultaneously with ART	161	46.7
	After ART	145	42.0
Duration of CPT (months)	1 month	9	2.6
	1-3 months	104	30.2
	4-6 months	147	42.6
	Above 6 months	85	24.6
Reason for CPT discontinuation	CD 4>350cells/dL	27	40.3

	Allergies	2	3.0
	Pregnancy	38	56.7
CPT beneficial	No	18	5.2
	Yes	327	94.8
Purpose of CPT	Reduce signs and symptoms	129	37.4
	Cure	11	3.2
	Support	205	59.4
CPT dose in take	Inadequate	245	71.0
	Adequate	100	29.0

Clinical manifestation related characteristics

Most (86.1%) of the participants were classified as stage III by the WHO clinical staging, while only 32 participants (3.5%) were in stage I (Table 4). Among the participants

40(11.6%) were reported having comorbid conditions, while hypertension was the most prevalent (57.5%) of the comorbidity (Table 4). Furthermore, 294 (85.2%) had CD4 counts below 350 cells/dL, and 309 (89.6%) exhibited hemoglobin levels above 7 g/dL (Table 4).

Table 4: Clinical manifestation related characteristics of an adult with known HIV clients Addis Ababa, Ethiopia, 2022

Variable	Category	Frequency	Percentage
WHO Clinical Stage	I	12	3.5
	II	32	9.3
	III	297	86.1
	IV	4	1.2
Comorbid Illnesses	Hypertension	23	57.5
	Diabetic Mellites	6	15.0
	Tuberculosis	8	20.0
	Others	3	7.5
Level of CD4	CD 4<350 cells/dl	294	85.2
	CD4>350 cells/dl	51	14.8
Level of Haemoglobin	Less 7 g/dl	3	0.9
	From 7 to 11 g/dl	33	9.6
	Above 11 g/dl	309	89.6

CD4-Cluster of differentiation

Drugs related factors

Among the participants, 40 (11.6%) had a history of medication use, predominantly using anti-hypertensive medications, which were used by 23 (57.5%) participants (Table 5).

Furthermore, 63 (18.3%) participants were reported a history of using street drugs, with alcohol being the most used substance (74.6%) (Table 5). Of those who used street drugs, 40(63.5%) participants were indicated that their use was habitual (Table 5)

Table: 5 Other drugs related factors among adult people living with HIV in Lami Kira sub-city, Addis Ababa, Ethiopia, 2022

Variables	Category	Frequency	Percentage
History of medication	Yes	40	11.6
	No	305	88.4
Types of medication used	Anti-hypertension	23	57.5
	DM drugs	6	15.0
	Anti-tuberculosis	8	20.0
	Others*	3	7.5
History of street drugs	No	282	81.7
	Yes	63	18.3
Type of street drugs used	Alcohol	47	74.6
	Chat	16	25.4
Why do you use the drugs	Stress	23	36.5

Habitual

40

63.5

Other: Anti-epilepsy, drug for asthma*

Health facilities-related factors

The majority (86.7%) of the participants resided within 5 km of a healthcare facility, and 301(87.2%) refilled their CPT at every visit (Table 6).

Table 6: Health facilities-related characteristics in Lami-Kura sub-city, Addis Ababa, Ethiopia, 2022

Variables	Category	Frequency	Percentage
Distance to the health center	Less than 5km	299	86.7
	More than 5 km	46	13.3
Refilled CPT during visit	No	44	12.8
	Yes	301	87.2
Duration of contact with physician	≤15 minute	114	33.0
	>15 minute	231	67.0
Got adequate information on how to take a drug	No	178	51.6
	Yes	167	48.4
Adequate Counseling CPT upon refill	No	182	52.8
	Yes	163	47.2

CPT-Cotrimoxazole prophylaxis therapy, Km-Kilometer

Cotrimoxazole prophylaxis therapy adherence level

A total of 186 (53.9%) participants were non-adherence to CPT, while 160 (46.4%) (Fig 1).

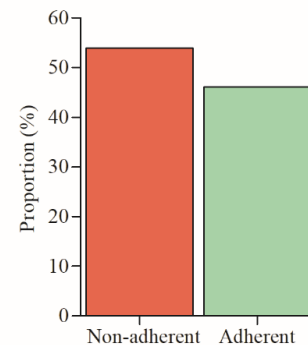


Figure 1: Cotrimoxazole prophylaxis therapy adherence level among adult people living with HIV in Lami-Kura sub-city, Addis Ababa, Ethiopia, 2022

Factors associated with cotrimoxazole prophylaxis therapy adherence

The findings of multivariable logistic regression model revealed that four variables were significantly associated with the CPT adherence. Pregnant women [AOR = 8.9, 95% CI: (4.1–

66.5)], being single marital status [AOR = 2.8, 95% CI: (1.3–5.9)], being initiated CPT concurrently with ART [AOR = 4.9, 95%CI: (1.7–14.5)], being on CPT for over three months [AOR = 3.82, 95% CI: (1.6–10.9)] were significantly associated with CPT adherence (Table 7).

Table 7: Factors associated with Cotrimoxazole prophylaxis therapy adherence among adult living with HIV in Lami-Kura sub-city, Addis Ababa, Ethiopia, 2022

Variable		CPT adherence status		COR (95% CI)	AOR (95% CI)
		Adherent	Non-adherent		
Pregnancy status	Yes	9	29	2.2 (2.1–4.6)	8.9 (4.1–16.5) *
	No	87	125	1	1
Educational status	Unable to read and write	16	10	1	1
	Primary and above	73	102	0.35(0.77–4.4)	0.23(0.08–0.67)
Marital status	Single	48	99	2.6(1.5–3.7)	2.8(1.3–5.9)*
	Married	11	87	1	1
Income status	Lower	15	95	1	1
	Middle	57	91	4.0(1.1–3.0)	2.7(1.2–5.9)

Comorbidities	Yes	11	29	1	1
	No	148	157	2.7(0.85–3.4)	0.60(0.23–1.6)
Time of initiation of CPT	Before ART	9	30	1	1
	Simultaneously with ART	58	103	5.8(2.6–13.1)	4.9(1.7–14.5) *
Duration of CPT intake	1-3 months	60	86	1	1
	More than 3 months	57	27	3.4(2.0–5.7)	3.8(1.6–10.9) *
Inadequate dose intake	Yes	60	40	1	1
	No	99	146	2.2(1.38–3.6)	0.61(0.24–1.5)
Distance from health facility	Less than 5km	17	29	1	1
	More than 5km	142	157	1.5(0.81–2.9)	0.47(0.14–1.3)

CPT- Cotrimoxazole prophylaxis therapy, COR- Crude odds ratio, AOR- Adjusted odds ratio

DISCUSSION

The adherence rate of CPT among adult clients with HIV was 53.9%. Being pregnant, single marital status, starting CPT and ART at the same time, and taking CPT for over three months were significantly associated with CPT adherence.

In comparison to research done in Malawi (37%) and North-Western Morocco (16.2%) the adherence rate of the current study is higher (22). However, it is lower than the adherence rates reported from Indonesia (55.57%) (13) and Egypt (58.7%) (21). These variations between the current study finding on the level of CPT adherence and the previously report could be attributed to differences in sample sizes, study groups, geographical locations, study period, and socioeconomic conditions.

The present study results showed that pregnant clients tended to have lower adherence to CPT. This finding aligns with the studies reported from Egypt (12), Somaliland (19), Gonder Town (21), and Haramaya(9). This agreement might be due to the fact that pregnancy can be a time of heightened emotional stress, especially for women who are managing an HIV diagnosis. Factors like stigma, partner rejection, and fear of disclosure could cause some women to hide or skip medications.

Being single was linked to non-adherence rates. Being single marital status had 2.8 times more likely to exhibit non-adherence level compared to their married counterparts. This observation is consistent with research reported from Iluababor in Southwest Ethiopia (23). This suggesting that individuals with single marital status might experience less social support and

face more stigma, which could adversely affect their adherence.

In the present study, initiating CPT simultaneously with ART was linked to non-adherence. Participants who started CPT at the same time with ART were more likely to struggle with adherence than those who began CPT afterward. This finding is in line with previous studies reported from Gonder (24) and Jimma (25). This may result from increased pill burden causing overwhelming feeling, especially for newly diagnosed clients, leading to non-adherence to one or both therapies. In addition, both CPT and ART can have side effects when taken together for the first time, and could be difficult for people living with HIV to identify which drug is causing discomfort. This confusion may prompt them to stop CPT (which is sometimes perceived as optional).

People living with HIV who have been on CPT for over three months were more prone to report non-adherence, which different from the findings of the study reported from Tanzania (26). This could be related to a reduced perception of risk. People living with HIV who have been on CPT for an extended period and feel healthy may start to think that the medication is no longer needed. This false sense of security can lead to decreased motivation to maintain consistent use, particularly when there are no apparent symptoms or infections.

The cross-sectional study design nature is the main limitation of this study in the ability to establish causal relationships and is subject to recall bias, which may affect the accuracy of reported adherence. The adherence is self-reported and it might over or under estimate the

level of adherence. Despite these limitations, the results of this study were not affected.

Conclusion

Adherence to CPT in the present study considerably lower than the previously reported findings. Interventions targeted pregnant mothers, individuals with single marital status, simultaneous initiation of CPT and ART, and those on CPT for longer than three months are required to increase CPT adherence.

Declaration

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Availability of data and materials

All data generated and/or analyzed during this study is included in the results of this study and are available from the corresponding author upon reasonable request.

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Ethical consideration

Ethical approval for this study was obtained from the Addis Ababa Public Health Research and Emergency Management Directorate as well as Rift Valley University. Written informed consent was obtained from all participants receiving antiretroviral therapy (ART) prior to their inclusion in the study.

Consent for publication: Not applicable.

Competing interests: The authors declare that they have no competing interests.

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