

# Level of Adherence and Associated Factors Among HIV-Infected Patients on Antiretroviral Therapy in Northern Ethiopia: Retrospective Analysis

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**Background:** Poor adherence to ART increases viremia, which leads to disease progression and transmission of drug-resistant HIV strains. This study aimed to assess the level of ART adherence and associated factors among adolescents and adult patients enrolled in ART care in Northern Ethiopia.

**Methods:** A retrospective analysis was conducted among 19,525 patients from April 2015 to March 2019. Data verification and filtration were done in Excel 2013 before exporting to STATA 14.0. Ordinal logistic regression was used to analyze the data.

**Results:** About 94.84%, 95% CI (94.52%, 95.14%) of the study subjects were in good adherence. However, about 1.46%, 95% CI (1.30%, 1.64%) and 3.70%, 95% CI (3.44%, 3.97%) of them had poor and fair adherence respectively. In the adjusted analysis, being male (AOR = 0.75; 95% CI: 0.65, 0.87), patients from general hospitals (AOR = 0.52; 95% CI: 0.39, 0.69), WHO staging IV (AOR = 0.57; 95% CI: 0.41, 0.81) and non-suppressed viral load (VL) status (AOR = 0.54; 95% CI: 0.47, 0.63) were negatively associated with good adherence. Whereas, age of 50+ years old (AOR = 1.68; 95% CI: 1.13, 2.50), recent CD4 count of 200–499 (AOR = 1.45; 95% CI: 1.21, 1.74) and recent CD4 count of 500 and above (AOR = 1.84; 95% CI: 1.47, 2.32) were positively associated with good ART drug adherence.

**Conclusion:** There was a higher level of adherence compared to the previous studies conducted in Ethiopia. Being male, patients from general hospitals, WHO staging II, III and IV and non-suppressed VL status were negatively associated with good adherence. Whereas, older ages, recent CD4 count of 200–499 and  $\geq 500$  CD4 count were positively associated with good ART drug adherence. The health system should recognize a higher need of younger age groups and males to design targeted counseling and support to encourage consistently high levels of adherence for a better ART treatment outcome.

**Keywords:** adherence and compliance, antiretroviral therapy, retreatment

## Background

Standard antiretroviral therapy (ART) consists of at least three antiretroviral (ARV) drugs in combination to maximally suppress the HIV virus and stop the progression of HIV disease.<sup>1</sup> Based on the 2017 World Health Organization's (WHO) report, 36.7 million people were living with HIV/AIDS worldwide.<sup>2</sup> Access to highly active antiretroviral therapy (HAART) in low- and middle-income countries has expanded dramatically.<sup>3</sup> Subsequently, HAART coverage is increasing; and nearly

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20.9 million people were taking HAART in June 2017.<sup>2</sup> It is estimated that 1% of the Ethiopian population were living with HIV and 66% of the adults and adolescents aged 15 years and above were on ART treatment in 2018.<sup>4</sup>

The introduction of ART played a significant role in improving the lives of people living with HIV/AIDS (PLWHA).<sup>5</sup> However, the efficacy and durability of the ART drug regimens are mainly determined on adherence to the drugs.<sup>6</sup> ART requires near perfect adherence rates (as high as 95%).<sup>7,8</sup> Poor adherence can cause serious consequences, such as increasing viremia which may lead to disease progression, development and transmission of drug-resistant HIV strains to others.<sup>9,10</sup>

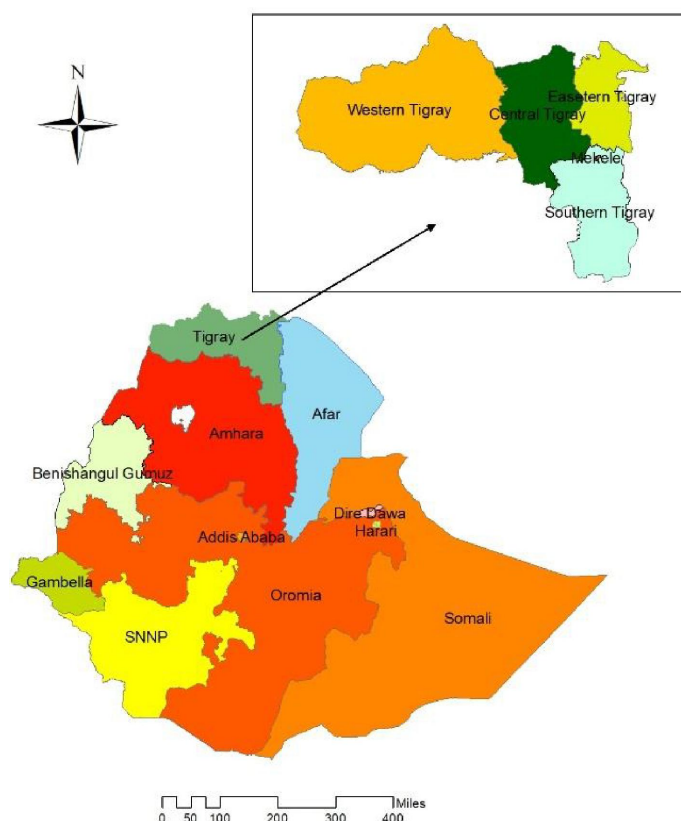
Optimal adherence to HAART depends on socio-demographic (age, gender), clinical (WHO staging, VL and CD4 count) and health system-related factors.<sup>13–15</sup> Although assessing the level of ART adherence and its determinant factors is crucial for further improvement of ART, there were no studies in Northern Ethiopia with a large representative sample size. Therefore, this study aimed to assess the level of self-reported adherence and associated factors among adolescent and adult patients enrolled in ART care in Northern Ethiopia. The finding of this study could

supplement achieving the Sustainable Development Goal (SDG) to “end AIDS epidemic” by 2030.

## Methods

### Study Design, Setting and Data Source

A retrospective analysis was conducted from April 2015 to March 2019 in Tigray Health Research Institute (THRI), the only center of viral load (VL) determination in Tigray region and some parts of Afar region. Tigray region is the 4th most populous out of the 9 Regional States of Ethiopia (Figure 1). As part of the intensive program of the three 90s (by 2020; 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy, and 90% of all people receiving antiretroviral therapy will have viral suppression),<sup>14</sup> ART treatment and response (the third 90) was being monitored by VL which was commenced in April 2015 in Tigray region. Data were obtained from the standard sample referral form of VL. The study was done among 19,525 patients, who had complete data on demographic, clinical, immunological and viral load in the database of THRI. Adherence was



**Figure 1** Map of the study area.

one of the independent variables in the previously published studies. However, the level of self-reported adherence and its determinants were not presented. To come up with the sample, all records in the database were reviewed and all the data that fulfill the eligibility criteria were included in the study.<sup>15–17</sup>

## Eligibility Criteria

Patients enrolled in ART care for at least 6 months were included in the study. Whereas, subjects younger than 15 years were excluded from the study.<sup>17</sup>

## Operational Definitions

### Adherence

The level of compliance to taking ART medications by the patients during ART care.

### Good Adherence

Drug adherence of 95% or  $\leq 2$  missed drug doses of 30 doses or  $< 3$  missed drug doses of 60 doses.<sup>18</sup>

### Fair Adherence

Drug adherence of 85–94% or 3–5 missed drug doses of 30 doses or 4–9 missed drug doses of 60 doses.<sup>18</sup>

### Poor Adherence

Drug adherence of  $< 85\%$  or  $\geq 6$  doses of missed ART drug doses of 30 doses or  $> 9$  doses missed ART drug doses of 60 doses.<sup>18</sup>

### Incomplete adherence

If the patients reported either poor or fair adherence.

### Viral Non-Suppression

Elevated VL Ribonucleic Acid (RNA) copies of  $> 1000$  copies/mL in plasma in a patient who has been on ART for at least 6 months.<sup>18</sup>

### Declined Immunological Response

A recent CD4 count of less than the baseline CD4 T-cells count where (Recent CD4 count minus the Baseline CD4 count = Negative).

### Same Immunological Response

The recent and the baseline CD4 counts are the same where (Recent CD4 count minus Baseline CD4 count = 0).

### Enhanced Immunological Response

A recent CD4 count of greater than the baseline CD4 T-cells count where (Recent CD4 count minus Baseline CD4 count = Positive).

## Data Collection Tools and Procedure

All the data in the database of the VL were exported to Microsoft Excel 2013 and then data verification and filtration were done before exporting to STATA 14.0 for analysis. During the filtration, complete regimens, meaningful range of biological measures and clients from Tigray region health care facilities were filtered, and overall 19,525 subjects with complete data were filtered from the total 55,104 clients for the analysis. HIV-1 RNA was extracted from 0.2 mL of plasma using the Abbott m2000sp automated sample preparation system (Abbott Molecular, USA) at THRI. Extracted RNAs were measured using Abbott m2000rt quantitative Real Time HIV-1 assay (Abbott Molecular, USA) with an HIV-1 RNA detection level of 40 to 10 million copies/mL based on the manufacturer's procedures. Adherence was measured by self-report and it was sent through the standard VL referral form. Immunological response after ART initiation was assessed by subtracting the baseline CD4 count from a recent CD4 count; categorized as deteriorated, the same and positively responded.

## Data Quality Assurance

Data completeness and consistency were checked in Microsoft Excel. High and low positive controls were checked before performing the patient sample for VL determination. However, CD4 count quality controls were done based on low, medium and high controls to evaluate the run validity in each laboratory, where the CD4 count was done.

## Data Management and Analysis

Analysis was done using STATA 14.0 to estimate the proportion of adherences and identify factors associated with adherences. Levels of adherences and the CD4 count were categorized based on the Ethiopian ART follow-up guideline and WHO respectively. The proportion of adherence levels was further evaluated by age group, sex, pregnancy status, breastfeeding status, WHO staging, CD4 baseline, CD4 recent, immunological response status, regimen, treatment line, reason for VL test, health facility ownership and health facility level. Cross tabulation was done for each of the independent variables with the outcome variable. Missed values were filtered and excluded for all variables; hence there was no issue of missing values in the final dataset.

The outcome variable has natural order, and hence the model analytic approach used to identify factors associated with adherence levels was the ordinal logistic regression.

The outcome variable was adherence level (0 = Poor adherence, 1 = Fair adherence and 2 = Good adherence). Statistical significance was considered at 95% CI (two-sided) in the examination of variables and interpretation of crude and adjusted odds ratios. Unadjusted association was used to determine the strength of the association between the independent variables and the outcome variable in the bivariable ordinal logistic regression. Whereas, adjusted associations were used to determine the strength of associations in the multivariable ordinal logistic regression. All significant variables at  $P$ -value  $\leq 0.05$  in the bivariable ordinal logistic regression were entered into the multivariable ordinal logistic regression. As pregnancy and breastfeeding status apply to females, both variables were excluded from statistical model building in the multivariable ordinal logistic regression. Variables which have a collinearity effect (Variation Inflation Factor (VIF)) were removed/omitted in the statistical modeling.

## Result

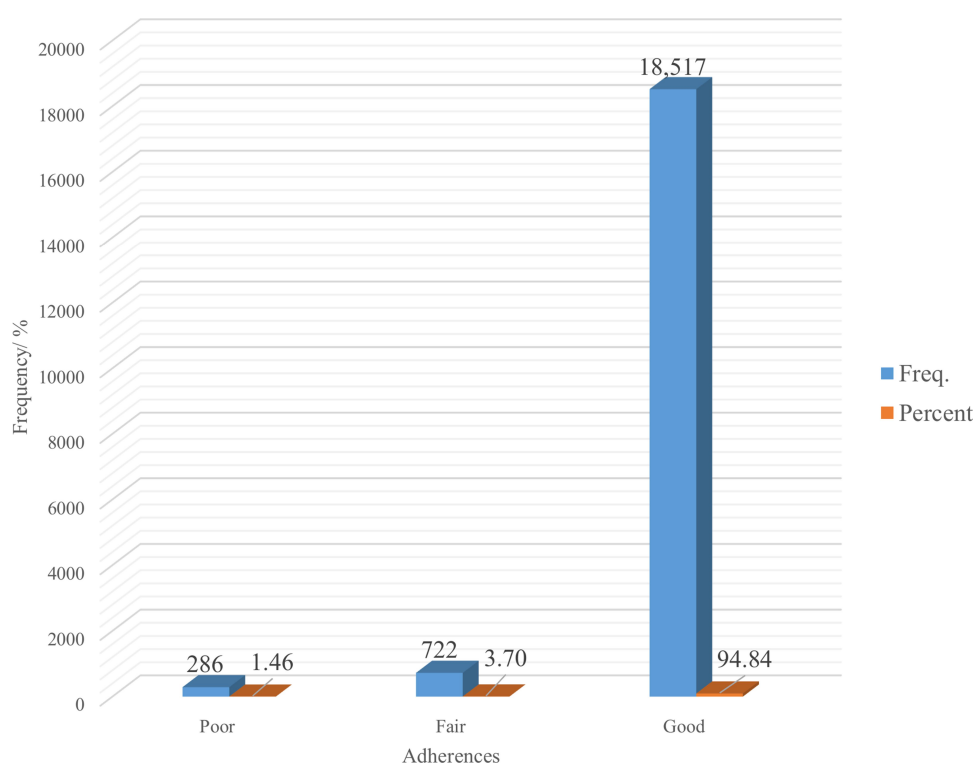
### Level of Self-Reported ART Adherence

About 94.84%, 95% CI (94.52%, 95.14%) of the study subjects were at a good level of self-reported ART adherence. However, about 1.46%, 95% CI (1.30%, 1.64%) and

3.70%, 95% CI (3.44%, 3.97%) of them had poor and fair adherence respectively. The incomplete adherence level of this study was 5.16%, 95% CI (4.86%, 5.48%) (Figure 2).

### Factors Associated with Self-Reported ART Drug Adherences

The bivariable ordinal logistic regression showed that age, gender, WHO stage, viral load status, 2h (TDF-3TC-ATV/R) regimen, baseline CD4 count and recent CD4 count were associated with self-reported ART drug adherence. After adjusting for possible effects of confounding variables in the multivariable ordinal logistic regression, being male (AOR = 0.75; 95% CI: 0.065, 0.87), patients from general hospitals (AOR = 0.52; 95% CI: 0.39, 0.69), WHO staging II (AOR = 0.47; 95% CI: 0.36, 0.60), WHO staging III (AOR = 0.25; 95% CI: 0.19, 0.34), WHO staging IV (AOR = 0.57; 95% CI: 0.41, 0.81) and non-suppressed VL status (AOR = 0.54; 95% CI: 0.47, 0.63) were negatively associated with good adherence. Whereas, age categories from 30 to 34 years (AOR = 1.54; 95% CI: 1.04, 2.26), 35–39 years (AOR = 1.47; 95% CI: 1.01, 2.15), 45–49 years (AOR = 1.87; 95% CI: 1.24, 2.83) and 50+ years old (AOR = 1.68; 95% CI: 1.13, 2.50), recent CD4 count of 200–499 (AOR = 1.45; 95% CI: 1.21, 1.74) and



**Figure 2** Levels of adherences of ART medication among HIV-positive adolescents and adults in Tigray region, North Ethiopia, 2015–2019 (n = 19,525).

**Table I** Bivariable and Multivariable Ordinal Logistic Regression Analysis of Adherence to Antiretroviral Therapy Among HIV-Positive Adolescents and Adults in Tigray Region, North Ethiopia, 2015–2019 (N = 19,525)

Variables	Category	ART Adherence			Total	COR (95% CI)	AOR (95% CI)
		Poor, n (%)	Fair, n (%)	Good, n (%)			
Age	15–19	13 (4.55)	23 (3.19)	384 (2.07)	420 (2.15)	1 (Ref.)	1 (Ref.)
	20–24	11 (3.85)	15 (2.08)	529 (2.86)	555 (2.84)	1.91 (1.13, 3.22)*	1.55 (0.91, 2.62)
	25–29	31 (10.84)	65 (9.00)	1736 (9.38)	1832 (9.38)	1.70 (1.14, 2.54)**	1.33 (0.88, 2.01)
	30–34	58 (20.28)	119 (16.48)	3539 (19.11)	3716 (19.03)	1.88 (1.29, 2.74)***	1.54 (1.04, 2.26)*
	35–39	53 (18.53)	163 (22.58)	4014 (21.68)	4230 (21.66)	1.75 (1.21, 2.54)**	1.47 (1.01, 2.15)*
	40–44	56 (19.58)	167 (23.13)	3490 (18.85)	3713 (19.02)	1.48 (1.02, 2.14)*	1.32 (0.90, 1.93)
	45–49	28 (9.79)	69 (9.56)	2051 (11.08)	2148 (11.00)	1.99 (1.34, 2.97)***	1.87 (1.24, 2.83)**
	50+	36 (12.59)	101 (13.99)	2774 (14.98)	2911 (14.91)	1.91 (1.30, 2.81)***	1.68 (1.13, 2.50)*
Gender	Female	158 (55.24)	412 (57.06)	12,296 (66.40)	12,866 (65.90)	1 (Ref.)	1 (Ref.)
	Male	128 (44.76)	310 (42.94)	6221 (33.60)	6659 (34.10)	0.66 (0.58, 0.75)***	0.75 (0.65, 0.87)***
Pregnant mother	No	157 (99.37)	410 (99.51)	12,204 (99.25)	12,771 (99.26)	1 (Ref.)	
	Yes	1 (0.63)	2 (0.49)	92 (0.75)	95 (0.74)	1.42 (0.45, 4.51)	
Lactating mother	No	155 (98.10)	402 (97.57)	12,107 (98.46)	12,664 (98.43)	1 (Ref.)	
	Yes	3 (1.90)	10 (2.43)	189 (1.54)	202 (1.57)	0.67 (0.38, 1.18)	
Facility ownership	Government	277 (96.85)	661 (91.55)	17,733 (95.77)	18,671 (95.63)	1 (Ref.)	
	NGO	9 (3.15)	61 (8.45)	770 (4.16)	840 (4.30)	0.59 (0.46, 0.76)	
	Private	0	0	14 (0.08)	14 (0.07)	–	
Facility type	Clinic	0	0	43 (0.23)	43 (0.22)		
	Health center	69 (24.13)	134 (18.56)	5479 (29.59)	5682 (29.10)	1.05 (0.77, 1.41)	
	Primary hospital	28 (9.79)	81 (11.22)	2022 (10.92)	2131 (10.91)	0.72 (0.52, 1.002)	
	General hospital	163 (56.99)	461 (63.85)	9205 (49.71)	9829 (50.34)	0.57 (0.43, 0.76)***	0.52 (0.39, 0.69)***
	Referral hospital	16 (5.59)	40 (5.54)	1443 (7.79)	1499 (7.68)	1 (Ref.)	
	Other	10 (3.50)	6 (0.83)	325 (1.76)	341 (1.75)	0.77 (0.44, 1.38)	
Service provided at defense facility	No	276 (96.50)	692 (95.84)	17,882 (96.57)	18,850 (96.54)	1 (Ref.)	
	Yes	10 (3.50)	30 (4.16)	635 (3.43)	675 (3.46)	0.86 (0.62, 1.19)	
WHO staging	I	220 (76.92)	582 (80.61)	17,027 (91.95)	17,829 (91.31)	1 (Ref.)	1 (Ref.)
	II	23 (8.04)	64 (8.86)	688 (3.72)	775 (3.97)	0.37 (0.30, 0.47)***	0.47 (0.36, 0.60)***
	III	28 (9.79)	50 (6.93)	330 (1.78)	408 (2.09)	0.20 (0.15, 0.25)***	0.25 (0.19, 0.34)***
	IV	15 (5.24)	26 (3.60)	472 (2.55)	513 (2.63)	0.54 (0.39, 0.75)***	0.57 (0.41, 0.81)**
Viral load test reason	First at 6 months	177 (61.89)	427 (59.14)	11,355 (61.32)	11,959 (61.25)	1 (Ref.)	1 (Ref.)
	Routine annual VL test	37 (12.94)	175 (24.24)	5820 (31.43)	6032 (30.89)	1.47 (1.25, 1.72)***	1.40 (1.19, 1.65)***
	Suspected ART failure clinical	0	4 (0.55)	46 (0.25)	50 (0.26)	0.63 (0.23, 1.75)	
	Suspected ART failure–immunological	8 (2.8)	8 (1.11)	65 (0.35)	81 (0.41)	0.21 (0.12, 0.36)***	0.45 (0.24, 0.82)**
	Suspected ART failure – initial viral load	56 (19.58)	92 (12.74)	943 (5.09)	1091 (5.59)	0.33 (0.28, 0.41)***	0.55 (0.44, 0.69)***
	Not indicated in the form	8 (2.8)	16 (2.22)	288 (1.56)	312 (1.60)	0.64 (0.42, 0.97)*	0.62 (0.41, 0.94)
Viral load status	Suppressed	123 (43.01)	413 (57.20)	13,836 (74.72)	14,372 (73.61)	1 (Ref.)	1 (Ref.)
	Non-suppressed	163 (56.99)	309 (42.80)	4681 (25.28)	5153 (26.39)	0.38 (0.34, 0.43)***	0.54 (0.47, 0.63)***

(Continued)

Table 1 (Continued).

Variables	Category	ART Adherence			Total	COR (95% CI)	AOR (95% CI)
		Poor, n (%)	Fair, n (%)	Good, n (%)			
Regimen	1c (AZT–3TC–NVP)	85 (29.72)	222 (30.75)	5525 (29.84)	5832 (29.87)	1 (Ref.)	1 (Ref.)
	1d (AZT–3TC–EFV)	28 (9.79)	85 (11.77)	1794 (9.69)	1907 (9.77)	0.88 (0.71, 1.10)	
	1e (TDF–3TC–EFV)	141 (49.30)	309 (42.80)	8940 (48.28)	9390 (48.09)	1.10 (0.95, 1.28)	
	1f (TDF–3TC–NVP)	29 (10.14)	90 (12.47)	2023 (10.93)	2142 (10.97)	0.95 (0.76, 1.18)	
	1g (ABC–3TC–EFV)	0	0	6 (0.03)	6 (0.03)	–	
	1h (ABC–3TC–NVP)	0	1 (0.14)	6 (0.03)	7 (0.04)	0.35 (0.04, 2.88)	
	2a (ABC–ddI–LPV/R), 2c (TDF–ddI–LPV/R), 2d (TDF–ddI–NVP) and 2g (TDF–3TC–LPV/r)	0	0	12 (0.06)	12 (0.06)	–	
	2f (AZT–3TC–ATV/r)	0	3 (0.42)	59 (0.32)	62 (0.32)	1.11 (0.35, 3.55)	
	2h (TDF–3TC–ATV/R)	3 (1.05)	12 (1.66)	152 (0.82)	167 (0.86)	0.57 (0.33, 0.98)*	1.04 (0.59, 1.83)
Baseline CD4 count	<200	164 (57.34)	392 (54.29)	9131 (49.31)	9687 (49.61)	1 (Ref.)	1 (Ref.)
	200–499	103 (36.01)	250 (34.63)	7252 (39.16)	7605 (38.95)	1.25 (1.09, 1.43)**	1.03 (0.88, 1.21)
	500 and above	19 (6.64)	80 (11.08)	2134 (11.52)	2233 (11.44)	1.32 (1.06, 1.64)*	0.95 (0.71, 1.27)
Recent CD4 count	<200	88 (30.77)	206 (28.53)	2749 (14.85)	3043 (15.59)	1 (Ref.)	1 (Ref.)
	200–499	125 (43.71)	325 (45.01)	8459 (45.68)	8909 (45.63)	2.01 (1.73, 2.35)***	1.45 (1.21, 1.74)***
	500 and above	73 (25.52)	191 (26.45)	7309 (39.47)	7573 (38.79)	2.96 (2.50, 3.52)***	1.84 (1.47, 2.32)***
Immunological response compared to baseline	Negative	80 (27.97)	180 (24.93)	3279 (17.71)	3539 (18.13)	1 (Ref.)	1 (Ref.)
	No change	6 (2.10)	12 (1.66)	232 (1.25)	250 (1.28)	0.72 (0.43, 1.21)	
	Positive response	200 (69.93)	530 (73.41)	15,006 (81.04)	15,736 (80.59)	1.63 (1.41, 1.89)***	1.14 (0.93, 1.40)

Notes: \*P-value ≤ 0.05; \*\*P-value ≤ 0.01; \*\*\*P-value ≤ 0.001.

Abbreviations: 3TC, lamivudine; ABC, abacavir; AOR, adjusted odds ratio; ART, antiretroviral therapy; ATV/r, atazanavir/ritonavir; AZT, zidovudine; CD4, cluster of differentiation 4; COR, crude odds ratio; ddI, didanosine; EFV, efavirenz; LPV/R, lopinavir/ritonavir; n, number; NVP, nevirapine; P-value, precession value; Ref., reference; TDF, tenofovir disoproxil fumarate; WHO, World Health Organization; VL, viral load.

recent CD4 count of 500 and above (AOR = 1.84; 95% CI: 1.47, 2.32) were positively associated with good ART drug adherence (all associations assessed are presented in Table 1).

## Discussion

The main aim of this study was to assess the level of adherence and associated factors among adolescent and adult patients on ART care in Northern Ethiopia. The good adherence rate in this study was 94.84%. This is near the current recommendation of at least 95% of ART adherence level required to suppress viral replication to achieve clinical improvement, and increased CD4 count.<sup>19</sup> The finding of this study showed a better ART medication adherence compared to the studies conducted in Gobba, Southeast Ethiopia (90.8%),<sup>20</sup> Eastern Ethiopia (85%),<sup>21</sup> Hara Town and its Surroundings, Northeast Ethiopia (71.8%)<sup>22</sup> and Gondar Referral Hospital, Northwest Ethiopia (88.2%).<sup>23</sup> On the other hand, the incomplete adherence level of this study was 5.16%, 95% CI (4.86%, 5.48%), which is lower

compared to the study conducted in Southern Ethiopia which was 13%, 95% CI (11%, 15%) of incomplete adherence level.<sup>24</sup> The differences for these findings might be due to differences in the definition of incomplete adherence, the impact of the ART program over time in creating beneficiary awareness and care provider skill in the provision of counseling. The other possible explanation might be that many of the participants included in this study had longer ART duration, and those taking the drugs for a longer duration usually acquire skills on how to deal with some of the obstacles hindering their adherence. Further, other context variations may also explain the difference observed, like the method of adherence measuring.

With regard to the age of the patients, patients in the age groups 30–34, 35–39, 45–49 and 50+ years old, their odds of having good adherence compared with those who had fair and poor adherences combined were 1.54, 1.47, 1.87 and 1.68 times higher keeping all the other variables in the model constant. Studies from Gondar, Northwest Ethiopia,<sup>23</sup> Northeast Ethiopia<sup>25</sup> and Gobba Hospital, Southeast



Ethiopia<sup>20</sup> reported that age has no significant associations with adherences. However, a study from Kenya had found that adherence to ART increased with increased age and decreased as the age goes beyond 60 years.<sup>26</sup> Another study from Rwanda has also shown that being in the age groups 18–24, 25–34 and 35–44 vs  $\geq 44$  years respectively were associated with non-perfect ART adherence.<sup>27</sup> Moreover, there are different studies contradicting the finding of this study. A study from Eastern Ethiopia showed patients who were in the age group 35–44 years old were more adherent than older age groups ( $\geq 45$  years).<sup>21</sup> The differences of these findings might be due to differences in study design and measurements and the exact reasons for poor adherence were not explored in different age groups. However, there were previous studies that reported reasons for poor adherence among young people, including denial and fear of HIV infection, low self-esteem, and unstructured and chaotic lifestyles.<sup>28,29</sup> Also, a few studies have documented high levels of risky sexual behavior among young age groups on ART.<sup>30</sup> Poor adherence to ART among young individuals may increase treatment failure and the spread of drug-resistant HIV viruses. Incomplete treatment adherence may also affect, in the future, drug choice.

For male patients, the odds of good adherence compared with fair and poor adherences combined were 0.75 times less, keeping all the other variables in the model constant. Similar findings from sub-Saharan Africa and Rwanda evidenced that being male was the main determinant for ART non-adherence.<sup>27,31</sup> Likewise, a prospective cohort observational study conducted in four health facilities in south Tigray revealed that being male was an independent risk factor for attrition from HIV care which translates into non-adherence.<sup>32</sup> However, studies from Goba Hospital, Southeast Ethiopia and Northeast Ethiopia have shown that gender was not significantly associated with ART adherence.<sup>20,25</sup> The reason why males were prone to viral non-suppression might be due to low health-seeking behavior.<sup>32–34</sup> Compared to females, males were more likely to forgo ART because of side effects.<sup>35</sup> This indicates intensive counseling support to males is in need to minimize treatment failure and drug mutations.

The odds of good adherence versus the combined poor and fair adherence were 0.52 times less among patients served in general hospitals compared to those served in referral hospitals, given that all other variables in the model are held constant. Although there were no studies which contradict or support the finding of this study, the differences might be attributed due to variation in the level of setup, experience, training and skills of the service providers.

The odds of good adherence versus the combined poor and fair adherence were 1.45 times higher among patients with a recent CD4 count of 200–499 cells/mm<sup>3</sup> compared to those patients with a recent CD4 count of  $< 200$  cells/mm<sup>3</sup>, given that all other variables in the model are held constant. Likewise, the odds of good adherence versus the combined poor and fair adherence were 1.84 times higher among patients with a recent CD4 count of  $\geq 500$  cells/mm<sup>3</sup> compared to those patients with a recent CD4 count of  $< 200$  cells/mm<sup>3</sup>, given that all other variables in the model are held constant. A previous study evidenced that patients with higher recent CD4 count were significantly associated with adherence.<sup>23</sup> A similar study also showed that low CD4 cell counts were associated with increased risk of non-adherence.<sup>35</sup> This is because good adherence contributes to greater growth of CD4 cell counts.<sup>36</sup> Or in those patients who miss building immunity, it is due to viral non-clearance from the blood in the absence of optimal adherence. Likewise, for patients with WHO staging II, III and IV compared with WHO staging I, the odds of good adherence versus the combined poor and fair adherence were 53%, 75% and 43% lower respectively, given that all of the other variables in the model held constant. However, a study from Northeast Ethiopia indicated that WHO clinical staging was not associated with medication adherence.<sup>25</sup> This difference might be in study method difference, in which the later one was with a small sample size that cannot ensure external validity. On the other hand, for patients with viral non-suppression taking viral suppression as reference, the odds of good adherence versus the combined poor and fair adherence was 46% lower, given that all of the other variables in the model held constant. There were other similar studies which support non-adherence was associated with unsustained viral suppression patients.<sup>37</sup> Likewise, higher viral loads are associated with increased risk of non-adherence.<sup>35</sup> This is because as viremia increases, the probability of complication increases, which results in forgetting the medication time.

## Strengths and Limitations of the Study

The strengths of the study are that the study was done in a relatively higher sample size with an appropriate analysis technique that provides important information regarding patients' medication adherence to ART treatment in Northern Ethiopia. Despite these strengths, the study was not without limitation. Adherence was measured based on self-report and is susceptible to recall and social

desirability bias. Due to the nature of secondary data, the analysis misses some important variables such as the existence of family support, disclosure, co-morbidity and grade of ART experience in HIV-infected patients.

## Conclusion

There was a higher level of adherence compared to the previously conducted studies in Ethiopia. Being male, patients from general hospitals, WHO staging II, III and IV and non-suppressed VL status were negatively associated with good adherence. Whereas, older ages, recent CD4 count of 200–499 and  $\geq 500$  CD4 count were positively associated with good ART drug adherence. The health system should recognize a higher need of the younger age groups and males to design targeted counseling and support for this high-risk group. The present study supports the need to promote adherence and encourage consistently high levels of adherence to achieve a good treatment outcome and slow the development of drug resistance.

## Data Sharing Statement

The data that support the findings of this study are available from the Tigray Regional Health Bureau and Tigray Health Research Institute but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data can be accessed from Tigray Health Research Institute, Institutional Review Board (IRB) via institutional.review.board.thri@gmail.com. Upon permission, de-identified data will be shared.

## Ethics Approval and Informed Consent

Ethical clearance and approval were obtained from Tigray Health Research Institute (THRI) Institutional Review Board (IRB) with a reference no. of THRI/00132/19. The dataset owned by Tigray Regional Health Bureau (TRHB) and THRI and are the legally authorized representative of the patient's data. Permission to use the data only for research purpose. Informed written consent was obtained from THRI and TRHB.

## Patient Data Confidentiality and Compliance

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki

Declaration and its later amendments or comparable ethical standards. Personal identifiers were de-identified when extracting the data from the database to maintain privacy and confidentiality of the patients.

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## Author Contributions

All authors made a significant contribution to the conception, study design, execution, and acquisition of data, analysis and interpretation. All authors involved in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

Authors' declare that there are no competing interests.

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