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Level of adherence to antiretroviral therapy and associated factor among HIV infected adults in south Gondar zone, Northwest Ethiopia.

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Abstract

Objectives: The purpose of this study was to identify levels of adherence to ART drugs and factors associated with them in northwest Ethiopia. We hypothesize that in the era of COVID-19 adherence level to ART among people living with HIV have been jeopardized.

Design: cross-sectional study.

Setting: the study was conducted in one specialized hospitals and three district hospital found in the south Gondar zone, northwest Ethiopia.

Participants: people living with HIV receiving highly Active Antiretroviral Therapy in South Gondar zone public hospitals. 432 adult peoples living with HIV receiving ART in selected public hospitals and who have been on treatment for more than 3 month period participated in the study.

Primary and secondary outcome measures: magnitude of optimal adherence and predictors for low level of adherence were assessed.

Results: among 432 study participants 81.5% (95% CI; 78-85.2) of participants were 100% adherent by using self-reported data. Determinants of lower adherence included Stigma or discrimination (OR, 0.4, p=0.016), missed scheduled clinical visit (OR, 0.45 p=0.034), being on anti-TB treatment (OR, 0.45 p=0.01], recent CD4 cells cunt less than 500 cell/mm³ (OR, 0.3 p=0.023) and patients in WHO clinical stage three at the time of ART initiation (OR, 0.24 p=0.027) were factors significantly associated with adherence to ART drugs

Conclusions: level of adherence was relatively low. Stigma or discrimination, patients who missed scheduled clinical visits, patients who had been on anti-TB treatment, respondents whose

recent CD4 cells count less than 500 cell/mm³, and patients in WHO clinical stage three were factors significantly affecting the level of adherence.

Strength and limitation of this study

- Our measurement of adherence is only based on patients' announcement of missed doses so Recall bias and social desirability bias is inherent limitations of our study.
- Self-report is proving to be a less reliable measure of adherence so interpretation needs caution.
- The study was conducted in four different public hospitals so the finding is widely applicable in the study area.

INTRODUCTION

HIV/AIDS is one of the pandemic public health problems still affecting many people. At the end of 2015, globally 36.7 million people were living with HIV. In the same year, 2.1 million people were newly infected by HIV/AIDS and 1.1 million people died from HIV-related causes [1]. Countries are taking different actions to tackle the HIV/AIDS virus epidemic as well as to improve the quality of life among people infected by the virus; one of these was the treatment of the patient with antiretroviral therapy (ART) [2]. Achievement of optimal adherence and patient retention are becoming the greatest challenges in the management of HIV/AIDS in Ethiopia. A five-year retrospective medical record review of 3012 adult patients who were enrolled in therapy at Gondar University Hospital ART clinic demonstrated that 31.4% of patients had been lost to follow-up [3]. Highly active antiretroviral therapy (HAART) includes complex regimens that require strict adherence to complicated treatment schedules due to great concern on treatment-resistant variants

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66 of HIV that rapidly develop in response to underdosing and intermittent, irregular use of
67 antiretroviral agents[4].

68 Adherence to multi-drug antiretroviral regimens has been a focus of attention since ART drugs
69 introduction owing to their complexity, frequent adverse effects, and chronic nature [5,6].

70 To get optimal viral suppression and prevent treatment failure individual should take more than
71 95% of prescribed drugs. If once the individual fails to take more than 95% of prescribed drugs
72 virologic failure rate will be more than 50% [7,8].

73 Lack of optimal adherence to antiretroviral therapy (ART) increases viral resistance, immune
74 suppression, and risk for opportunistic infection and death [9,10]. According to a World Health
75 Organization (WHO) survey study in developing countries, the HIV drug resistance rate among
76 people starting ART ranged from 4.8% in 2007 to 6.8% in 2010[11].

77 A large percentage of patients on ART find it difficult to achieve a high level of adherence.
78 Previous studies have shown that approximately 12-50% of HIV-positive patients fail to achieve
79 optimal adherence [12]. A study conducted in rural Tanzania showed that 70% of the participants
80 achieved the desired level of adherence [13]. In Soweto South Africa 88% of patients report more
81 than 95% adherence rate and the main reasons given for missing doses were being away from
82 home (30%), difficulty with the daily routine (23%), and running out of pills (12%)[14].

83 A study done in Addis Ababa city describes that only 73.3% of patients were adherent to ART.
84 The study also showed that Stigma, discrimination, and poor relationship with the health care
85 provider to be associated with low adherence [15]

86 The ability of patients to follow treatment plans optimally is frequently compromised by more
87 than one barrier, usually related to different aspects; some of them are the social and economic

88 factors, the health care team or/and system, characteristics of the disease, disease therapies and
89 patient-related factors [16].

90 A review shows that fear of disclosure, concomitant substance abuse, forgetfulness, suspicions of
91 treatment, regimens that are too complicated, number of pills required, decreased quality of life,
92 work and family responsibilities, falling asleep, and access to medication were barriers to
93 adherence [17].

94 Now on the country has developing HIV/AIDS prevention, care strategic plan in an investment
95 case approach. This is in line with the three 90's target set by UNAIDS to help end the AIDS
96 epidemic by 2030[18]. The target states that 90% of all people receiving ART will have viral
97 suppression. The plan and strategic objectives are fruitless if adherence to HAART is not well
98 recognized.

99 Having a strategy to sustain an optimal level of adherence among people living with HIV is an
100 essential step towards ensuring treatment success. So the main purpose of this study is to
101 determine the level of adherence and its predictors among people living with HIV who have been
102 using HAART. The knowledge will help to evaluate the clinical management strategies and define
103 relevant, efficient, acceptable adherence support measures for patients within the health system.

104 MATERIALS AND METHODS

105 Study setting, design, and periods

106 An institution-based cross-sectional study was conducted from August 1, 2020, to January 31,
107 2021 in four hospitals found in the south Gondar zone, Amhara region. One hospital was
108 specialized hospital (Debre tabor comprehensive specialized hospital) and the other three were
109 district hospitals (mekane eyesus hospital, addis zemen hospital and nifas mewchia hospital). All

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3 110 hospitals provide services related to ART. However; very severe cases may be referred to debre
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5 111 tabor comprehensive specialized hospital.
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9 112 **Population**

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11 113 people living with HIV (≥ 18 years old) receiving highly Active Antiretroviral Therapy (HAART)
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13 114 in South Gondar zone public hospitals were the study populations and the study participants were
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15 115 adult people living with HIV (≥ 18 years old) receiving Highly Active Antiretroviral Therapy
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17 116 (HAART) in selected public hospitals and who have been on treatment for more than 3 month
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19 117 period.
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23 118 **Sample size calculation**

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26 119 The sample size in this cross-sectional study was determined using a single proportion formula $n =$
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28 120 $(Z_{\alpha/2})^2 pq/d^2$. The minimum sample size required for the study was estimated to be 432 using the
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30 121 above formula where n is the sample size, z is the standard normal deviate set at 1.96 (for 95%
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32 122 confidence level), d margin of error acceptable or measure of precision (taken as 0.035) and
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34 123 $p = 85.3\%$ taken from the previous study [19] and sample size adjusted by 10% non-response.
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39 124 **Operational definitions**

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41 125 **Good (optimal) Adherence:** when taking all antiretroviral treatment in a correctly prescribed dose
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43 126 in the one week before the study [20].
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47 127 **Sampling technique and procedure**

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49 128 The study was conducted in four randomly selected hospitals. Then the possible number of
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51 129 participants in each of the Hospitals of the study area was allocated proportionally based on their
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53 130 patient's flow. Study participants who fulfill the inclusion criteria were included in the study using
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131 a systematic random sampling technique and every 5th interval, patient was recruited in the study
132 based on their order of arrival.

133 **Data collection instruments**

134 The data collection tool was adapted from two main sources. Questionnaire from AIDS Clinical
135 Trial Groups (AACTG)[12] adherence instrument and questionnaire from The Community
136 Programs for Clinical Research on AIDS (CPCRA)[21]. Other information, including the clinical
137 aspect of the patient, retrieves from patient medical records. Optimal adherence was considered
138 when taken all antiretroviral treatment incorrectly prescribed doses at a right time in the week
139 before the study. Otherwise, it is categorized as non-adherent. If they report having missing doses
140 during the last seven days, the questionnaire asks a range of multiple-choice questions about why
141 they miss their pills. Patients' clinical data such as WHO clinical stage and the CD4 counts were
142 retrieved from their medical records at the ART clinic by using a checklist. Data collection was
143 performed by five-diploma nurses (supervised by three BSC nurses). A two days comprehensive
144 training was given for data collectors and supervisors. The questionnaire was compiled in English
145 and evaluated by experts who had expertise in AIDS care and treatment situations in our country.
146 Five AIDS experts were invited to review the Amharic version of the questionnaire for face
147 validity and readability. The questionnaire had pilot tested on 30(5% of the sample) HIV-infected
148 people. Data collectors were trained to have a common understanding of the objective and the
149 methodology of the research. The investigators were closely supervised the performance of the
150 data collectors daily.

151 Data entry and editing were performed by EPI info and then exported to SPSS version 23 for
152 analysis. We have computed the Frequencies and percentages of different variables for description
153 as appropriate. Using Chi-square test bivariate analysis of variables was completed with Odds

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ratio at 95% confidence interval to assess the presence and degree of association between the dependent and independent variables. All explanatory variables associated with outcome variables with $p<0.2$ were entered into multivariable logistic regression analysis. Statistically significant associated factors were identified based on a $p\text{-value}<0.05$.

Patient and public involvement (PPI)

Members of the public were not involved in the study concept or design.

RESULTS

Demographic and economic characteristics

A total of 432 HIV-positive participants, who reported using ART were interviewed about their adherence to their medication, giving a response rate of 100%. The population consists of one hundred seventy-two (39.8%) male and two hundred sixty female (60.2%) and 335(77.5%) were urban residents. Out of the total population, 257(50.2%) were in the age group between 25-34 years and the mean age of study participants was 30.6 ± 8 years. The majority of participants 322(74.5%) were married. From the total population 211(48.8%) participants were government employees and the majority of patient's monthly income full between more or equal to 1000 Ethiopian birr (table 1).

Family and clinical related characteristics

Out of the total population, 255(59%) of patients disclose their serostatus. From the overall population, only 45(10.4%) of participants were got ever stigma and discrimination. Of 432 participants, 81(18.8%) of them use complementary medicine in addition to their ART drugs. Regular mealtimes 193(44.7%) was the most common reminder (Table 2).

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176 Adherence and health care service characteristics

177 Based on the patient's self-report 81.5 % (95% CI; 78-85.2) of participants had optimal adherence
178 level (take their entire daily dose) one week before the interview. The reason given for missing
179 their treatment was forgetting 31 (7.1%) and being away from home 19 (4.4%). Only 46(10.6%)
180 of study participants miss the scheduled clinical visit and 104(24.1%) patients were taking drugs
181 other than their ART medicine (table 3)

182 Factors associated with adherence to ART

183 Stigmatized or discriminated patients were 60% less likely to adhere to ART treatment compared
184 to non-stigmatized and non-discriminated patients [AOR=0.4, 95%CI (0.2-0.84)]. Patients who
185 missed scheduled clinical visits were 55% less likely to adhere to their ART treatment compared
186 to patients who didn't miss scheduled clinical visits 55%[AOR=0.45(0.21-0.94)]. Patients who
187 had been on anti-TB treatment have been 55% less likely to adhere to ART treatment compared to
188 patients who had no anti-TB treatment [(AOR=0.45(0.24-0.83)]. Respondents whose recent CD4
189 cells count less than 500 cells/mm³ were 70% less likely to adhere to treatment compared to
190 respondents whose CD4 count was greater than 500 cells/ mm³ [AOR=0.3(0.14-0.73)]. patients in
191 WHO clinical stage three at the time of ART initiation were 76% less adherent to ART therapy
192 compared to their counterpart [AOR=0.24(0.098-0.57)] (table 4).

193 DISCUSSION

194 This study focus on the magnitude of ART drug adherence and associated factors in public
195 hospitals in the south Gondar zone. This study found that 81.5 % of participants were having an

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3 196 optimal adherence rate based on a one-week recall before the actual interview. This is far less than
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5 197 finding in southwest Ethiopia where 95% of the patients were adherent with $\geq 95\%$ (optimal) of
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7 198 prescribed doses in the last 7 days [22] and northeast Ethiopia where 95.5% were taking all their
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9 199 medication [23]. Comparably higher than found in Tanzania (70%) of the participants achieved
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11 200 the desired level of adherence [13]. Other studies conducted in northeastern Ethiopia explain that
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13 201 the adherence rate was found to be 71.8% in the past seven days of respondents' recall of missed
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15 202 doses [24]. But it is almost consistent with study findings in Addis Ababa reporting 82.8%
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17 203 adherence of patients had optimal adherence [25].
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22 204 Stigmatized or discriminated patients were 60% [AOR0.4, 75%CI (0.2-0.84) less likely to adhere
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24 205 to ART treatment compared to patients who had not been stigmatized or discriminated against.
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26 206 Stigma and discrimination are major obstacles leading to reduced treatment-seeking behavior and
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28 207 ineffective HIV/AIDS prevention and care, especially in sub-Saharan Africa [26]. Patients often
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30 208 missed their doses as a result of fear of being identified as HIV-positive.
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35 209 Patients who missed appointments were 55% less likely to adhere to ART treatment compared to
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37 210 patients who didn't miss appointments [AOR=0.4595%CI (0.21-0.94)]. Achievement of optimal
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39 211 adherence and patient retention are becoming the greatest challenges in the management of
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41 212 HIV/AIDS in Ethiopia. A five-year retrospective medical record review of 3012 adult patients
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43 213 who were enrolled in therapy at Gondar University Hospital ART clinic demonstrated that 31.4%
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45 214 had been lost to follow-up [3]. Study in Uganda found that patients on ART that missed their
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47 215 appointments were more likely to miss their doses compared to those that did not miss scheduled
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49 216 appointment [27]. Suboptimal retention in care is associated with lower ART receipt and worse
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51 217 biological outcomes, including higher viral load, which can contribute to increased infectivity and
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53 218 transmission [28, 29]. Emerging system and individual level literature that describes the influence
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219 of patient satisfaction, health care empowerment, patient-provider relationships, and clinical
220 interactions on retention in care also shows promise for improving appointment attendance, and
221 for implementation of retention interventions at multiple levels [3, 30].

222 Patients who had been on anti-TB treatment have been 55% less likely to adhere to ART treatment
223 compared to patients who didn't have anti-TB treatment [(AOR=0.45(0.24-0.83)]. A cross-
224 sectional study found high levels of non-adherence (42.4%) among patients after 1 month of
225 concurrent treatment(TB and HIV treatment) [31]. We found that patients were more frequently
226 adhere to TB treatment compared to ART. This finding might be due to the shorter duration that a
227 patient must take TB treatment compared to life-long ART but may also suggest that the
228 preference for ART may be diminished when patients are receiving integrated TB/HIV treatment
229 support[32].

230 Respondents whose recent CD4 count less than 500 cell/mm³ were 70% less likely adhere to
231 treatment compared to respondent whose CD4 count greater than 500 cell/mm³
232 [AOR=0.3,95%CI,(0.14-0.73)]. Consistently high levels of adherence were an important
233 determinant of virologic and immunologic outcomes. Study shows that CD4 cell count was
234 increased by 179, 159, and 53 cells/mm³ among the groups with 100%, 80%–99%, and 0%–79%
235 adherence level respectively [33]. A review conducted in a developing country found that the
236 likelihood of the treatment failure was almost 5 times higher among patients with CD4 < 200
237 cells/mm³ compared to those with CD4 ≥ 200 CD4 cells/mm³[34]. As CD4 cell count increases,
238 viral replication decreases, which means it has an inverse relationship with viral load. As patients'
239 immune status drops, and the rate of viral load increases compared to the immune competent
240 individuals with HIV infection. In addition, users with compromised immunity are more
241 susceptible to different opportunistic infections that endure the cruel cycle of immunity depletion

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242 and viral replication [35]. Patients who had been on WHO clinical stage three at the time of ART
243 initiation were 76% less adherent to ART therapy compared to their counterparts. It has been
244 proven that HAART is effective in suppressing human immunodeficiency virus (HIV) replication,
245 decreasing morbidity and mortality associated with HIV, suppressing development and spread of
246 ART drug-resistant HIV, and improving quality of life in adults as well as children infected with
247 HIV. However, drugs don't work in patients who don't take them properly so that optimum
248 adherence to HAART is critical to the successful outcome of patients receiving therapy [7, 8].

249 **CONCLUSIONS**

250 This study demonstrated that level of adherence was relatively low compared with other local
251 studies. Stigma or discrimination, missing schedule clinical visits, being in anti-TB treatment,
252 recent CD4 cells cunt less than 500 cell/mm³, and patients in WHO clinical stage three at the time
253 of ART initiation were factors associated with adherence to ART drugs. The establishment of a
254 monitoring and evaluation system during clinical visits helps to achieve optimal adherence.

255 **ABBREVIATIONS**

256 AACTG: Adult AIDS Clinical Trial Groups; AIDS: Acquired immune deficiency syndrome;
257 ART: Antiretro Viral therapy; ARV: Antiretroviral;; CD4: Cluster differentiation; CPCRA:
258 Community Programs for Clinical Research on AIDS, HIV: human immunodeficiency; HAART:
259 highly active antiretroviral therapy UNAIDS: United Nation Acquired Immune Deficiency
260 Syndrome WHO: world health organization.

261 **Ethics approval and consent to participate**

262 Ethical approval letter was obtained from the institutional review board of Wollo university
263 college of medicine and health Sciences (no: 0156/CMHS/IRB/2020). Official Permission letter
264 was obtained from the south Gondar zone Health Department and each hospital. The objective of
265 the study was explained to all study subjects to obtain their verbal or written consent before the
266 interview. Participants were informed that they had the full right to discontinue participating in the
267 study if they felt discomfort. They were also assured that all the data provided by them would be
268 kept confidential. In addition, no personal identifiers were used.

269 **Consent for publication**

270 Not required.

271 **Availability of data and materials**

272 Full data set and other materials pertaining to this study can be obtained from corresponding
273 author on reasonable request.

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277 **Competing interests**

278 None.

279 **Acknowledgments**

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281 also grateful to the data collectors and professionals working in the ART clinic for facilitating the
282 data collection.

283 **Contributors**

284 SB conceives the research project, develops the proposal, supervised the data collection process,
285 conducts the analysis, and wrote the manuscript. TM develops the proposal, supervised data
286 collection, was involved in data analysis, and wrote the manuscript. Both authors read and
287 approved the final manuscript.

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Table 1: demographic and economic characteristics of the study participants in south Gondar zone, August 1, 2020 to January 31 2021 (n = 432)

variables	Frequency(n=432)	Percentage (%)
sex		
male	172	39.8

	female	260	60.2
Place of residence			
	urban	335	77.5
	rural	97	22.5
Aage			
	18-24	103	23.8
	25-34	217	50.2
	35-45	70	16.3
	>45	42	9.7
Monthly income			
	<1000	79	18.3
	≥1000	353	81.7
Educational status			
	Primary level of education	55	12.7
	Secondary level of education	314	72.7
	College and above	63	14.6

Table 2: family and clinical related characteristics of the study participants in south Gondar zone, August 1, 2020 to January 31 2021 (n = 432)

variables		Frequency(n=432)	Percentage (%)
Serostatus of sexual partner	positive	226	52.3
	negative	17	3.9
	unknown	189	43.7
disclosure status	Not-disclosed	177	41
	disclosed	255	59.0
To whom Serostatus disclosed	family	79	31
	Sexual partner	173	68.2
	friend	3	0.8
Stigma and discrimination	no	387	89.6

		yes	45	10.4
	Do you use complementary medicine	No	351	81.3
		Yes	81	18.8
	Do you use reminder	No	40	9.3
		Yes	392	90.7
	Base line CD4 count	≤500cells/mm ³	51	13.2
		>500cells/mm ³	336	86.8
	treatment regimens	tdf +3tc +efv	259	60.0
		azt + 3tc+efv	143	33.1
		azt +3tc +nvp	30	6.9
		tdf +3tc +efv	259	60.0
	WHO clinical disease stage during initiation of ART	Stage-I	50	11.6
		Stage-II	352	81.5
		Stage-III	30	6.9
	Recent CD4 count	≤500cells/mm ³	87	20.1
		>500cells/mm ³	341	78.9

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397 **Table 3: Adherence and health care service related characteristics of the study participants**
398 **in south Gondar zone, August 1, 2020 to January 31 2021 (n = 432)**

Variables	Frequencies(n=432)	Percentage (%)
Do you miss your dose in the last 7days		
No	352	81.5
Yes	80	18.5
No of missed doses		
1-2 doses	57	13.2
3-4 doses	23	5.3
Reason for missing to take ART medication		
Away from home	19	23.75
forgot	31	38.75

	Busy with other things	12	15
	sickness	18	22.5
Missed scheduled clinical visit			
	No	386	89.4
	Yes	46	10.6
Do you take Drugs other than ARV			
	No	328	75.9
	Yes	104	24.1

Table 4: Factors associated with ART adherence among adult patients on ART in public health institutions in south Gondar zone, August 1, 2020 to January 31, 2021.

		Adherence to ARV		COR(95%CI)	AOR(95%CI)	p-value
		adherent	Non-adherent			
drug other than ARV						
	no	275	53	1	1	
	yes	77	27	0.55(0.3-0.9)	1.14(0.53-2.45)	
stigma and discrimination patients on ART						
	no	326	61	1	1	
	yes	26	16	0.26(0.13-0.5)	0.4(0.2-0.84)	0.016
missed scheduled clinical visit						
	no	325	61	1	1	
	yes	27	19	0.27(0.14-0.51)	0.45(0.21-0.94)	0.034
Patients on TB treatment						

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	no	297	50	1	1	
	yes	55	30	0.41(0.18-0.53)	0.45(0.24-0.83)	0.01
Recent CD4 count						
	≥500 cells/mm ³	328	65	1	1	0.023
	<500 cells/mm ³	27	17	0.23(0.12-0.56)	0.3(0.14-0.73)	0.007
WHO clinical stage three at the time of ART initiation						
	Stage-I	42	8	1		
	Stage-II	291	61	0.208(0.68-0.633)		
	Stage-III	12	11	0.23(0.1-0.55)	0.24(0.098-0.57)	0.027

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Magnitude of optimal adherence and predictors for a low level of adherence among HIV/AIDS infected adults in south Gondar zone, Northwest Ethiopia: A multi-facility cross-sectional study

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Abstract

Objectives: This study aims to identify levels of adherence to ART drugs and factors associated with them in northwest Ethiopia. We hypothesize that in the era of covid -19 there would be suboptimal adherence to ART drugs.

Design: An observational cross-sectional study was conducted. Factors associated with the level of adherence were selected for multiple logistic regressions at a p-value of less than 0.2 in the analysis. Statistically significant associated factors were identified at a p-value less than 0.05 and adjusted OR (AOR) with a 95% CI.

Setting: the study was conducted in one specialized hospital and three district hospitals found in the south Gondar zone, northwest Ethiopia.

Participants: About 432 people living with HIV/AIDS receiving HAART in South Gondar zone public hospitals and who have been on treatment for more than three months period participated in the study.

Primary and secondary outcome measures: levels of adherence to ART drugs and their associated factors.

Results: among 432 study participants 81.5% (95% CI; 78-85.2) of participants had optimally adherent to ART drugs. Determinants of lower adherence included Stigma or discrimination (OR, 0.4, p=0.016), missed scheduled clinical visit (OR, 0.45 p=0.034), being on TB treatment (OR, 0.45 p=0.01], recent CD4 cells count less than 500 cell/mm³ (OR, 0.3 p=0.023) and patients who had been a WHO clinical stage three at the time of ART initiation (OR, 0.24 p=0.027) were factors significantly associated with adherence to ART drugs.

Conclusions: level of adherence was relatively low compared with some locale studies. The intervention targeted to reduce discrimination, counseling before initiation of treatment, and awareness regarding compliance is advised to improve adherence to antiretroviral regimens.

Limitation of this study

- Our measurement of adherence is based on patients' announcement of missed doses, Recall bias and social desirability bias is inherent limitations of our study.

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64 **INTRODUCTION**

65 HIV/AIDS is one of the pandemic public health problems still affecting many people. At the end
66 of 2020, globally 37.7 million people globally were living with HIV. In the same year, 1.5 million
67 people were newly infected by the virus and 680000 people died from AIDS-related illnesses [1].
68 Countries are taking different actions to tackle the HIV/AIDS virus epidemic as well as to improve
69 the quality of life among people infected by the virus; one of these was the treatment of the patient
70 with ART therapy [2].
71 Achievement of optimal adherence and patient retention are becoming the greatest challenges in
72 the management of HIV/AIDS in Ethiopia. A five-year retrospective medical record review of
73 3012 adult patients who were enrolled in therapy at Gondar University Hospital ART clinic
74 demonstrated that 31.4% of patients had been lost to follow-up [3].
75 Highly active antiretroviral therapy (HAART) includes complex regimens that require strict
76 adherence to complicated treatment schedules due to great concern on treatment-resistant variants
77 of HIV that rapidly develop in response to underdosing and intermittent, irregular use of
78 antiretroviral agents[4].
79 Adherence to multi-drug antiretroviral regimens has been a focus of attention since ART drugs
80 introduction owing to their complexity, frequent adverse effects, and chronic nature [5,6].
81 To get optimal viral suppression and prevent treatment failure individual should take more than
82 95% of prescribed drugs. If once the individual fails to take more than 95% of prescribed drugs
83 virologic failure rate will be more than 50% [7,8].
84 Lack of optimal adherence to antiretroviral therapy (ART) increases viral resistance, immune
85 suppression, and risk for opportunistic infection and death [9,10]. According to a World Health

86 Organization (WHO) survey study in developing countries, the HIV drug resistance rate among
87 people starting ART ranged from 4.8% in 2007 to 6.8% in 2010[11].

88 A large percentage of patients on ART find it difficult to achieve a high level of adherence.
89 Previous studies have shown that approximately 12-50% of HIV-positive patients fail to achieve
90 optimal adherence [12]. A study conducted in rural Tanzania showed that 70% of the participants
91 achieved the desired level of adherence [13]. In Soweto South Africa 88% of patients report more
92 than 95% adherence rate and the main reasons given for missing doses were being away from
93 home (30%), difficulty with the daily routine (23%), and running out of pills (12%)[14].

94 A study done in Addis Ababa city describes that among patients on ART drugs, 73.3% of
95 participants had an optimal level of adherence. Stigma, discrimination, and poor relationship with
96 health care providers were predictors for a suboptimal level of adherence [15].

97 The ability of patients to follow treatment plans optimally is frequently compromised by more
98 than one barrier, usually related to different aspects; some of them are the social and economic
99 factors, the health care team or/and system, characteristics of the disease, disease therapies and
100 patient-related factors [16].

101 A review shows that fear of disclosure, concomitant substance abuse, forgetfulness, suspicions of
102 treatment, regimens that are too complicated, number of pills required, decreased quality of life,
103 work and family responsibilities, falling asleep, and access to medication were barriers to
104 adherence [17].

105 Now on the country has developing HIV/AIDS prevention, care strategic plan in an investment
106 case approach. This is in line with the three 90's target set by UNAIDS to help end the AIDS
107 epidemic by 2030[18]. The target states that 90% of all people receiving ART will have viral

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108 suppression. The plan and strategic objectives are fruitless if adherence to HAART is not well
109 recognized.
110 Currently, our world including Ethiopia has been struggling to prevent and control a new
111 pandemic disease called SARS-COV-2 however, chronic diseases like HIV/AIDS were put aside
112 especially in developing countries. We hypothesize that there may be suboptimal adherence to
113 ART drugs among people living with HIV. Having a strategy to sustain an optimal level of
114 adherence among people living with HIV is an essential step towards ensuring treatment success.
115 The knowledge would help to evaluate the clinical management strategies and define relevant,
116 efficient, acceptable adherence support measures for patients within the health system. So the
117 main purpose of this study was to determine the level of adherence and its predictors among
118 people living with HIV who have been using HAART.
119 Therefore, this observational study hypothesize that in the era of covid -19 there would be
120 suboptimal adherence to ART drugs among people living with HIV/AIDS.

MATERIALS AND METHODS

Study setting, design, and periods

A multicenter facility-based observational cross-sectional study was conducted from August to January 2021 in the south Gondar zone, Amhara region. South Gondar zone is divided into 19 woredas and structured with one general hospital, seven primary hospitals. All of them are providing ART care and treatment for its consumer. In the zone, there is 6870 HIV/AIDS infected patient enrolled in ART care and treatment. In this study, four public hospitals were selected randomly which provide ART care and treatment for HIV/AIDS infected people.

Population

people living with HIV/AIDS (≥ 18 years old) receiving HAART in South Gondar zone public hospitals were the study populations and the study participants were adult people living with HIV/AIDS (≥ 18 years old) treated as out-patients in selected public hospitals and who have been on treatment for more than three month period.

Eligibility criteria

HIV/AIDS infected people whose age greater than or equal to eighteen years, PLHIV who have been on treatment for more than three month period and continuing their ART during the study period were eligible for this study.

Sampling technique and procedure

The study was conducted in four randomly selected hospitals. Then the possible number of participants in each of the Hospitals of the study area was allocated proportionally based on their patient's flow. Using the eligibility criteria each study participant was included in the study and a systematic random sampling technique (every 5th interval) was applied based on their order of arrival in the ART clinic.

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155 **Explanatory variables**

156 Socio-demographic (age, educational status, residence, marital status), personal and family-related
157 (disclosure of serostatus, stigma, and discrimination, use of complementary medicine), medication-related
158 (drug other than ARV, patients on ART, missed scheduled clinical visit), clinical (Patients on TB
159 treatment), immunological factors (Recent CD4 count, WHO clinical stage) were factors included in the
160 regression analysis.

161 **Data collection instruments**

162 The data collection tool was adapted from two main sources. Questionnaire from AIDS Clinical
163 Trial Groups (AACTG) [12] adherence instrument which measured level of adherence based on
164 patients self-report. A questionnaire from the Community Programs for Clinical Research on
165 AIDS (CPCRA) [19] was used to collect other information including the clinical aspect of the
166 patient. Taking all antiretroviral treatment at a right time in the week before the study was a cut-
167 off value to consider optimal adherence to the ART medication. Otherwise, it is categorized as
168 non-adherent. If they report having missing doses during the last seven days, the questionnaire
169 asks a range of multiple-choice questions about why they miss their pills. Patients’ clinical data
170 such as WHO clinical stage and the CD4 counts were extracted from their medical records at the
171 ART clinic by using a checklist which was adapted from different literature. Data collection was
172 performed by five diploma nurses (supervised by three BSC nurses). A two days comprehensive
173 training was given for data collectors and supervisors.

174 The questionnaire was compiled in English and evaluated by experts who had expertise in AIDS
175 care and treatment situations in our country. Five AIDS experts were invited to review the
176 Amharic version (local language) of the questionnaire for face validity and readability. The
177 questionnaire had pilot tested on 30(5% of the sample) HIV-infected people. It was reported

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3 178 reliable and valid with 0.83 α -Cronbach, shows high level of internal consistency, 85% general
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5 179 inter-observer agreement, 78% sensitivity, and 95% specificity, so it had been appropriate and
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8 180 easy to understand by participants. Data collectors were trained to have a common
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10 181 understanding of the objective and the methodology of the research. The investigators were
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12 182 closely supervised the performance of the data collectors daily.

13 14 15 183 **Operational definitions**

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17 184 **Good (optimal) Adherence:** when taking all antiretroviral treatment in a correctly prescribed dose
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19 185 in the one week before the study [20].

20 21 22 186 **Sample size calculation**

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25 187 The sample size in this cross-sectional study was determined using a single proportion formula $n =$
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27 188 $(Z_{\alpha/2})^2 pq/d^2$. The minimum sample size required for the study was estimated to be 432 using the
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29 189 above formula where n is the sample size, z is the standard normal deviate set at 1.96 (for 95%
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31 190 confidence level), d margin of error acceptable or measure of precision (taken as 0.035) and
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33 191 $p=85.3\%$ taken from the previous study [21] and sample size adjusted by 10% non-response.

34 35 36 192 **Statistical analysis**

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39 193 Data entry and analysis were done by using Epi info V.7.1 and SPSS V.23 respectively. We have
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41 194 computed the Frequencies and percentages of different variables for description as appropriate.
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43 195 Using Chi-square test bivariate analysis of variables was completed with Odds ratio at 95%
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45 196 confidence interval to assess the presence and degree of association between the dependent and
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47 197 independent variables. We hypothesize that there would be suboptimal adherence to ART drugs
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49 198 among people living with HIV so a one-tailed p-value was applied. Explanatory variables

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3 199 associated with outcome variables with $p<0.2$ were entered into multivariable logistic regression
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5 200 analysis. Statistically significant associated factors were identified based on a $p\text{-value}<0.05$.
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9 201 **Patient and public involvement (PPI)**

10 202 Members of the public were not involved in the study concept or design.
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15 204 **RESULTS**

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18 205 **Demographic and economic characteristics**

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21 206 A total of 432 HIV-positive patients, who reported using ART were interviewed about adherence
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23 207 to their medication, giving a response rate of 100%. The population consists of one hundred
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25 208 seventy-two (39.8%) male and two hundred sixty female (60.2%) and 335(77.5%) were urban
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27 209 residents. Out of the total population, 217(50.2%) were in the age group between 25-34 years and
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29 210 the mean age of study participants was 30.6 ± 8 years. The majority of participants 322(74.5%)
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31 211 were married. From the total population 211(48.8%) participants were government employees and
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33 212 the majority of patients' monthly income was more or equal to 1000 Ethiopian birr (**table 1**).
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39 213 **Family and clinical related characteristics**

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41 214 Out of the total population, 255(59%) of patients disclose their serostatus. From the overall
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43 215 population, only 45(10.4%) of participants were stigmatized and/or discriminated by their family,
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45 216 friends, or community. Of 432 study participants, 81(18.8%) were using traditional medicine in
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47 217 addition to their ART drugs. Regular mealtimes 193(44.7%) was the most common reminder
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49 218 (**Table 2**).
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220 Adherence and health care service characteristics

221 Based on the patient's self-report 81.5 % (95% CI; 78-85.2) of participants had optimal adherence
222 level (take their entire daily dose) one week before the interview. The reason given for missing
223 their treatment was forgetting 31 (7.1%) and 19 (4.4%) being away from home. Only 46(10.6%)
224 of study participants miss the scheduled clinical visit and 104(24.1%) patients were taking drugs
225 other than their ART medicine (**table 3**)

226 Factors associated with adherence to ART

227 Stigmatized or discriminated patients were 60% less likely to adhere to ART treatment compared
228 to non-stigmatized and non-discriminated patients [AOR=0.4, 95%CI (0.2-0.84)]. Patients who
229 missed scheduled clinical visits were 55% less likely to adhere to their ART treatment compared
230 to patients who didn't miss scheduled clinical visits 55%[AOR=0.45(0.21-0.94)]. Patients who
231 had been on TB treatment have been 55% less likely to adhere to ART treatment compared to
232 patients who had no TB treatment [(AOR=0.45(0.24-0.83)]. Respondents whose recent CD4 cells
233 count, less than 500 cells/mm³ were 70% less likely to adhere to treatment compared to
234 respondents whose CD4 count was greater than 500 cells/ mm³ [AOR=0.3(0.14-0.73]. patients in
235 WHO clinical stage three at the time of ART initiation were 76% less adherent to ART therapy
236 compared to their counterpart [AOR=0.24(0.098-0.57)] (**table 4**).

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241 **DISCUSSION**

242 This study focus on the magnitude of ART drug adherence and associated factors in public
243 hospitals in the south Gondar zone. This study found that 81.5 % of participants were having an
244 optimal adherence based on a one-week recall before the actual interview. This is far less than
245 finding in southwest Ethiopia where 95% of the patients were adherent with $\geq 95\%$ (optimal) of
246 prescribed doses in the last 7 days [22] and northeast Ethiopia where 95% were taking all their
247 medication [23]. Comparably higher than found in Tanzania (70%) of the participants achieved
248 the desired level of adherence [13]. Other studies conducted in northeastern Ethiopia explain that
249 the adherence rate was found to be 71.8% in the past seven days of respondents' recall of missed
250 doses [24]. But it is almost consistent with a study finding in Addis Ababa reporting 82.8% of
251 patients had optimal adherence [25].

252 Stigmatized or discriminated patients were 60% [AOR0.4, 75%CI (0.2-0.84) less likely to adhere
253 to ART treatment compared to patients who had not been stigmatized or discriminated. Stigma
254 and discrimination are major obstacles leading to reduced treatment-seeking behavior and
255 ineffective HIV/AIDS prevention and care, especially in sub-Saharan Africa [26]. Patients often
256 missed their doses as a result of fear of being identified as HIV-positive. A systematic review
257 conducted among 26,715 HIV-positive persons in 32 countries found that HIV-related stigma
258 compromised ART adherence, primarily by undermining social support and adaptive coping. The
259 study reveals the importance of social ties in promoting adherence, particularly in resource-limited
260 settings, and reflects the centrality of social integration to the experience of HIV-positive persons
261 engaged in treatment [27].

262 Patients who had been on TB treatment have been 55% less likely to adhere to ART treatment
263 compared to patients who didn't have TB treatment [(AOR=0.45(0.24-0.83)]. A cross-sectional
264 study found high levels of non-adherence (42.4%) among patients after 1 month of concurrent
265 treatment (TB and HIV treatment) [28]. Patients were more frequently adhere to TB treatment
266 compared to ART. This might be due to the shorter duration that a patient must take TB treatment
267 compared to life-long ART but may also suggest that the preference for ART may be diminished
268 when patients are receiving integrated TB/HIV treatment support[29].

269 Respondents whose recent CD4 count less than 500 cell/mm³ were 70% less likely adhere to
270 treatment compared to respondent whose CD4 count greater than 500 cell/mm³
271 [AOR=0.3,95%CI,(0.14-0.73)]. Consistently high levels of adherence were an important
272 determinant of virologic and immunologic outcomes. Study shows that CD4 cell count was
273 increased by 179, 159, and 53 cells/mm³ among the groups with 100%, 80%–99%, and 0%–79%
274 adherence level respectively [30]. A review conducted in a developing country found that the
275 likelihood of the treatment failure was almost 5 times higher among patients with CD4 < 200
276 cells/mm³ compared to those with CD4 ≥ 200 cells/mm³[31]. As CD4 cell count increases, viral
277 replication decreases, which means it has an inverse relationship with viral load. As patients'
278 immune status drops, and the rate of viral load increases compared to the immune-competent
279 individuals with HIV infection. In addition, users with compromised immunity are more
280 susceptible to different opportunistic infections that endure the cruel cycle of immunity depletion
281 and viral replication [32].

282 Patients who had been on WHO clinical stage three at the time of ART initiation were 76% less
283 adherent to ART therapy compared to their counterparts. It has been proven that HAART is
284 effective in suppressing human immunodeficiency virus (HIV) replication, decreasing morbidity

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3 285 and mortality associated with HIV, suppressing development and spread of ART drug-resistant
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5 286 HIV, and improving quality of life in adults as well as children infected with HIV. However, drugs
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7 287 don't work in patients who don't take them properly so that optimum adherence to HAART is
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10 288 critical to the successful outcome of patients receiving therapy [7, 8].
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13 289 Poor adherence has several effects on patient health. Some of them severely compromise the
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15 290 effectiveness of treatment; make this a critical issue in population health from the perspective of
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17 291 quality of health and health economics. So there should be intervention aimed at improving
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19 292 adherence because it has a significant positive return on investment through primary prevention
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21 293 and control of adverse health outcomes [33].
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25 294 Our measurement of adherence is based on PLHIV self-reports of missed doses which may be
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27 295 subject to social desirability and recall biases. This observational cross sectional study was limited
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29 296 to participants at south Gondar zone selected hospital and it include PLHIV who have been treated
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31 297 as out-patients so it exclude patients treated at in-patient level. Therefore, the results might not be
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33 298 generalizable. Using health belief model further exploration is important to identify possible
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35 299 trigger that enforcing adherence behavior. The health belief model helps to have deep insight on
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37 300 the consequences of non-adherence to ART, the personal risk of problems with regard to ART
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39 301 medication non-adherence, the value of adhering to ART, and the obstacles for not to taking their
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41 302 ART medication.
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47 303 **CONCLUSIONS**
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50 304 Stigma or discrimination, missing schedule clinical visits, being in anti-TB treatment, recent
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52 305 CD4 cells count less than 500 cell/mm³, and patients in WHO clinical stage three at the time of
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54 306 ART initiation were factors associated with adherence to ART drugs. The establishment of a
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monitoring and evaluation system during clinical visits helps to achieve optimal adherence. Maintaining relatively high CD4 cell counts during HAART encourages patients on ART to have optimal adherence, again this reduces disease severity. The intervention targeted to reduce discrimination, counseling before initiation of treatment, and educational therapy during follow-up is advised to have maximum effect on improving ART adherence.

ABBREVIATIONS

AACTG: Adult AIDS Clinical Trial Groups; AIDS: Acquired immune deficiency syndrome; ART: Antiretro Viral therapy; ARV: Antiretroviral;; CD4: Cluster differentiation; CPCRA: Community Programs for Clinical Research on AIDS, HIV: human immunodeficiency; HAART: highly active antiretroviral therapy UNAIDS: United Nation Acquired Immune Deficiency Syndrome WHO: world health organization.

Ethics approval and consent to participate

An ethical approval letter was obtained from the institutional review board of Wollo university college of medicine and health Sciences (no: 0156/CMHS/IRB/2020). Official Permission letter was obtained from the south Gondar zone Health Department and each hospital. The objective of the study was explained to all study subjects to obtain their verbal or written consent before the interview. Participants were informed that they had the full right to discontinue participating in the study if they felt discomfort. They were also assured that all the data provided by them would be kept confidential. In addition, no personal identifiers were used.

Consent for publication

Not required.

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328 Availability of data and materials

329 The full data set and other materials of this study can be obtained from the corresponding author
330 on reasonable request.

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333 not-for-profit sectors.

334 Competing interests

335 All authors declare that they have no competing interests.

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339 data collection.

340 Contributors

341 SB conceives the research project, develops the proposal, supervised the data collection process,
342 conducts the analysis, and wrote the manuscript. TM develops the proposal, supervised data
343 collection, was involved in data analysis, and wrote the manuscript. Both authors read and
344 approved the final manuscript.

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Table 1: demographic and economic characteristics of the study participants in south Gondar zone, August 1, 2020 to January 31 2021 (n = 432)

variables	Frequency(n=432)	Percentage (%)
sex		
male	172	39.8
female	260	60.2
Place of residence		
urban	335	77.5
rural	97	22.5
age		
18-24	103	23.8
25-34	217	50.2
35-45	70	16.3
>45	42	9.7
Monthly income		
<1000	79	18.3
≥1000	353	81.7
Educational status		
Primary level of education	55	12.7
Secondary level of education	314	72.7
College and above	63	14.6

Table 2: family and clinical related characteristics of the study participants in south Gondar zone, August 1, 2020, to January 31, 2021 (n = 432)

variables	Frequency(n=432)	Percentage (%)
Serostatus of sexual partner		
positive	226	52.3
negative	17	3.9
unknown	189	43.7
disclosure status	Not-disclosed	41

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	disclosed	255	59.0
To whom Serostatus disclosed	family	79	31
	Sexual partner	173	68.2
	friend	3	0.8
Stigma and discrimination	no	387	89.6
	yes	45	10.4
Do you use complementary medicine	No	351	81.3
	Yes	81	18.8
Do you use reminder	No	40	9.3
	Yes	392	90.7
Baseline CD4 count	≤500cells/mm ³	51	13.2
	>500cells/mm ³	336	86.8
treatment regimens	tdf +3tc +efv	259	60.0
	azt + 3tc+efv	143	33.1
	azt +3tc +nvp	30	6.9
	tdf +3tc +efv	259	60.0
WHO clinical disease stage during initiation of ART	Stage-I	50	11.6
	Stage-II	352	81.5
	Stage-III	30	6.9
Recent CD4 count	≤500cells/mm ³	87	20.1
	>500cells/mm ³	341	78.9

Table 3: Adherence and health care service-related characteristics of the study participants in south Gondar zone, August 1, 2020, to January 31, 2021 (n = 432)

Variables	Frequencies(n=432)	Percentage (%)
Do you miss your dose in the last 7days		
No	352	81.5
Yes	80	18.5
No of missed doses		

1-2 doses	57	13.2
3-4 doses	23	5.3
Reason for missing to take ART medication		
Away from home	19	23.75
forgot	31	38.75
Busy with other things	12	15
sickness	18	22.5
Missed scheduled clinical visit		
No	386	89.4
Yes	46	10.6
Do you take Drugs other than ARV		
No	328	75.9
Yes	104	24.1

Table 4: Factors associated with ART adherence among adult patients on ART in public health institutions in south Gondar zone, August 1, 2020, to January 31, 2021.

	Adherence to ARV		COR(95%CI)	AOR(95%CI)	p-value
	adherent	Non-adherent			
drug other than ARV					
no	275	53	1	1	
yes	77	27	0.55(0.3-0.9)	1.14(0.53-2.45)	
stigma and discrimination patients on ART					
no	326	61	1	1	
yes	26	16	0.26(0.13-0.5)	0.4(0.2-0.84)	0.016
missed scheduled clinical visit					
no	325	61	1	1	
yes	27	19	0.27(0.14-0.51)	0.45(0.21-0.94)	0.034
Patients on TB treatment					

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Recent CD4 count	no	297	50	1	1	
	yes	55	30	0.41(0.18-0.53)	0.45(0.24-0.83)	0.01
	≥500 cells/mm ³	328	65	1	1	0.023
	<500 cells/mm ³	27	17	0.23(0.12-0.56)	0.3(0.14-0.73)	0.007
WHO clinical stage three at the time of ART initiation						
	Stage-I	42	8	1		
	Stage-II	291	61	0.208(0.68-0.633)		
	Stage-III	12	11	0.23(0.1-0.55)	0.24(0.098-0.57)	0.027

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Line no
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	23-65
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	66-120
Objectives	3	State specific objectives, including any prespecified hypotheses	121-122
Methods			
Study design	4	Present key elements of study design early in the paper	135
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	136-140
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	141-155
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	157-162
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	164-175
Bias	9	Describe any efforts to address potential sources of bias	176-184
Study size	10	Explain how the study size was arrived at	186-191
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	192-193
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed	
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	195-202
		(e) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	207-208
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	208-219
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	222-228
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	229-238
		(b) Report category boundaries when continuous variables were categorized	
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	244-295
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	296-304
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	306-309
Generalisability	21	Discuss the generalisability (external validity) of the study results	310-313
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	334-355

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Magnitude of optimal adherence and predictors for a low level of adherence among HIV/AIDS infected adults in south Gondar zone, Northwest Ethiopia: A multi-facility cross-sectional study

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Keywords:	HIV & AIDS < INFECTIOUS DISEASES, PUBLIC HEALTH, Adverse events < THERAPEUTICS, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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Magnitude of optimal adherence and predictors for a low level of adherence among HIV/AIDS infected adults in south Gondar zone, Northwest Ethiopia: A multi-facility cross-sectional study

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Abstract

Objectives: This study aims to identify levels of adherence to ART drugs and factors associated with them in northwest Ethiopia. We hypothesize that in the era of covid -19 there would be suboptimal adherence to ART drugs.

Design: An observational cross-sectional study was conducted. Factors associated with the level of adherence were selected for multiple logistic regressions at a p-value of less than 0.2 in the analysis. Statistically significant associated factors were identified at a p-value less than 0.05 and adjusted OR (AOR) with a 95% CI.

Setting: the study was conducted in one specialized hospital and three district hospitals found in the south Gondar zone, Northwest Ethiopia.

Participants: About 432 people living with HIV/AIDS receiving HAART in South Gondar zone public hospitals and who have been on treatment for more than three months period participated in the study.

Primary and secondary outcome measures: levels of adherence to ART drugs and their associated factors.

Results: among 432 study participants 81.5% (95% CI; 78-85.2) of participants had optimally adherent to ART drugs. Determinants of a low level of adherence; Stigma or discrimination (OR, 0.4, p=0.016), missed scheduled clinical visit (OR, 0.45 p=0.034), being on TB treatment (OR, 0.45 p=0.01], recent CD4 cells count less than 500 cell/mm³ (OR, 0.3 p=0.023) and patients who had been a WHO clinical stage three at the time of ART initiation (OR, 0.24 p=0.027) were factors significantly associated with adherence to ART drugs.

Conclusions: level of adherence was relatively low compared with some local studies. The intervention targeted to reduce discrimination, counseling before initiation of treatment, and awareness regarding compliance is advised to improve adherence to antiretroviral regimens.

Strength and Limitations of the study

- There is a possibility of recall bias and social desirability bias.
- Findings are also generalizable only for patients treated as out-patients.
- Being a cross-sectional survey, causality cannot be inferred from those findings.
- Adherence level is a snapshot of adherence behavior during covid-19 infection.
- The present study has strength due to the use of robust data collection tools that ensured the quality of the study.

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65 **INTRODUCTION**

66 HIV/AIDS is one of the pandemic public health problems still affecting many people. At the end
67 of 2020, globally 37.7 million people globally were living with HIV. In the same year, 1.5 million
68 people were newly infected by the virus and 680000 people died from AIDS-related illnesses [1].
69 Countries are taking different actions to tackle the HIV/AIDS virus epidemic as well as to improve
70 the quality of life among people infected by the virus; one of these was the treatment of the patient
71 with ART therapy [2].
72 In Ethiopia, achieving optimal adherence and sustainable follow up in care and treatment are the
73 most difficulties in HIV/AIDS management. A five-year retrospective medical record review of
74 3012 adult patients who were enrolled in therapy at Gondar University Hospital ART clinic
75 demonstrated that 31.4% of patients had been lost to follow-up [3].
76 Highly Active Antiretroviral Therapy (HAART) involves sophisticated regimens that necessitate
77 careful adherence to intricate treatment schedules owing to the high risk of developing treatment-
78 resistant forms of HIV as a result of missing, underdosing, and irregular use of antiretroviral
79 drugs[4].
80 Adherence to multi-drug antiretroviral regimens has been a focus of attention since ART drugs
81 introduction owing to their complexity, frequent adverse effects, and chronic nature [5,6].
82 To get optimal viral suppression and prevent treatment failure individual should take more than
83 95% of prescribed drugs. If once the individual fails to take more than 95% of prescribed drugs
84 virologic failure rate will be more than 50% [7,8].
85 Antiretroviral medication noncompliance can result in negative clinical, immunological, and
86 virological effects. In the absence of good adherence, the immune system continues to be
87 distracted, resulting in lower CD4 cell levels and the establishment of resistant virus strains [9,10].

88 According to a World Health Organization (WHO) survey study in developing countries, the
89 HIV/AIDS drug resistance rate among people starting ART ranged from 4.8% in 2007 to 6.8% in
90 2010[11].

91 A considerable number of ART patients struggle to maintain a high level of adherence. According
92 to previous studies, 12 to 50 percent of HIV-positive patients do not attain adequate adherence
93 [12]. A study conducted in rural Tanzania showed that 70% of the participants achieved the
94 desired level of adherence [13]. In Soweto, South Africa 88% of patients report more than 95%
95 adherence rate, and the main reasons given for missing doses were being away from home (30%),
96 difficulty with the daily routine (23%), and running out of pills (12%)[14].

97 A study done in Addis Ababa city describes that among patients on ART drugs, 73.3% of
98 participants had an optimal level of adherence. Stigma, discrimination, and poor relationship with
99 health care providers were predictors for a suboptimal level of adherence [15].

100 Social and economic difficulties, the health-care policies, disease traits, disease therapies, and
101 patient-related factors are all potential impediments to patients complying with treatment
102 plans[16].

103 Fear of disclosure, concurrent substance abuse, forgetfulness, suspicions of treatment, overly
104 complicated regimens, number of pills required, decreased quality of life, work and family
105 responsibilities, falling asleep, and access to medication were all identified as obstacles to
106 adherence in a systematic review study[17].

107 Now on countries devised a comprehensive plan to address HIV/AIDS prevention and care. This
108 is in line with the three 90's target set by UNAIDS to help end the AIDS epidemic by 2030[18].

109 The target states that 90% of all people receiving ART will have viral suppression. The plan and
110 strategic objectives are fruitless if adherence to HAART is not well recognized.

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111 Currently, our world including Ethiopia has been struggling to prevent and control a new
112 pandemic disease called SARS-COV-2 however, chronic diseases like HIV/AIDS were put aside
113 especially in developing countries. We hypothesize that there may be suboptimal adherence to
114 ART drugs among people living with HIV. Having a strategy to sustain an optimal level of
115 adherence among people living with HIV is an essential step towards ensuring treatment success.
116 The knowledge would help to evaluate the clinical management strategies and define relevant,
117 efficient, acceptable adherence support measures for patients within the health system. So the
118 main purpose of this study was to determine the level of adherence and its predictors among
119 people living with HIV who have been using HAART.
120 Therefore, this observational study hypothesizes that in the era of covid -19 there would be
121 suboptimal adherence to ART drugs among people living with HIV/AIDS.
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MATERIALS AND METHODS

Study setting, design, and periods

A multicenter facility-based observational cross-sectional study was conducted from August to January 2021 in the south Gondar zone, Amhara region. South Gondar zone is divided into 19 woredas and structured with one general hospital, seven primary hospitals. All of them are providing ART care and treatment for its consumer. In the zone, there is 6870 HIV/AIDS infected patient enrolled in ART care and treatment. In this study, four public hospitals were selected randomly which provide ART care and treatment for HIV/AIDS infected people.

Population

people living with HIV/AIDS (≥ 18 years old) receiving HAART in South Gondar zone public hospitals were the study populations and the study participants were adult people living with HIV/AIDS (≥ 18 years old) treated as out-patients in selected public hospitals and who have been on treatment for more than three month period.

Eligibility criteria

HIV/AIDS infected people greater than or equal to eighteen years of age, PLHIV who have been on treatment for more than three months period and continuing their ART during the study period were eligible for this study.

Sampling technique and procedure

The study was conducted in four randomly selected hospitals. Then the possible number of participants in each of the hospitals of the study area was allocated proportionally based on their order of arrival. Using the eligibility criteria each study participant was included in the study and a systematic random sampling technique (every 5th interval) was applied based on their order of arrival in the ART clinics.

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158 **Explanatory variables**

159 Socio-demographic (age, educational status, residence, marital status), personal and family-related
160 (disclosure of serostatus, stigma, and discrimination, use of complementary medicine),
161 medication-related (drug other than ARV, patients on ART, missed scheduled clinical visit),
162 clinical (Patients on TB treatment), immunological factors (Recent CD4 count, WHO clinical
163 stage) were factors included in the regression analysis.

164 **Data collection instruments**

165 The data collection tool was adapted from two main sources. Questionnaire from AIDS Clinical
166 Trial Groups (AACTG) [12] adherence instrument which measured level of adherence based on
167 patients self-report. A questionnaire from the Community Programs for Clinical Research on
168 AIDS (CPCRA) [19] was used to collect other information including the clinical aspect of the
169 patient. Taking all antiretroviral treatment at a right time in the week before the study was a cut-
170 off value to consider optimal adherence to the ART medication. Otherwise, it is categorized as
171 non-adherent. If they report missed doses during the last seven days, the questionnaire asks a
172 range of multiple-choice questions about why they miss their daily dose. Patients' clinical data
173 such as WHO clinical stage and the CD4 counts were extracted from their medical records at the
174 ART clinic by using a checklist which was adapted from different literature. Data collection was
175 performed by five-diploma nurses (supervised by three BSC nurses). A two days comprehensive
176 training was given for data collectors and supervisors.

177 The questionnaire was compiled in English and evaluated by experts who had expertise in AIDS
178 care and treatment situations in our country. Five AIDS experts were invited to review the
179 Amharic version (local language) of the questionnaire for face validity and readability. The
180 questionnaire had pilot tested on 30(5% of the sample) HIV-infected people. It was reported

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3 181 reliable and valid with 0.83 α -Cronbach, shows high level of internal consistency, 85% general
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5 182 inter-observer agreement, 78% sensitivity, and 95% specificity, so it had been appropriate and
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8 183 easy to understand by participants. Data collectors were trained to have a common
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10 184 understanding of the objective and the methodology of the research. The investigators were
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12 185 closely supervised the performance of the data collectors daily.
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15 186 **Operational definitions**

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17 187 **Good (optimal) Adherence:** when taking all antiretroviral treatment in a correctly prescribed dose
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19 188 in the one week before the study [20].
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22 189 **Sample size calculation**

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25 190 The sample size in this cross-sectional study was determined using a single proportion formula $n =$
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27 191 $(Z_{\alpha/2})^2 pq/d^2$. The minimum sample size required for the study was estimated to be 432 using the
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29 192 above formula where n is the sample size, z is the standard normal deviate set at 1.96 (for 95%
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31 193 confidence level), d margin of error acceptable or measure of precision (taken as 0.035) and
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33 194 $p=85.3\%$ taken from the previous study [21] and sample size adjusted by 10% non-response.
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38 195 **Statistical analysis**

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41 196 Data entry and analysis were done by using Epi info V.7.1 and SPSS V.23 respectively. We have
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43 197 computed the Frequencies and percentages of different variables for description as appropriate.
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45 198 Using Chi-square test bivariate analysis of variables was competed with Odds ratio at 95%
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47 199 confidence interval to assess the presence and degree of association between the dependent and
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49 200 independent variables. We hypothesize that there would be suboptimal adherence to ART drugs
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51 201 among people living with HIV so a one-tailed p-value was applied. To control possible
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53 202 confounding variables explanatory variables associated with outcome variables with $p<0.2$ were
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203 entered into multivariable logistic regression analysis. Statistically significant associated factors
204 were identified based on a p-value<0.05.

205 **Patient and public involvement (PPI)**

206 Members of the public were not involved in the study concept or design.

207 **RESULTS**

208 **Demographic and economic characteristics**

209 A total of 432 HIV/AIDS infected patients who reported using ART were interviewed about
210 adherence to their medication, giving a response rate of 100%. The population consists of one
211 hundred seventy-two (39.8%) male and two hundred sixty female (60.2%) and 335(77.5%) were
212 urban residents. Out of the total population, 217(50.2%) were in the age group between 25-34
213 years and the mean age of study participants was 30.6±8 years. The majority of participants
214 322(74.5%) were married. From the total population 211(48.8%) participants were government
215 employees and the majority of patients' monthly income was more or equal to 1000 Ethiopian birr
216 (table 1).

217 **Family and clinical related characteristics**

218 Out of the total population, 255(59%) patients disclose their serostatus. From the overall
219 population, 45(10.4%) participants were stigmatized and/or discriminated by their family, friends,
220 or community. Again 81(18.8%) were using traditional medicine in addition to their ART drugs.
221 Regular mealtimes 193(44.7%) was the most common reminder (Table 2).

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224 Adherence and health care service characteristics

225 Based on the patient's self-report 81.5 % (95% CI; 78-85.2) of participants had optimal adherence
226 level (take their entire daily dose) one week before the interview. The reason given for missing
227 their treatment was forgetting 31 (7.1%) and being away from home 19 (4.4%). Only 46(10.6%)
228 of study participants miss the scheduled clinical visit and 104(24.1%) patients were taking drugs
229 other than their ART medicine (**table 3**)

230 Factors associated with adherence to ART

231 Stigmatized or discriminated patients were 60% less likely to adhere to ART treatment compared
232 to non-stigmatized and non-discriminated patients [AOR=0.4, 95%CI (0.2-0.84)]. Patients who
233 missed scheduled clinical visits were 55% less likely to adhere to their ART treatment compared
234 to patients who didn't miss scheduled clinical visits 55% [AOR=0.45(0.21-0.94)]. Patients who
235 had been on TB treatment have been 55% less likely to adhere to ART treatment compared to
236 patients who had been no TB treatment [(AOR=0.45(0.24-0.83)]. Respondents whose recent CD4
237 cells count, less than 500 cells/mm³ were 70% less likely to adhere to treatment compared to
238 respondents whose CD4 count was greater than 500 cells/ mm³ [AOR=0.3(0.14-0.73]. patients in
239 WHO clinical stage three at the time of ART initiation were 76% less adherent to ART therapy
240 compared to their counterpart [AOR=0.24(0.098-0.57)] (**table 4**).

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245 **DISCUSSION**

246 This study was focused on the magnitude of optimal ART drug adherence and associated factors
247 for a low level of adherence among HIV/AIDS infected patients at public hospitals in the south
248 Gondar zone. The study found that 81.5 % of participants were having an optimal adherence based
249 on a one-week recall before the actual interview. This is far less than the finding in southwest
250 Ethiopia where 95% of patients had optimal adherence to their prescribed doses [22] and similarly,
251 in northeast Ethiopia, 95% of patients also had optimal adherence to their medication [23].
252 However, our findings were comparably higher than those found in Tanzania, only 70% of the
253 participants achieved the desired level of adherence [13]. Another study conducted in northeastern
254 Ethiopia explains that the level of optimal adherence was found to be 71.8% in the past seven days
255 of recall of their daily doses [24]. But it is almost consistent with a study finding in Addis Ababa
256 reporting 82.8% of patients had optimal adherence [25].

257 Stigmatized or discriminated patients were 60% [AOR0.4, 75%CI (0.2-0.84) less likely to adhere
258 to ART treatment compared to their counterparts. Stigma and discrimination, especially in Sub-
259 Saharan Africa play the main role for poor patient follow up in treatment care and extensive
260 contribution for inadequate HIV/AIDS prevention [26]. Patients frequently skipped doses due to
261 fear of being identified as HIV-positive. A systematic review of 26,715 HIV-positive people in 32
262 countries discovered that HIV-related stigma hampered adherence to antiretroviral therapy (ART),
263 principally through impairing social support and adaptive measure taken to manage stigma during
264 medication. The study highlights the relevance of social relationships in improving adherence,
265 particularly in resource-constrained contexts, and highlights the importance of social integration in
266 HIV-positive people treatment experiences [27].

267 Patients who had been on TB treatment have 55% less likely to adhere to ART treatment
268 compared to patients who didn't have TB treatment [(AOR=0.45(0.24-0.83)]. A cross-sectional
269 study found that individuals who had been on TB treatment in addition to ART drugs have a high
270 level of ART non-adherence [28]. Patients were more frequently adhere to TB treatment compared
271 to antiretroviral treatment. This might be due to the shorter duration of TB treatment compared to
272 life-long ART medication. Another possible reason, patients prioritize TB treatment and would
273 have less attention to life-long ART medication to avoid the burden of medications [29].

274 Respondents whose recent CD4 count less than 500 cell/mm³ were 70% less likely adhere to
275 treatment compared to respondent whose CD4 count greater than 500 cell/mm³
276 [AOR=0.3,95%CI,(0.14-0.73)]. Study finding show that optimal level of adherence was found to
277 be a key factor in virologic and immunologic results. A CD4 cell count was increased by 179, 159,
278 and 53 cells/mm³ in the groups had 100%, 80 to 99 %, and 0% to 79 % level of adherence
279 respectively [30]. A study conducted in a developing nation, patients with CD4 counts below 200
280 cells/ mm³ had a nearly 5 times higher chance of treatment failure than those with CD4 counts
281 above 200 cells/mm³[31]. Viral replication reduces when CD4 cell count rises, implying that viral
282 burden is inversely proportional to CD4 cell count. When compared to immune-competent
283 patients with HIV infection, patients with deteriorated immune status had raised viral load.
284 Furthermore, individuals with weakened immunity are more vulnerable to a variety of
285 opportunistic illnesses, which suffer from the vicious cycle of immune depletion and viral
286 replication [32].

287 Patients who had been on WHO clinical stage three at the time of ART initiation were 76% less
288 adherent to ART therapy compared to their counterparts. It has been proven that HAART is
289 effective in suppressing human immunodeficiency virus (HIV) replication, decreasing morbidity

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3 290 and mortality associated with HIV, suppressing development and spread of ART drug-resistant
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5 291 HIV, and improving quality of life in adults as well as children infected with HIV. However, drugs
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7 292 don't work in patients who don't take them properly so optimal adherence to HAART is a crucial
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10 293 step towards the successful outcome of therapy [7, 8].
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13 294 Poor adherence has several effects on patient health. Some of them severely compromise the
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15 295 effectiveness of treatment; making this a critical issue in the population health from the
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17 296 perspective of quality of health and health economics. So there should be an intervention aimed at
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20 297 improving adherence because it has a significant positive return on patient's health through
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22 298 primary prevention and control of adverse outcomes [33].
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25 299 Using the health belief model further exploration is important to identify the possible trigger that
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27 300 enforces adherence behavior. The health belief model helps to have deep insight on the
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29 301 consequences of non-adherence to ART, the personal risk of problems about medication non-
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31 302 adherence, the value of adhering to ART drugs, and the obstacles for not taking ART medication.
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35 303 The limitations of this study were, measurement of adherence is based on PLHIV self-reports of
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37 304 missed doses which may be subject to social desirability and recall biases. Findings are also
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39 305 generalizable only for patients treated as out-patients; it excludes patients treated at the in-patient
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41 306 level. This condition may limit to conclude in-patient treated people living with HIV/AIDS.
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44 307 Since the study was conducted during the covid-19 pandemic disease, the actual magnitude of
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46 308 optimal adherence may not be similar to our finding. As this is a cross-sectional study, cause-
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48 309 effect relation could not be analyzed. Despite these limitations, our study demonstrates strengths.
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50 310 One of the strengths, it was conducted using two standardized sounded adherence measurement
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52 311 tools which helped in ensuring the quality of the studies.
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312 CONCLUSIONS

313 Stigma or discrimination, missing scheduled clinical visits, being in anti-TB treatment, recent
314 CD4 cells count less than 500 cells/mm³ and patients in WHO clinical stage three at the time of
315 ART initiation were factors associated with a low level of adherence to ART drugs. The
316 establishment of a monitoring and evaluation system during clinical visits helps to achieve
317 optimal adherence. Maintaining relatively high CD4 cell counts during HAART encourages
318 patients on ART to have optimal adherence, again this reduces disease severity. The intervention
319 targeted to reduce discrimination, counseling before initiation of treatment, and educational
320 therapy during follow-up is advised to have maximum effect on improving ART adherence.

321 ABBREVIATIONS

322 AACTG: Adult AIDS Clinical Trial Groups; AIDS: Acquired immune deficiency syndrome;
323 ART: Antiretro Viral therapy; ARV: Antiretroviral;; CD4: Cluster differentiation; CPCRA:
324 Community Programs for Clinical Research on AIDS, HIV: human immunodeficiency; HAART:
325 highly active antiretroviral therapy UNAIDS: United Nation Acquired Immune Deficiency
326 Syndrome WHO: world health organization.

327 Ethics approval and consent to participate

328 An ethical approval letter was obtained from the institutional review board of Wollo university
329 college of medicine and health Sciences (no: 0156/CMHS/IRB/2020). Official Permission letter
330 was obtained from the south Gondar zone Health Department and each hospital. The objective of
331 the study was explained to all study subjects to obtain their verbal or written consent before the
332 interview. Participants were informed that they had the full right to discontinue participating in the

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333 study if they felt discomfort. They were also assured that all the data provided by them would be
334 kept confidential. In addition, no personal identifiers were used.

335 **Consent for publication**

336 Not required.

337 **Availability of data and materials**

338 The full data set and other materials of this study can be obtained from the corresponding author
339 on reasonable request.

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342 not-for-profit sectors.

343 **Competing interests**

344 All authors declare that they have no competing interests.

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347 Office. We are also grateful to the data collectors and professionals working in the ART clinic for
348 facilitating the data collection.

349 **Contributors**

350 SB conceives the research project, develops the proposal, supervised the data collection process,
351 conducts the analysis, and wrote the manuscript. TM develops the proposal, supervised data

collection, was involved in data analysis, and wrote the manuscript. Both authors read and approved the final manuscript.

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Table 1: demographic and economic characteristics of the study participants in south Gondar zone, August 1, 2020, to January 31 2021 (n = 432)

variables	Frequency(n=432)	Percentage (%)
sex		
male	172	39.8
female	260	60.2
Place of residence		
urban	335	77.5
rural	97	22.5
age		
18-24	103	23.8
25-34	217	50.2
35-45	70	16.3
>45	42	9.7
Monthly income		
<1000	79	18.3
≥1000	353	81.7
Educational status		
Primary level of education	55	12.7
Secondary level of education	314	72.7
College and above	63	14.6

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Table 2: family and clinical related characteristics of the study participants in south Gondar zone, August 1, 2020, to January 31, 2021 (n = 432)

variables		Frequency(n=432)	Percentage (%)
Serostatus of sexual partner	positive	226	52.3
	negative	17	3.9
	unknown	189	43.7
disclosure status	Not-disclosed	177	41
	disclosed	255	59
To whom Serostatus disclosed	family	79	31
	Sexual partner	173	68.2
	friend	3	0.8
Stigma and discrimination	no	387	89.6
	yes	45	10.4
Do you use complementary medicine	No	351	81.3
	Yes	81	18.8
Do you use reminder	No	40	9.3
	Yes	392	90.7
Baseline CD4 count	≤500cells/mm ³	51	13.2
	>500cells/mm ³	336	86.8
treatment regimens	tdf +3tc +efv	259	60.0
	azt + 3tc+efv	143	33.1
	azt +3tc +nvp	30	6.9
	tdf +3tc +efv	259	60.0
WHO clinical disease stage during initiation of ART	Stage-I	50	11.6
	Stage-II	352	81.5
	Stage-III	30	6.9
Recent CD4 count	≤500cells/mm ³	87	20.1
	>500cells/mm ³	341	78.9

Table 3: Adherence and health care service-related characteristics of the study participants in south Gondar zone, August 1, 2020, to January 31, 2021 (n = 432)

Variables	Frequencies(n=432)	Percentage (%)
Do you miss your dose in the last 7days		
No	352	81.5
Yes	80	18.5
No of missed doses		
1-2 doses	57	13.2
3-4 doses	23	5.3
Reason for missing to take ART medication		
Away from home	19	23.75
forgot	31	38.75
Busy with other things	12	15
sickness	18	22.5
Missed scheduled clinical visit		
No	386	89.4
Yes	46	10.6
Do you take Drugs other than ARV		
No	328	75.9
Yes	104	24.1

Table 4: Factors associated with ART adherence among adult patients on ART in public health institutions in south Gondar zone, August 1, 2020, to January 31, 2021.

				Adherence to ARV	COR(95%CI)	AOR(95%CI)	p-value
				adherent	Non-adherent		
drug other than ARV							
	no	275	53	1		1	
	yes	77	27	0.55(0.3-0.9)		1.14(0.53-2.45)	

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Line no	Page no
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1-3	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	23-46	2-3
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	66-118	4-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	119-120	6
Methods				
Study design	4	Present key elements of study design early in the paper	135	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	136-140	7
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	142-149	7
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	N/A	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	158-162	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	164-184	8
Bias	9	Describe any efforts to address potential sources of bias	N/A	
Study size	10	Explain how the study size was arrived at	189-193	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	195-196	9
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	199-200	9
		(b) Describe any methods used to examine subgroups and interactions	N/A	
		(c) Explain how missing data were addressed	192	9
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	189-203	9-10
		(e) Describe any sensitivity analyses		

Continued on next page

Results				
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	208-209	10
	*	(b) Give reasons for non-participation at each stage	100% response rate	10
		(c) Consider use of a flow diagram	N/A	
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	209-221	10
	*	(b) Indicate number of participants with missing data for each variable of interest	No missed data	10
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N/A	
Outcome data	15	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	N/A	
	*	<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	N/A	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	224-228	11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	230-239	11
		(b) Report category boundaries when continuous variables were categorized	Table 1-4	21-24
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A	
Discussion				
Key results	18	Summarise key results with reference to study objectives	245-300	12-14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	301-309	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	311-313	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	314-318	15
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	339-340	16

N/A: Not Applicable

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.