


Antiretroviral treatment failure and associated factors among HIV patients on the first-line antiretroviral therapy at Mizan-Tepi University teaching hospital, Southwest Ethiopia

A cross-sectional study

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Abstract

The use of Antiretroviral therapy (ART) has become a standard of care for the treatment of HIV infection. The therapy restores immune function and reduces HIV-related adverse outcomes. However, treatment failure erodes this advantage and leads to an increased morbidity and compromised quality of life in HIV patients. Thus, this study aimed to assess anti-retroviral treatment failure and associated factors among HIV patients on the first line ART at Mizan-Tepi University Teaching Hospital. A cross-sectional study was undertaken among adult patient who have been on ART and attending ART Clinic of Mizan-Tepi University Teaching Hospital from September 2014 to September 2018. Data were collected retrospectively by reviewing patients' medical charts using a standard structured questionnaire. Data were entered into Epi data version 4.0.2 and then exported to SPSS version 21.0 for analysis. To identify the predictors of anti-retroviral treatment failure, multiple stepwise backward logistic regression analysis were done. P value $< .05$ was considered as statistically significant. Among 221 patients included in the study, 118 (53.39%) were females. The mean weight of study participants at ART initiation was 57.04 kg. Of the 221 patients on the first line ART, 10 (4.5%) experienced treatment failure. Of these patients, 5 (50%) and 3 (30%) experienced virological failure and clinical failure, respectively. Functional status (AOR: 3, CI: [1.13–6.5], $P < .001$) and low baseline CD4 cell count (AOR: 4.3, CI: [3.4–10.6], $P < .0001$) were found to be an independent predictors of treatment failure. The rate of first-line ART treatment failure in the study setting was substantial. Functional status and low baseline CD4 cell count were found to be an independent predictors of virological, clinical and immunological failure. Therefore, more attention should be given for the lifestyle of patients' on ART and maximize virological tests for monitoring treatment failures.

Abbreviations: AIDS = Acquired Immune Deficiency Syndrome, ART = Anti Retroviral Therapy, cART = Combination Anti-Retroviral Therapy, CD4 = Clusters of Differentiation, HAART = Highly Active Anti-retroviral Therapy, HIV = Human Immunodeficiency Virus, HIVDR = HIV Drug Resistance, MDR-TB = Multi-Drug Resistance Tuberculosis, MTUTH = Mizan Tepi University Teaching Hospital, NRTI = Nucleoside Reverse-Transcriptase Inhibitors, PCP = Pneumocystis Carnivi Pneumonia, PTB = Pulmonary Tuberculosis, PUD = Peptic Ulcer Disease, UTI = Urinary Tract Infection, WHO = World Health Organization.

Keywords: antiretroviral, Ethiopia, Mizan Tepi University teaching hospital, treatment failure

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1. Introduction

The identification and management of first-line ART failure is a key challenge for HIV programs in resource-limited settings. Staying on a failing first-line therapy is associated with an increased mortality. In addition to this, development of drug resistance limits the ability to construct new, potent, and tolerable regimens in the future. This study was aimed to determine the first-line ART failure and factors associated with it. Highly active antiretroviral treatment (HAART) has been effective in prolonging and improving the quality of life of people living with HIV by transforming it from a fatal acute disease to a manageable chronic condition.^[1]

Human immunodeficiency virus (HIV) is responsible for a worldwide pandemic, and is the cause of acquired immune deficiency syndrome (AIDS). The 2020 Joint United Nations programmes on HIV/AIDS (UNAIDS) report indicated about 3.5 million more HIV infections and 820,000 people died from AIDS-related illnesses in the same year.^[2,3] Over the past three decades, there has been an unparalleled effort to provide access to antiretroviral therapy (ART) for HIV-infected individuals in sub-Saharan Africa, the region with the highest HIV burden.^[4] Global scale-up of antiretroviral therapy has been the primary contributor to a 48% decline in deaths from AIDS-related causes.^[5]

Viral load monitoring has become the standard of care for monitoring the success of and diagnosing the failure of ART and has been explicitly recommended by the World Health Organization (WHO) since 2010. In settings in which there is no access to viral load testing, clinical monitoring alone or a combination of clinical and immunologic monitoring is used to assess response to ART and to determine treatment failure.^[6–8]

Studies conducted in different parts of Ethiopia showed the presence of treatment failure. The immunological failure rate in Deberemarkos Hospital was found to be high.^[9] Conversely, a study conducted in Gondar University Hospital showed that virologic failure rate was low (4.1%).^[10] HIV treatment failure in Ethiopia found to be high. Being on advanced WHO clinical stage, presence of opportunistic infections, and poor adherence to highly active antiretroviral therapy were the contributing factors of HIV treatment failure.^[11] In another study, treatment failure among ART users in Ethiopia was significant. Adherence, co-infection, advanced WHO clinical stage, regimen change, and disclosure are determinant factors for treatment failure.^[12]

Studies revealed that baseline clinical factors (e.g., high pretreatment viral load, low pretreatment CD4 count, prior WHO stage), drug–drug interactions, poor adherence, primary infection with drug-resistant strains of HIV were associated with treatment failure.^[13,14] In addition, inappropriate prescribing, poor patient retention on ART or late initiation or when stock-outs occur have been shown to be associated with the development of HIV treatment failure.^[15–18] Lower prevalence of HIV treatment failure based on the definition of HAART, immunological, and virological failure was 13.7% in Amhara, 6.5% in Tigray, and 1.5% in Addis Ababa, respectively.^[11] Failure can be assessed, based on WHO criteria, as clinical, immunologic, virologic or a combination. Regular treatment failure detection is low because of inadequate capacity and lack of laboratory facilities in resource-limited settings including Ethiopia.^[19]

The timing and accuracy of treatment failure in resource-limited settings is fundamental. Early detection of treatment

failure is crucial to sustain first-line therapy effectiveness. Inability to do so may lead to the accumulation of drug resistance-associated mutations and may result in increased morbidity and mortality. However, misclassification due to the need for early detection of treatment failure lead to the premature switch and use of valuable second-line regimens, which are costly and may represent the last available regimen.^[20–23]

Identification of risk factors helps to early define predictors of treatment efficacy that permit better use of these potent drugs, avoid unnecessary side effects of second-line drugs, prevent drug resistance, and reduce economic burden, especially in a resource-limited setting like Ethiopia. It also helps as a guide for health professionals and higher officials to alleviate the problem and to develop strategies to decrease the rate of treatment failure. Despite such importance, information regarding anti-retroviral treatment failure and associated factors is null in the present study setting and therefore, this study aimed to assess anti-retroviral treatment failure and associated factors among HIV patients on first line ART at Mizan-Tepi University Teaching Hospital.

2. Methods

2.1. Study setting and period

The study was conducted in Mizan-Tepi University Teaching Hospital (MTUTH), Bench Sheko Zone, Southern Nations, Nationalities and Peoples Region (SNNPR), Ethiopia. The Hospital is located 585 km away from Addis Ababa, the capital city of Ethiopia and 830 km away from Hawasa, the capital city of SNNPR. The hospital has inpatient and outpatient departments and 4 different wards including medical ward, gynecology and obstetrics ward, pediatrics ward and surgical ward. It delivers diversified health services including emergency services, dental clinic, psychiatry clinic, laboratory services, X-ray, and follow up of chronic diseases like TB, and HIV/AIDS. The Hospital has Outpatient, Inpatient, Emergency and ART Pharmacies. The study was conducted from March 19 to April 5, 2019 through patient's chart review to assess first line ART treatment failure and factors associated with ARV treatment failure.

2.2. Study design

A hospital based cross-sectional study was conducted among HIV patients on first line ART from September 2014 to September 2018 at MTUTH.

2.3. Source and study population

All adult patients living with HIV/AIDS who have enrolled for treatment at ART clinic of MTUTH were source population whereas, adult HIV patients who had received ART for at least 6 months within September 2014 to September 2018 time period and fulfilled the inclusion criteria were the study population. Adult HIV patients aged ≥ 18 years, patients who had started standard first-line ART and had taken ART for at least 6 months were included in the study whereas, patients who were on second-line ART and had incomplete data were excluded from the study.

2.4. Patient and public involvement

Since the data were collected from patients' medical chart, the patients were not directly involved in data collection process.

2.5. Outcomes variables

The dependent variable was ART treatment failure whereas, the independent variables consisted: base line CD4 cell count, sex, age, WHO disease stage during ART initiation, marital status, educational status, religion, types of ART regimen, co-morbidity, presence of opportunistic infection, and duration of initial therapy.

Treatment failure can be defined as a progression of disease after initiation of Highly active Antiretroviral Therapy (HAART).^[6] ART failure is associated with virologic failure, immunologic failure, and/or clinical failure. Immunological failure is defined as a fall in CD4 cell count to baseline (or below) or a 50% reduction from on treatment peak value or presence of persistent CD4 cell count below 100 cells/mm.^[3,24,25] Clinical failure is the occurrence of new or recurrent WHO stage 4 or some stage 3 conditions. Virological failure is said to have occurred when plasma viral load exceeds 1000 copies/mL in two consecutive measurements within a 3-month interval with adherence support after at least 6 months of following ART.^[26]

2.6. Sample size determination and sampling technique

The sample size was determined based on the single population proportion formula: $[(Z\alpha/2)^2 p(1-p)]/d^2$ with the assumption of 95% confidence interval (CI), marginal error (d) of 5%, $Z\alpha/2 = (1.96)$, and $P = 50\%$. Accordingly, the sample size was found to be 384. Then, using the correction formula ($N_f = n/(1 + n/N)$ with $N = 521$ (the number of patients on ART from September 2014 to September 2018), the required total sample size was calculated to be 221. Simple random sampling was utilized to include adult patients who fulfilled the inclusion criteria and whose charts were complete during the data collection period.

2.7. Data collection tool

The data was collected by reviewing patient charts of HIV patients who fulfilled the inclusion criteria. A data abstraction format which contained patient's socio-demographic data, baseline characteristics and treatment related data was prepared. After the abstraction format was prepared patient charts were reviewed and baseline demographic data at the time of ART initiation were recorded including sex, age at ART initiation, weight at ART initiation, marital status, religion, educational status, and substance abuse. Baseline data including significant co-morbid illness, laboratory data such as functional status at ART initiation, AIDS defining illness prior to ART were collected. Treatment related data such as, WHO stage at ART initiation, CD4 count initially, history of treatment interruption, initial first line regimen and ART failure related data such as type of treatment failure, reason for treatment failure, failing ART regimen were studied.

2.8. Data collection and procedures

Data was collected from patients medical chart through reviewing. That means, collecting important and detailed information present in the medical chart and used for study. The medical chart review (data collection process) took place at Mizan-Tepi university teaching hospital. To avoid errors and omissions, the data collectors were trained professionals who have been working at this area for more than 2 years and also

training was given before data collection. The supervisors were assigned and followed the data collectors daily. Daily thorough reviews of the collected data were put in place and important corrections were given on the subsequent days. Double entry was made to prevent error.

2.9. Quality assurance and control

Data abstraction format were prepared based on literature. To assure the quality of collected data appropriately, designed data collection instrument was used and the collected data were reviewed and checked for completeness and consistency. The Cronbach's alpha coefficient of the data collection tool was calculated to check internal consistency and it was 0.79 which is within the acceptable range.^[9,10]

Unavailable data on patient charts and which were not related to the study objectives were omitted (specially WHO disease stage, CD4 count level, initial first line ART regimen, functional status). Flow diagram of numbers of potentially eligible, examined for eligibility, confirmed eligible, included in the study, and analyzed was expressed in Figure 1.

2.10. Data processing and analysis

The data were explored to check for outliers, missing data and assumptions. During analysis, frequencies and percentages were used to describe categorical variables, while means and standard deviations were used to describe continuous variables. Bivariate logistic regression was run for all independent variables to identify variables that fits for multivariable logistic regression. Variables with a P -value $< .25$ in the bivariate analysis were included in multivariable logistic regression model to identify the predictors of ART treatment failure. A P -value $< .05$ was considered significant.

2.11. Ethical clearance

The ethical clearance was obtained from Mizan-Tepi University research ethical board. The hospital director was informed about the purpose of the study to get agreement. Patients had requested for informed consent. To ensure patient confidentiality, name and address of the patient was not recorded in the data collection format.

2.12. Operational definition

- **cART** is defined as a treatment regimen containing a non-nucleoside reverse transcriptase inhibitor (NNRTI) (either nevirapine or efavirenz), or a protease inhibitor (PI) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs), or triple NRTIs (zidovudine/lamivudine/ abacavir).
- **Treatment failure** is defined as progression of disease after initiation of HAART.
- **Virological failure** is defined as an inability to reach a viral load > 1000 copies/mL after a defined amount of time.
- **Immunologic failure** is when CD4 count falls to the base line (below or 50%) from on treatment peak value or persistent CD4 level below 100 cell/mm^3 without concomitant infection to cause transient CD4 cell decrease.
- **Clinical failure** is defined as New or recurrent WHO stage 4 conditions occurred and certain WHO stage 3 conditions.

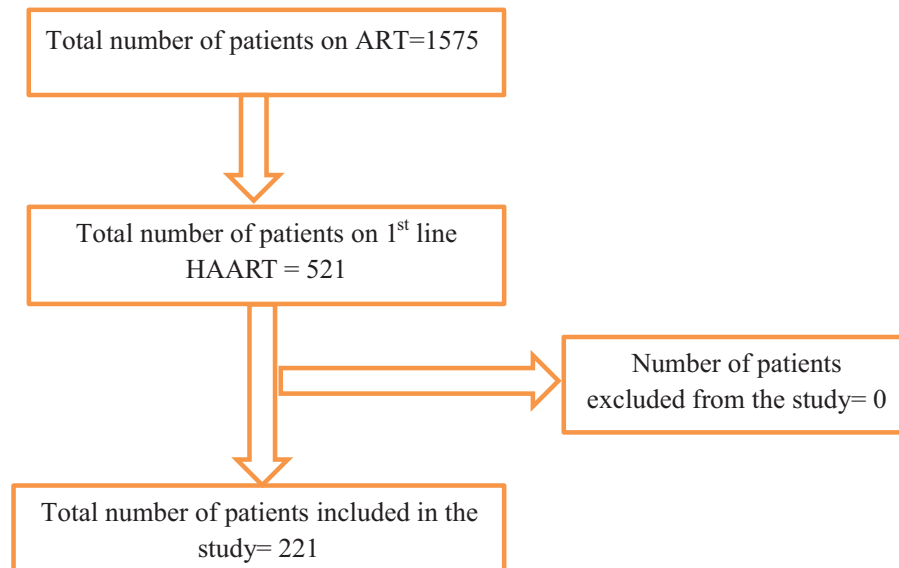


Figure 1. Schematic presentation of the sampling procedure of the study subjects.

3. Results

3.1. Socio-demographic characteristics of study participants

Out of 221 patients included in the study, 118 (53.39%) patients were females. The mean age of patients at the start of ART was 31.16 ± 0.34 years (range 18–70 years). Nearly half of the patients were the Orthodox Christians (52.5%) and had attended primary education (48.9%). Nearly one fourth of them had a history of substance abuse (27.3%) (Table 1).

Table 1
Socio-demographic characteristics of HIV/AIDS patients on antiretroviral therapy at MTUTH from September 2014 to September 2018.

Variable	Category	Frequency (%)
Sex	Female	118 (53.4)
	Male	103 (46.6)
Age	18–30	120 (54.29)
	31–45	89 (40.27)
	46–60	11 (4.9)
	>60	1 (0.45)
Weight at ART initiation	35–50	59 (26.69)
	51–65	123 (55.65)
	>65	39 (17.64)
Marital status	Never married	48 (21.7)
	Married	119 (53.8)
	Divorced	38 (17.7)
	Widowed	16 (7.2)
Religion	Orthodox	116 (52.5)
	Muslim	67 (30.3)
	Protestant	36 (16.3)
	Other*	2 (0.9)
Educational status	Primary education	108 (48.9)
	No education	50 (22.6)
	Secondary education	42 (19)
	Higher education	21 (9.5)
Substance Abuse	No	174 (78.7)
	Yes	47 (27.3)

* Catholic.

3.2. Baseline clinical characteristics of patients

The mean CD4 count at ART initiation was 255.35 cells/mm³ (range 19–848 cell/mm³). Majority of study participants, 86 (38.6) and 65(29.4) were at WHO stage I and stage III condition at time of ART initiation, respectively. Fifty-two (23.5%) of patients had one or more opportunistic infection at the time of their HAART initiation. Most of the patients 190(86%) were working by their functional status and 34 (15.4%) had significant co-morbid illness at the start of HAART, of which the majority of them 18(52.94%) suffered pulmonary tuberculosis (PTB) (Table 2).

3.3. Treatment-related information

The majority of the patients were on tenofovir-lamivudine-efavirenz 174(78.7%). All most 207(93.7%) had good adherence to their treatment. Majority of patients 80.01% were followed their treatment for >12 months and, all most 205(92.8%) have no history of treatment interruption (Table 3).

3.4. Treatment failure

A total of 10(4.5%) patients were found to have treatment failure. The main documented reason for treatment failure was non-adherence 8 (80%) of patients. As shown in Table 4, majority of treatment failure cases were on a regimen with zidovudine +lamivudine backbone which is 70%. In most of the cases, the patients had both virological and clinical failure (Table 4).

3.5. Factors associated with treatment failure

Bedridden functional status, history of treatment failure, and low baseline CD4 count (<100 cells/mm³) were the factors associated with treatment failure in binary logistic regression analysis.

Treatment failure was most likely to occur for the patients who had bedridden as compare to the patients with working functional status AOR = 3 (1.13–6.5). Similarly when compared to the patients with baseline CD4 cell count >200 cells/mm³, the

Table 2

Baseline clinical characteristics of HIV/AIDS patients on antiretroviral therapy at MTUTH ART clinic, Mizan-Aman, south west Ethiopia, June 2019.

Variable	Category	Frequency (%) N = 221
Initial CD4 cell count (cells/mm ³)	<50	8 (3.61)
	50–100	19 (8.59)
	101–199	58 (26.24)
	200–349	91 (41.17)
	350–500	29 (13.12)
	>500	16 (7.23)
WHO staging at initiation of ART	Stage 1	86 (38.6)
	Stage 2	59 (26.7)
	Stage 3	65 (29.4)
	Stage 4	11 (5)
Presence of opportunistic infections	Yes	52 (23.5)
	No	169 (76.5)
Significant comorbid illness	Yes	34 (15.4)
	No	187 (84.6)
Specified comorbidity	PTB	18 (52.94)
	Hypertension	3 (8.82)
	Asthma	2 (5.88)
	Diabetic mellitus	2 (5.88)
	MDR-TB	3 (8.82)
	PCP	1 (2.94)
	UTI	1 (2.94)
	HBV	1 (2.94)
	PTB + PUD	1 (2.94)
	Severe Anemia	2 (2.94)
Functional status	Working	190 (86)
	Ambulatory	25 (11.3)
	Bed ridden	6 (2.7)
AIDS-defining illness prior to ART	Yes	187 (84.6)
	No	34 (15.4)
Mode exposure	Sexually	58 (26.2)
	Missing	163 (73.8)

patients who had a baseline CD4 cell count <200 cells/mm³ were more likely to develop treatment failure AOR = 4.3 (1.04–10.6) (Table 5). Therefore, being bedridden and low CD4 count (<200 cell/mm³) are independent predictors of treatment failure among patients on first-line ART in the study setting.

4. Discussion

This study showed that the prevalence of first-line ART failure rate was 4.5%. This finding was comparable with study conducted in Gondar which was 4.1%.^[10] However, this result was far from what was found in the study at DebreMarkos Hospital, Ethiopia in which the failure rate was reported as 21%.^[9] The possible explanation for the observed variations could be attributed to methodological difference in the assessment of failure, sample size, socio-economic, and medical service that has a great impact on treatment failure detection. This discrepancy might be also due to the difference in study setting and difference in experienced health care professionals involved in medication adherence and counseling.

In Ethiopia, the threat of HIV treatment failure is becoming a continuing discussion. This might be due to poor HIV care services, delayed to recognize treatment failure, late initiation of HAART, high burden of opportunistic infections, lack of appropriate nutritional support, ART-associated adverse reac-

Table 3

Treatment-related information of HIV/AIDS patients on antiretroviral therapy at MTUTH from September 2014 to September 2018.

Variables	Category	Frequency (%) N = 221
Initial first-line ART regimen	TDF/3TC/EFV	174 (78.7)
	AZT/3TC/NVP	30 (13.6)
	AZT/3TC/EFV	13 (5.9)
	TDF/3TC/NVP	4 (1.8)
Duration on ART (month)	6–12	44 (19.9)
	>12	177 (80.1)
Adherence to first line regimen	Good	207 (93.7)
	Fair	8 (3.6)
	Poor	6 (2.7)
History of treatment interruption	Yes	16 (7.2)
	No	205 (92.8)
Interruption period (months)	<6	12 (75)
	6–12	4 (25)

Table 4

Treatment failure after initiation of HAART in HIV/AIDS patients at MTUTH from September 2014 to September 2018.

Variables	Category	Frequency (%) n = 221
Presence of treatment failure	Yes	10 (4.5)
	No	211 (95.5)
Reason for treatment failure	Non adherence	8 (80)
	Other	2 (20)
Type of treatment failure	Virological failure	5 (50)
	Clinical failure	3 (30)
	Immunological failure	2 (20)
Failing regimen backbone	3TC + TDF	3 (30)
	3TC + AZT	7 (70)
Months from ART initiation to second-line ART	<6	0 (0)
	6–12	9 (90)
	>12	1 (10)
CD4 at switch to second-line ART	<50	1 (10)
	50–100	3 (30)
	101–200	5 (50)
	>200	1 (10)
WHO Stage at switch to second-line regimen	Stage2	6 (60)
	Stage3	4 (40)

tion, and frequent psychological problem. Besides, the absence of frequent therapeutic drug monitors and/or resistance testing while the patient is still on the suspect or failing regimen. All four markers of lower socioeconomic status (financial hardship, non-employment, rented or unstable housing status, and non-university education) can be considered for the higher burden of HIV treatment failure in Ethiopia.^[11]

Even though the binary logistic regression showed many variables to have significant association with ART failure, multivariate logistic regression indicates that only poor adherence and low baseline CD4 cell count have strongest association with treatment failure. In the present finding, the main reason for treatment failure was non-adherence 8 (80%) of the patients. In addition, majority of treatment failure cases were on a regimen with zidovudine + lamivudine backbone which is 70%. This is in line with the study done in Felege-Hiwot Referral hospital, Ethiopia where zidovudine + lamivudine backbone was the major regimen with treatment failure.^[3]

This study found that the patients with an initial CD4 cell count of <100 cells/mm³ have more risk of developing treatment

Table 5
Multiple logistic regression analysis of first-line ART failure at MTUTH ART Clinic, Mizan-Aman Southwest Ethiopia.

Variable	Category	Treatment failure		COR 95%CI	AOR 95%CI	P
		Yes	No			
Functional status	Working			1	1	
	Ambulatory/bedridden	4 (40%)	186 (88.1%)	23.50 (3.2–16.9)*	3 (1.13–6.5)*	.001
Hx of ART failure	No	5 (50%)	11 (5.22%)	1	1	
	Yes	5 (50%)	200 (94.78%)	0.05 (0.01–0.21)*	2.1 (0.08–0.09)	.67
Adherence to first line drug	Good	1 (10%)	206 (97.63%)	1.65 (1.89–3.54)	3.58 (2.35–5.62)	.072
	Fair	3 (30%)	5 (2.37%)	0.77 (2.23–5.71)	1.67 (0.81–3.45)	.93
	Poor	6 (60%)	0 (0%)	0.96 (0.67–3.89)	1.58 (1.46–4.71)	.68
OI	No	4 (40%)	48 (22.25%)	1	1	
	Yes	6 (60%)	163 (77.25%)	2.26 (0.61–8.35)	0.44 (0.12–1.63)	.57
CD4 count	<50	2 (20%)	6 (2.84%)	0.615 (0.133–2.83)	4.75 (3.63–7.34)	.083
	50–100	1 (10%)	18 (8.53%)	0.94 (0.14–0.617)*	4.3 (1.04–10.6)*	.0001
	101–200	3 (30%)	58 (27.48%)	1.43 (0.26–0.864)*	3.6 (1.6–8.3)	.037
	>200	4 (40%)	139 (65.87%)	1	1	

ART = Antiretroviral therapy, CI = confidence interval, OI = opportunistic infection.

* Statistically significant.

failure than the patients with a higher baseline CD4 count. This might be due to the reason that the patients with a low baseline CD4 cell count have a lesser immunity that may favor the probability of developing immunological failure. Similarly, the study done in Thailand,^[27] Debreworkos Ethiopia,^[9] and Felege-Hiwot Referral hospital^[3] reported that low baseline CD4 cell count is significant predictor of immunological failure. This might be due to the reason that the patients with a low baseline CD4 cell count have a lesser immunity that may favor the probability of developing immunological failure.

This study found that the patients with an initial ambulatory functional status have 23.50 times more risk of developing treatment failure than the patients with who had working functional status. This is inline with study done in Felege-Hiwot Referral hospital, Ethiopia^[3] where patients with initial ambulatory functional status had high risk of developing treatment failure as compared to patients with working functional status. But, this finding contrasts with the studies conducted in St. Luke and Tulu Bolo hospitals and Tanzania, which indicated baseline functional status did not have an association with the hazard of treatment failure.^[28,29] This inconsistency could be due to differences in criteria used to measure ART failure and follow-up period across studies. Bedridden functional status ART initiation reflects the deprived health condition and immunologic deterioration of patients. Therefore, patients are at increased risk of opportunistic infection, increased the burden of drugs and toxicity that could negatively affect adherence to ART medications and possibly increases the risk of ART failure.

4.1. Limitations of this study

This is a retrospective chart review which may be prone to errors and omissions and a single-centered study, the result may not also be generalized to all hospitals. Thus, we suggest further prospective and multi-centered studies to be done. The study misses some important variables like drug side effects during follow-up, body mass index, status disclosure, and substance abuse at start of first-line ART which were not recorded for most of the patients.

5. Conclusion

In the present study setting, the prevalence of first-line ART failure was substantial. Treatment failure was most likely to occur for the patients who had working functional status and those who were delayed to start ART till their CD4 cell count became very low (<100 cells/mm³). functional status and low baseline CD4 cell count were an independent predictor of treatment failure among patients on the first-line ART. Early assessment of patient's functional status and CD4 level may prevent treatment failure. Therefore, avoiding delays in ART initiation, reinforcing adherence interventions, and early CD4 cell count monitoring is important to prevent treatment failure.

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Author contributions

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

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