Research Article
Volume 16:3, 2025

Journal of AIDS & Clinical Research

ISSN: 2155-6113 Open Access

Treatment Failure and Associated Factors at Second Line Regimen among HIV Infected Patients in Government Hospitals in Amhara Region, Ethiopia

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Abstract

Background: Treatment failure a current issue that is related to patients to transfer from one regimen to a more advanced and a costly treatment result to the progress of HIV/AIDS control. Many HIV patients in the world transferred from first-regimen to the second-regimen because of treatment failure. This leads the program to be more resource intensive and needs to identify predictors for treatment failure at second line regimen. Therefore, the purpose of this study was to investigate the prevalence of treatment failure and the associated factors among HIV/AIDS under second line ART regimen in Amhara region, Ethiopia.

Materials and methods: An institutional based repeated follow ups of 700 HIV positive individuals, who were switched to second line regimen from January 2020 to December 2022 in 17 government hospitals in Amhara region was conducted. Inferential statistics including the *Chi-square* test and multivariable logistic regression analysis was applied to investigate factors associated with treatment failure. Associations between treatment failure and the predictors was based on a P-value of less than 5% and confidence intervals level of 95%.

Results: Among the covariates, age of the patients (AOR=1.122, 95% CI: 1.013, 2.234), baseline CD4 cell count (AOR=0.888, 95% CI: 0.714, 0.945), patients living without their partner (AOR=1.212, 95% CI: 1.051, 1.123), females under treatment (AOR=0.786, 95% CI; 0.564, 0.845), non-opportunistic diseases (AOR=0.865, 95% CI: 0.731, 0.938), patients not disclosed their HIV status (AOR=1.241, 95% CI: 1.087, 2.341), rural patients (AOR=1.135, 95% CI: 1.032, 1.453, patient with no education (AOR=1.125, 95% CI: 1.056, 1.546), patients with low adherence (AOR=1.225, 95% CI: 1.191, 2.453), bedridden patients (AOR=1.223, 95% CI: 1.131, 1.521), ambulatory patients (AOR=1.156, 95% CI:1.091, 1.267), non-smoker patients (AOR=0.854, 95% CI: 0.686, 0.935) significantly affected on the variable of interest. Similarly, alcohol intake, drug toxicity and baseline clinical WHO stages significantly affected for the development of tuberculosis in HIV-positive patients under treatment.

Conclusion: In this study, baseline CD4 cell count, female patients, non-opportunistic diseases, and non-smoking status were negatively associated with the development of TB, whereas, age of patients, living without partners, patients with no education, patients with low adherence, bedridden and ambulatory patients were positively associated to the development of TB in HIV patients. The findings obtained in this study are important for both service providers to conduct health-related education and patients to take care of their medication adherence. More attention should be given to those positively associated variables to response variables. The regional health bureau should open TB/HIV co-infection subsections like ART sections in each hospital.

Keywords: Second-line regimen • Treatment failure • HIV/AIDS • Amhara region • Government hospitals • Quality of life

Introduction

Since the start of the HIV/AIDS epidemic, about 76 million individuals have been affected by the disease and about 35 million of them have died due to HIV/AIDS [1]. In the year, 2016 about 37 million people were living with HIV and about 70% of such people belongs to Africa especially Sub-Saharan Africa (SSA) [2]. Ethiopia is one of the Sub-Saharan African countries with the high development

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Received: 02 October, 2024, Manuscript No. JAR-24-149416; **Editor assigned:** 07 October, 2024, PreQC No. JAR-24-149416 (PQ); **Reviewed:** 22 October, 2024, QC No. JAR-24-149416; **Revised:** 03 June, 2025, Manuscript No. JAR-24-149416 (R); **Published:** 10 June, 2025, DOI: 10.37421/2155-6113.2025.16.971

of TB among people living with HIV [3]. This accounts for the country to be 10th in the world and 4th in Africa, after Nigeria, South Africa, and the Democratic Republic of Congo [4]. About 85% of the country's population is living in rural areas with low living standards, where TB is highly distributed [5]. Amhara region, one of the regions in Ethiopia, has about 30% of the people living with HIV, followed by the Oromia region (26%) [6].

The introduction and scale-up of HAART has led to a reduction in HIV related mortalities up from 1.9 million AIDS-related deaths worldwide in 2005 down to 1 million people in 2016. ART scale-up has also contributed to a decline in new HIV infections by almost 11% since 2010 from 1.9 million people to 1.7 million people in 2016.1. The global expansion of the Combination Highly Active Anti-Retroviral Treatment (CHAART) has been contributed for the decrease of about 50% of AIDS-related deaths after the epidemic of HIV/AIDS [7]. In Ethiopia, ART began in 2003 and free ART was launched in 2005 [8]. By the test and treat all patient's policy of WHO 2016, above 73,800 HIV positive patients required ART in Ethiopia. However, only near of half of these took ARV nationwide [9].

Despite the WHO recommended viral suppression monitoring to ensure for lower viral load and early identification of the treatment failure, this is not happen in practice, especially in low and middle-income countries and rural areas [10].

About 21.7 million people living with the virus accessed treatment globally in the year 2017 and of these 15.3 million belongs to Africa. In Ethiopia, ART was started in 2003 and was launched freely in 2005 [11]. In this country, more than 73,800 HIV patients required ART based on the WHO 2016 the test and treat all patients' policy [9]. However, due to different reasons like inaccessibility, costs and technical demands of the HIV RNA test, immunologic (CD4 cell count) is still widely recommended in Ethiopia for monitoring treatment failures [9]. However, CD4 cell counts have lower accuracy in identifying virological failure, leading to premature changes or continuous uses of failed regimens [12]. This leads to a more advanced and complex treatment failures, and the burden of treatment increases morbidity and mortality rates in settings where virological tests are not available [13].

There has been a clear scarcity of information about treatment failure and associated risk factors among patients at second line regimen in Ethiopia, including in the catchment study area. In addition to this, the lack of early detection of the treatment failure is highly leads to delays in switching to efficacy drugs and this further leads to weaken the ability to prevent treatment failure at individual and population level [8]. Few studies have been conducted in identifying factors on the variable of interest among patients at first line regimen only one hospital [14,15]. Including more treatment sites with more advanced and complex regimen level may have additional information on the prevalence and associated factors of treatment failure. Hence, region wide studies having different treatment site is important for further information and to take remedial action on ART program [16]. Therefore, this study was conducted to investigate the prevalence of treatment failure and its associated factors at second line regimen among HIV patients in government hospitals of Amhara region, Ethiopia. The study also aimed to assess whether the factors related to the variable of study identified in developed country also worked in the study area.

Materials and Methods

Study area

This study was conducted in Amhara region which consists of about 12 zones. There are 17 government hospitals in the region with proper documentation of HIV patients' treatment result. The study was conducted in the periods between Oct 2018-June 2021. The selection frame consists of 6.500 HIV patients whose follow ups were in the study periods. The hospital laboratory at each of the government hospitals had a separate section for CD4 cell count and an estimated 2000 blood specimens were delivered for the purpose annually in all the government hospitals. Blood specimens were collected for viral load determination, processed and made ready for transport to Amhara region People Health Institute which is located in Bahir Dar.

Study design and population

A hospital-based retrospective study was conducted on 700 HIV patients transferred from first line regimen to second line regimen. All HIV patients whose follow ups were in the study period and transferred to second line regimen were included in this study. Hence, purposive sampling technique was used to enroll the participants.

Inclusion and exclusion criterion: All HIV patients at second line regimen whose follow ups were in the study period with at least two follow ups were included under study. Hence, both adult HIV patients and HIV infected children in the government hospitals in Amhara region were included in this study. All HIV patients whose follow ups were outside of the study period and patients who did not have at least two follow ups and all HIV patients followed up in the private hospitals were excluded in this study.

Study variables

Outcome variable: Treatment failure was the response variable in this investigation. Treatment failure fails to suppress viral replication to lower than 1000 copies/mL, while immunological failure is a fall of CD4 cell counts below 200 cells/μL.

Predictor variables: The socio-demographic variables consist of age, gender, educational level, occupation, marital status, distance from home to clinic, alcohol usage, disclosure, and monthly income. The clinical variables consist of WHO clinical stages, CD4 cell count, level of adherence, drug interruption, functional status, ART dose, frequency of drug substitute, tuberculosis in the course of therapy, duration of ART, and HIV prophylaxis.

Data collection procedures and quality control

Data were collected by the health staff from the patients' medical charts. The laboratory technicians collected 4 mL and 2 ml of whole blood into Plasma Preparation Tube (PPT) and ethylene diamine tetra acetic acid (K3 EDTA) tube, for viral load test and CD4 cell counts, respectively for each participant. After 30 min, PPT was centrifuged at 1500 rpm for 10 min to separate plasma (top), in between separator gel and the cell (bottom). Ten, the plasma containing PPT was transported in a triple package sample transportation box at 2–8°C to Amhara region public Health Institute.

The CD4 cell count determination was carried out using 50 µl of EDTA whole blood added to the cartridge and run by the Becton–Dickinson biosciences (BD) Fluorescent Activated Cell Sorter (FACS) Presto near patient machines. In the analysis, the software identifies the T-Lymphocyte populations and calculates the absolute counts of CD4 cell count and results printed out.

RNA extraction from 0.2 mL of plasma and amplification reagent (master mix) preparation was done by using the Abbott m2000sp HIV-1 assay. Ten both extracted RNA and master mix were dispensed into a 96 deep well plate (made ready for amplification). In the Abbott m2000rt analyzer extracted RNAs were changed to complementary Deoxyribonucleic Acid (DNA) by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), and DNA was continued for amplification. Then, the DNA product was measured using the Abbott m2000rt quantitative real-time HIV-1 assay with HIV-1 RNA detection level depend on the amount of samples ranging 40 to 10 × 10^6 copies/ml of blood. The data collection format was developed by the investigators in consultation to the health staff. Two day's awareness training about the variables included the study was given for data collectors. The potential predictors variables included in this study were selected based on the experience obtained from the literatures.

The quality of the data was confirmed by pre-testing the questionnaire on 50 randomly selected respondents before the actual data collection stared. Amendments on the data collection format were done based on the result obtained in the pre-test. The data collection process was supervised by the principal investigator daily. The Abbott real-time HIV-1 (m2000sp) assay internal control an RNA sequence unrelated to the HIV-1 target sequence was introduced into each specimen at the beginning of sample preparation. This unrelated RNA sequence was simultaneously amplified by RT-PCR and served as an Internal Control (IC) to demonstrate that the process proceeded correctly for each sample. Also, negative, low positive and high positive controls were used. For the CD4 test, the FACS Presto machine had internal performance control. Both viral load and CD4 cell counts tests were done by experts who used standard operating procedures.

Data analysis

Before data analysis, the collected data were scan. Cleaned and checked for completeness and entered to EPI-Info version 7 and exported to SPSS version 25 for analysis. In data analysis, descriptive statistics such as frequencies, percentages, averages and deviations were used. The binary logistic regressions were also used for investigating the associated factors for treatment failure in such a way that all factors/covariates whose p-values =<0.25 in the univariate analysis were included in multiple logistic regression for adjusted odds ratios. This was important in decreasing the confounding errors of the predictor variables.

Results

Socio-demographic information

Out of a total of 700 HIV positive people, 53.6% of them were males, 54.6% of them were living without their partners, 68.6% of them were educated, 63.1% were virally unsuppressed, and 77.3% of them were urban residents. The majority of them (81.4%) were at working status.

Among participants included in this investigation, about 32% of them did not disclose their HIV status to family members. In this investigation, about 35%, 33%, and 16.9%were at WHO clinical stages IV, III, and II respectively, and about 6% of the patients were HIV/TB co-infected at the enrolment stage (baseline HIV/TB co-infection). About 2.4%, 3.9%, and 4% of the patients were alcohol consumers, smokers, and opportunistic with other diseases respectively. The baseline characteristics of the participants on categorical variables are indicated in Table 1.

Name of variable	Categories	Frequency	Percentage (%)
Sex	Male	375	53.6
	Female	325	46.4
Patient category	Children	254	36.3
	Adult	446	63.7
	Living with partner	318	45.4
Marital status at initiation of second line regimen	Living without partner	382	54.6
Level of education	Not educated	220	31.4

	Educated	480	68.6
Viral suppression at initiation of second line regimen	Suppressed	258	36.9
	Unsuppressed	442	63.1
Clinical WHO stages at the time of initiation of second line regimen	Stage I	106	15.1
	Stage II	118	16.9
	Stage III	231	33
	Stage IV	245	35
Residence area	In rural area	159	22.7
	In urban area	541	77.3
Partner HIV status at initiation of second line region	Negative	81	11.6
	Not applicable	139	19.9
	Positive	230	32.9
	Unknown	250	35.7
Functional status on the time transfer to second line regimen	Ambulatory	107	15.3
	Bed ridden	23	3.3
	Working	570	81.4
HIV/TB co-infection at transferred to second line regimen	Negative	658	94
	Positive	42	6
Alcohol intake	No	683	97.6
	yes	17	2.4
HIV disclosure status	Disclosed	476	68
	Not disclosed	224	32
Smoking status	No	673	96.1
	Yes	79	3.9
Opportunistic infections	No	672	96
	Yes	80	4

Table 1. Socio-demographic, economic and clinical variables at the initiation of second line regimen (n=700).

Similar to the categorical variables, continuous variables were also summarized in this investigation. In this regard, the average (median) weight of the patients was 48 kg (IQR: 52, 64), and the average age in years of all patients was 30.67 years (st. dev=9.7 years). The average (median) baseline CD4 cell count at the initiation of second line regimen for all patients was 120 cells/mm^3 (IQR: 113,160).

Clinical variables during HAART

The clinical outcome variables at initiation of second line regimen and each visiting time of the second line regimen were also recorded. The clinical outcome variables recorded at the end of the study time are indicated in Table 2.

Name of variable	Categories	Frequency	Percentage (%)
Viral suppression	Suppressed	189	32.7
	Unsuppressed	389	67.3
Clinical WHO stages	Stage I	118	20.4
	Stage II	120	20.8

	Stage III	186	32.2
	Stage IV	154	26.6
Partner HIV status	Negative	54	9.3
	Not Applicable	120	20.8
	Positive	189	32.7
	Unknown	215	37.2
Functional status	Ambulatory	96	16.6
	Bed ridden	35	6.1
	Working	447	77.3
HIV/TB co-infection at enrollment	Negative	349	60.4
	Positive	229	39.6
Adherence status	Adherent	227	39.3
	Non-adherent	351	60.7
HIV disclosure status	Disclosed	445	77
	Not disclosed	133	23
Opportunistic status	No	254	43.9
	Yes	324	56.1
Drug toxicity	No	257	44.7
	Yes	321	55.5

Table 2. Clinical outcome variables after HAART (end of study period).

As it is indicated in Table 2, about 67.3% of the patients got treatment failure, 77.3% of the patients were at working status, 60.7% of the patients under treatment were non-adherent, 23%of the patients did not disclose to people living with them, 56% of them faced opportunistic with other infectious diseases and 55.5% of the patients faced drug toxicity. To identify the covariates that should be included in the multivariate data analysis, a univariate data analysis was conducted as shown in Table 3. As it is indicated in the univariate data analysis in Table 3, the covariates age of patients and CD4 cell count at initiation of second line regimen were significant at 25% CI. Similarly, the factors such as patient category, marital status, sex of patients, opportunistic infections, existence of mental depression, disclosure of HIV status, residence area, level of education, adherence to HAART, HIV functional status, smoking status alcohol intake status, drug toxicity and WHO clinical stages were also significant at 25% CI. Hence, all these variables should be included for multivariate data analysis in identification of associated factors for treatment failure. Among those patients who disclosed their disease status, a considerable number of them (65%) declared social support was given to them by families and communities around them. Similarly, an incidence of mental depression among the participants was also inventoried using Beck's depression inventory scale at each visit and the result showed that 27 (3.7%) of them were mentally depressed.

The nature of the missingness pattern in the current investigation was tested using a logistic regression model which is known to be monotone (dropouts). The pattern indicates that there were no missing observations in the first two visits and the number of dropouts increased linearly as follow-up times/visits increased. The result, in this regard, revealed that dropouts were not affected by the previous outcomes (β=0.5017, p=0.862). Hence, the missingness pattern was Missed Completely at Random (MCAR).

In data analysis, missed values were handled using multiple imputation techniques. The association between covariates and the variable of interest was assessed using the Chi-square test of association.

Hence, the potential predictor variables from univariate analysis were selected for multivariate analysis considering p-values less than 0.25 for variables to be significant. The result of multivariate data analysis for this investigation was indicated in Table 4. The significant predictors of the variable of interest under multivariate analysis are interpreted as follows.

Parameter	COR	Standard error	p-value
Age	1.022	1.122	0.064*
CD4 cell count at start of second line regimen	0.011	0.888	0.115*
Patient category	0.012	0.653	0.153*
Marital status	1.96	1.212	0.021*
Sex	0.015	0.786	0.021*
Opportunistic with other diseases	0.131	0.865	0.031*
Existence of mental depression/stress	0.021	1.021	0.173*
Disclosure of the HIV status to people living together	1.23	1.241	0.102*
Residence area	1.116	1.135	0.248*
Level of education	1.024	1.125	0.112*
Adherence to HAART	1.035	1.225	0.014*
HIV Functional status	1.424	1.223	0.223*
Smoking status	0.223	0.854	0.101*
Alcohol intake	0.124	0.874	0.202*
Drug toxicity	1.062	1.076	0.101*
WHO clinical stages	0.234	0.254	0.013*

Table 3. Univariate data analysis for treatment failure at second line regimen.

Among the participants under this investigation, about 39.6% of the HIV patients got treatment failure at the end of the study period. Different factors played a significant role for the event of treatment failure and these factors are discussed in Table 4. The significant predictors of the variable of interest under multivariate analysis are interpreted as follows.

Variables/Covariates	Coefficient	Standard error	AOR	95% for AOR	p-value
Age	0.022	0.831	1.122	(1.013, 2.234)	0.01*
Baseline CD4 cell count	-0.011	0.901	0.888	(0.714, 0.945)	0.01*
Patient category (Ref.=Adults)					
Children(age <15 years)	-0.014	0.698	0.043	(0.001, 0.231)	0.002*
Marital status (Ref. =With partner)					
Without partners	0.016	0.972	1.212	(1.051, 1.423)	0.021*
Sex (Ref.=Male)					
Female	-0.015	1.101	0.786	(0.564, 0.845)	0.021*
Opportunistic infections (Ref.=yes)					
No	-0.131	1.002	0.865	(0.731, 0.938)	0.031*
Existence of mental depression/stress (Ref.=yes)					
No	-0.021	0.963	1.021	(1.231, 1.282)	0.073
Disclosure of the HIV status to people living together(Ref.=yes)					
No	0.23	0.913	1.241	(1.087, 1.841)	0.002*
Residence area (Ref.=Urban)					
Rural	0.116	0.946	1.135	(1.032, 1.453)	0.048*
Level of education(Ref.=educated)					

Non-educated	0.024	0.921	1.125	(1.056, 1.546)	0.012*
Adherence to AART (Ref.=adherent)					
Non-adherent	0.035	1.018	1.225	(1.191, 2.453)	0.014*
Functional status (Ref.=working)					
Bed ridden	0.424	1.024	1.223	(1.031, 1.521)	0.023*
Ambulatory	0.013	1.001	1.156	(1.091, 1.267)	0.001*
Smoking status (Ref. =yes)					
No	-0.223	1.401	0.854	(0.686, 0.935)	0.001*
Alcohol intake (Ref.=yes)					
No	-0.124	1.103	0.874	(0.735, 0.972)	0.002*
Drug toxicity (Reference=yes)					
No	0.989	1.901	1.076	(1.064, 1.145)	0.001*
Baseline clinical stages (Ref.=Stage IV)					
Stage I	0.586	1.034	1.796	(0.043, 0.442)	0.013*
Stage II	0.621	1.032	2.272	(0.091, 0.342)	0.002*
Stage III	0.6129	0.931	1.86	(0.018, 0.143)	0.001*

Note: COR: Crude ODDS RATIO, AOR: Adjusted Odds Ratio, *stands for statistically significant variable

Table 4. Parameter estimates using multivariate data analysis for treatment failure.

Age had a significant effect on the development of treatment failure at second line regimen among HIV-infected patients. As age enlarged by one year, the expected odds of having treatment failure was also increased by 12.2%, keeping the other covariates constant (AOR=1.122, 95% CI: 1.013, 2.234, p-value<0.001).

As, CD4 cell count of HIV positive people at the start of second line regimen increase by one cell/mm3, the expected odds of developing treatment failure on HIV positive people was decreased by 11.2%, considering the other covariates the same (AOR=0.888, 95% CI: 0.714, 0.945, p-value<0.001).

Marital status had a significant effect on the development of TB in HIV positive patients. Hence, the expected odds of developing treatment failure for HIV patients living without partners was increased by 21.2% than patients living with partners, given the other covariates constant (AOR=1.212, 95% CI: 1.051, 1.323, p-value=0.021).

The sex of patients also significantly affected the variable of interest. Comparing female patients with males, the expected odds of developing treatment failure for female HIV-patients was decreased by 21.4% as compared to males (AOR=0.786, 95% CI: 0.564, 0.845, p-value=0.021), keeping the others constant.

Opportunistic infections significantly affected the development treatment failure. The expected odds of developing treatment failure for patients without opportunistic infections was decreased by 13.5% than patients with opportunistic infections, keeping the other covariates constant (AOR=0.865, 95% CI: 0.731, 0.938, p-value=0.031).

The expected odds of developing treatment failure for patients at second line regimen who did not disclose their disease status to people living with them was increased by 24% as compared to patients who disclosed their disease status (AOR=1.241, 95% CI: 1.087, 1.341, p-value=0.002).

The expected odds of developing treatment failure for HIV-patients living in rural areas was increased by 13.5% as compared to urban HIV patients, keeping the other variables constant (AOR=1.135, 95% CI: 1.056, 1.246, p-value=0.048).

Education significantly affected the variable of interest under investigation. The expected odds of developing treatment failure for non-educated patients was increased by 12.5% as compared to educated patients, keeping the other covariates constant (AOR=1.125, 95% CI: 1.056, 1.546, p-value=0.012).

Medication adherence played a significant for the development of treatment failure in HIV-positive adults. Hence, the expected odds of developing treatment failure for medication non-adherent patients was increased by 22.5% as compared to medication adherent patients (AOR=1.225, 95% CI: 1.191, 2.453, p-value=0.014).

The functional status of HIV patients played a significant contribution to the possibility of developing treatment failure in HIV positive people at second line treatment. Hence, the expected odds of developing treatment failure for bedridden functional status of HIV patients was increased by 22.3% as compared to working status, keeping the other variables constant (AOR=1.223, 95% CI: 1.131,

1.521, p-value=0.023). Similarly, the expected odds of developing treatment failure for ambulatory functional status of HIV patients was increased by 15.6% as compared to working status, keeping the other variables constant (AOR=1.156, 95% CI: 1.091, 1.267, p-value=0.001).

The expected odds of developing treatment failure for non-smoker HIV patients was decreased by 14.6% as compared to smokers, considering the others the same (AOR=0.854, 95% CI: 0.686, 0.935, p-value=0.001). Similarly, the expected odds of developing treatment failure for patients who did not drink alcohol was decreased by 12.6% than patients who drank alcohol, considering the others the same (AOR=0.874, 95% CI: 0.735, 0.972, p-value=0.002).

Similar to the above significant variables, WHO stages and drug toxicity also affected significantly for the development of TB on HIV-positive patients in this investigation.

Discussion

It is clear that the plasma viral load test is now increasingly used to check the success of patients on antiretroviral therapy since several studies have shown that the risk for HIV transmission is very low when the viral load is lower than 1000 copies/ml. Our study revealed that about 83.4% of the respondents' viral load was below 1000 copies/ml (suppressed), and most of them had chances to decrease treatment failure, minimize transmission to others and the risks for clinical conditions, indicating that a combination of ART was highly effective for patients' recover and the decline of opportunistic infection.

Significant HIV associated morbidity and mortality had been reported in pre-ART era. Following the introduction of HAART, however, the quality of life and disease related outcomes have been improved with specialty in high HIV burden countries like Ethiopia [17].

On the other hand, we reported that the prevalence of virological treatment failure was 16.6% (95% CI 12.5–20.9) among participants. The result was comparable to reports of previous studies in Gondar (14.7%) [8] and Addis Ababa (19.8%) [18]. Likewise, our report was consistent with findings in Uganda (14.5%) [10], India (12.7%) [7], Shenzhen, China (13.4%) [19], Haiti (14.2%) [20].

On the other hand, our result was higher when compared to the WHO 2015–2020 target of 10% virological treatment failure among HIV-1 positive patients with ART follow-ups. Our finding was also higher than what were reported by other Ethiopian studies (5.3 to 11.5%) [19].

The reasons for the higher failure might be poor adherence and longer duration on ART. Variations in virological failure might be related to the WHO guideline which varies over time. For instance, in our study virological failure was defined as viral load above 1000 copy/ml based on the 2016 WHO guideline [7]. However, some researches defined virological failure as a viral load >400 copy/ml in line with previous WHO guideline [18]. If studies were done on records, the results may be overestimated because patients are tested only when they are suspected to develop treatment failure, not on routine basis. Patients with poor adherence had above six times higher odds to develop treatment failure (AOR=6.367, 95% CI 2.355–17.2, P=001) compared to those who adhere. Poor adherence leads to a low level of antiretroviral effect in the body, and this causes insufficient to suppress viral replication, finally resulting in treatment failure. In addition, individuals with CD4+ count 72 months on treatment. Reasonably, if the duration of ART increases, the emergence of HIV-DR strain is expected as a result of HIV error-prone replication, mutation rate, and viral recombination [19]. Over time, acquired drug resistance (during on ART) might cause treatment failure; so patients with shorter duration (6–24 months) on ART have a less likely incidences of acquiring drug resistant viruses than those with longer (>73 month) among exposure to ART.

Thus a high burden of a drug-resistant virus with an increased viral load is expected among patients with more months than with lesser months on ART. Besides, the possible reason might be that as the duration of ART increases, the likelihood of poor adherence, drug interruption, and drug side effects also increase. Furthermore, immunological failure was found to be 6.1% (95% CI 3.4–9.5). The finding was in line with those of studies conducted in Ethiopia and reported 3.8–6.8%. However, it was lower than the results of other studies in Ethiopia 15–21%, Tanzania 19%, and Shenzhen China 18.4% [12]. Our work showed a lower immunological failure than some studies in Ethiopia and abroad. The possible reason for the low result might be the low sensitivity of the test. Immunological failure may also be related to the WHO guideline which varies over time. For instance, in our study immunological failure was defined as a fall of CD4+ count below 250 cells/μL following clinical failure or as a persistent CD4+ count below 100 cells/μL based on the 2016 WHO guideline. However, a former research defined immunological failure as a fall of CD4+ count to baseline or below severe immune suppression (CD4+ count)

Conclusion

In the present study, the burden of antiretroviral treatment failure according to WHO virological criteria was more than the 10% WHO target failure.

The Immunological test had low predictive values for detecting treatment failure compared to viral load estimation as a standard method. Poor adherence, CD4+ count <500 cells/μL and prolonged duration on ART were significant for virological failure. Therefore, our finding indicates the need for more focus and effort from the study area hospital and concerned bodies on significant risk factors to maximize the successes of patients' health by preventing, enhance early detection and monitoring of antiretroviral treatment failure and control further complications.

Limitations

The finding of the study is limited owing to the fact that specific drug resistance was not confirmed using genotypic method for resistance and susceptibility, for lack of resources. Being an institutional-based study, the result may not also be generalized to wider population. Despite its limitation, however, the work, we believe, provides important information which would be useful for the ART treatment programs in the country.

Declaration

All methods were performed in accordance with the ethical standards as laid down in the declaration of Helsinki. Hence, an informed consent was waived by Bahir Dar University research technical and ethical review board with ref. no Stat-S/ 166/2022, as a retrospective nature of the data used in the current study. The study was approved by Bahir Dar University research technical and ethical review board.

Authors' Contribution

Awoke Seyoum Tegegne contributed in proposal development, data collection, data analysis and writing the manuscript. Getu Degu participated in data analysis, writing the manuscript and edited the manuscript based on his rich experience in publication.

Competing Interests

Authors declared that there was no conflict of interest between authors and between authors and institutions.

Data Availability

The data used for the current investigation is available within the corresponding author.

Funding

This research did not receive any specific grant from funding agencies in the public.

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How to cite this article: Tegegne, Awoke Seyoum, and Getu Degu Alene. "Treatment Failure and Associated Factors at Second Line Regimen among HIV Infected Patients in Government Hospitals in Amhara Region, Ethiopia." *AIDS Clin Res* 16 (2025): 971.