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Research Article

Incidence Rate and Predictors of Switching to Second-Line Antiretroviral Therapy among Outpatient Adults with HIV at Adola and Negele General Hospitals in Guji Zone, South Ethiopia

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Abstract

Background: The emergence of drug resistance is of great concern, as it leads to failure of treatment. In Ethiopia, data on the causes and predictors of switching ART drug regimens between nonroutine viral load monitoring settings are limited, and the need for secondary ART regimens is unclear.

Objective: This study aimed to determine the incidence and predictors of switching to secondary ART in HIV-positive adult outpatients at Adola and Negele General Hospital, Gujii zone, southern Ethiopia, in 2021.

Methods: An institutional retrospective cohort study was carried out from June 2010 to June 2020. Data came from patient records that were chosen using simple random selection. EPI-Data version 4.6 was used to enter the data and STATA version 15 was used to analyze them. The survival rates of several groups of patients were compared using Kaplan-Meir curves and logarithmic rank tests. To find predictors, the Cox proportional hazards model is utilized.

Results: The incidence rate of the first change in ART regimen was 1.14 (95% CI: 0.88-1.17) per 100 person years, with a median survival of 104 months. Viral load 150–1000 copies/mL and >1000 copies/mL (Adjusted Hazard Ratio (AHR)=4.3, 95% CI=1.4 to 12.6 and 7.3, 95% CI=2.6 to 20.3), compliance rate <85% (AHR=5.9, 95% CI=3-11.5), baseline CD4 count <100 cells/mm3 (AHR=2, 95% CI=1.53-4), disclosure status (AHR=1.8, 95% CI=1.1-3.1) were significant predictors of initial regimen change.

Conclusions: The incidence of initial regimen change was considered low. The viral load from 150 to 1000 and >1000 copies/mL, adherence level <85%, baseline CD4 count <100 cells/mm3, and non-disclosure of HIV serostatus were independent of the initial change of the ART regimen. was shown to be a predictor. All stakeholders should focus on patients with high viral loads, low CD4 counts, and poor adherence to reduce the number of HIV patients who fail treatment.

Keywords: ART; Switch to second-line regimens; Predictors; Incidence rate; South Ethiopia

Abbreviations and Acronyms: 3TC: Lamivudine; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; ATV/r: Atazanavir/ritonavir; AZT: Stavudine; cART: Combined Antiretroviral Therapy; CD4: Cluster Differentiation T-Lymphocyte; HAART: Highly Active Antiretroviral Therapy; HIV: Human Immune Virus; HIVDR: Human Immune Virus Drug Resistant; MRD: Multiple Drug Resistant; NVP: Nevaprine; PI: Protease Inhibitors; PLWHA: People living with HIV/AIDS; PMTCT: Prevention Mother To Child Transmission; PY: Person-Years; SPSS: Statistical package for Social Science; TB: Tuberculosis; TDF: Tenofovir Disoproxil Fumarate; WHO: World Health Organization

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Background

The introduction of Highly Active Antiretroviral Therapy (HAART) is an important milestone in the history of HIV disease, dramatically reducing morbidity and mortality and improving the quality of life of people living with HIV/AIDS (PLWHA) [1]. However, due to several factors, including regimen nonadherence, mutations with resistant strains of the virus have been found to date, and reports of the MRD (multidrug resistant) virus in treatment-experienced HIV patients are increasing [2].

At the end of June 2020, 26 million people had access to antiretroviral therapy [3]. According to global estimates for 2016, approximately 5.5% of patients worldwide received second-line treatment [4]. Most people with HIV live in sub-Saharan Africa. Due to limited access to HIV diagnosis and treatment in these countries, AIDS-related morbidity and mortality remain among the highest in the world [5]. By 2015, nearly 2 of her 100 HIV patients in sub-Saharan Africa were transitioning to secondary ART each year [6]. In 2017, 1.5% of all ART patients in Ethiopia were second-line patients [7].

The World Health Organization (WHO) recommends switching to therapy of first- and second-line antiretroviral therapy for treatment-failed HIV patients to avoid drug resistance, severe immunosuppression, and increased morbidity and mortality [8]. As ART utilization increases, the risk of failure and resistance to treatment becomes more acute, and switching patients to second-line regimens is the preferred method for early detection of failure of treatment, thus reducing drug resistance. Reduce changes in cytotoxicity and improve clinical outcomes [9]. Second-line ART is a follow-up regimen used immediately after the failure of first-line therapy, where the goal of second-line therapy is to achieve complete viral suppression rather than complete viral suppression as in developed countries where multiple second-line therapies are used to prolong the survival of people living with HIV. Line options and salvage regimens are available, and early change is the norm [10]. Secondary ART involves agents that maintain activity across the viral strains of the patient, usually involving at least three active agents [11]. According to the National AIDS Control Program, it consists of at least one non-nucleoside reverse transcriptase inhibitor, a protease inhibitor [12]. Protease inhibitors are commonly used in combination with two nucleoside reverse transcriptase inhibitors to increase the therapeutic index and eliminate the possibility of resistance to ART [13].

The many reasons a patient switches to HAART therapy, plus interdependent and associated with switching from HAART therapy, include failure of treatment, side effects of antiretroviral drugs, and poor adherence to therapy. There are also several factors [14]. Treatment toxicity has been reported with all antiretroviral agents and is one of the most common reasons for switching, discontinuing and not adhering to medication [15].

Most of the studies conducted in Ethiopia focused specifically on switching therapy rather than switching ART therapy and were mainly from the northern, western, and central parts of the country and from the southern part of the country to Ethiopia, no studies have been conducted [16,17]. Therefore, this study aims to assess the incidence and rates of switching from initial HAART therapy (first-line treatment) to second-line therapy and determine predictors from June 2010 to June 2020 at the Adola and Negele General Hospital, Guji District, southern Ethiopia.

Methods and Materials

Setting and Study Period

The study was carried out at the Adola and Negele General Hospitals Adult Outpatient ART Clinic in the East Guji Zone, located 476 km and 596 km south of Addis Ababa, respectively. Within the zone, there are four hospitals, two of which were established in 2019, namely the primary hospitals of Uraga and Bole. These hospitals have completed the study period (June 2010 to June 2020) and have not yet started pharmacy services in 2019 and are therefore not included in the study.

The treatment protocol was carried out according to the WHO ART treatment guidelines for HIV infection in adults and adolescents. Baseline assessments are performed at week 0, followed by visits at weeks 1, 2, 4, 8, 12, 16 and 24. After 24 weeks of antiretroviral therapy, patients should return every 12 weeks [18].

These hospitals now provide secondary care to the majority of the population of the East Guji zone, and patients are referred from almost all parts of the East Guji zone. The hospital is now offering first-, second-, and third-line ART for him. The survey was conducted from May to June 2021.

Study Design and Study Population

An institutional retrospective cohort study design was conducted. All eligible HIV/AIDS-infected adults who initiated HAART between June 2010 and June 30, 2020, at the Adola and Negele General Hospital.

Inclusion and Exclusion Criteria

The inclusion criteria were adults (aged 15 years or older) who began a HAART regimen between June 2010 and June 2020 at the outpatient ART clinic of Adola and Negele General Hospital outpatient ART clinic. However, the woman who received her ART only for PMTCT did not have at least one follow-up appointment in the outpatient department, and the patient was transferred outside Adola and Negele General Hospital, with records sent from the study facility and had incomplete and unclear records.

Sample Size and Sample Method

The sample size was determined using the twice her population ratio formula for each target by Open EPI, version 7, open source. We use the following assumptions: 80% power [19]. The calculated sample size was 854. A simple random sample was used to select a given sample size. The inpatient card numbers/registration numbers were obtained from an electronic database. A patient record was then created using the card number. Patients who started ART but did not attend at least one of their follow-up visits were excluded from the study because the card was not transferred to the institution, excluding patients with incomplete baseline information. Next, assign all his MRNs his ID number and, using computer-generated random numbers, recruit his 854 data sets from study participants within 10 years from the follow-up period. The sampling frames were created for the rest of the data set (Figure 1).

Data Collection Procedure

Sociodemographic characteristics, baseline and follow-up clinical data, and laboratory data were collected from patient medical records using a structured and pretested data abstraction format. Candidate variables were identified from a patient

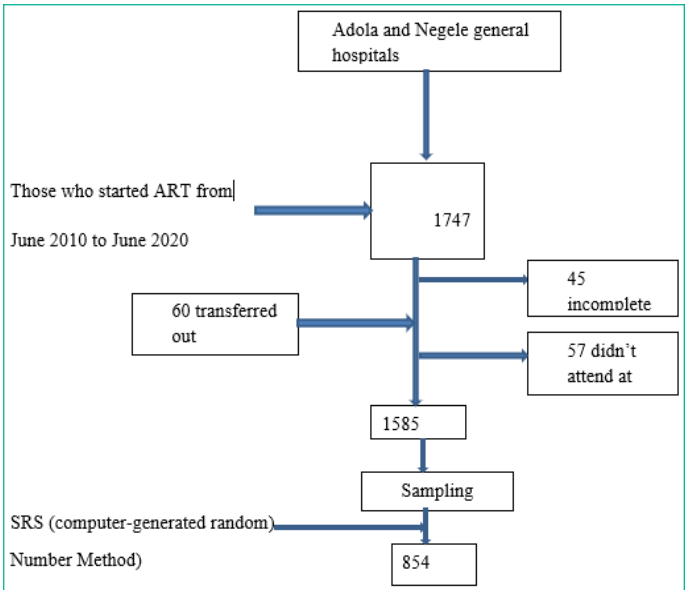

Figure 1: Schematic presentation of the sampling procedure for the study on incidence and predictors of the change in initial antiretroviral therapy regimen among adult patients on antiretroviral therapy at Adola and Negele General Hospitals South Ethiopia, 2021.

registry developed by the Ethiopian Federal Ministry of Health (FMOH) [18]. A unique ART number was used to identify the individual participants. The data abstraction form was adopted from the ART intake and follow-up forms from his ART clinic. It was pretested in 5% [43 of the total sample size found outside the Shakiso Health Center, a research facility. Patient admission forms, aftercare cards, ART registers, and electronic information databases served as data sources. Other clinical charts, including laboratory test results, were also used to document retroviral load and CD4 cell counts. Patients were retrospectively followed from the date of enrollment until the start of her HAART study. The investigators conducted training for data collectors and supervisors to familiarize themselves with data collection tools. The completeness of the questionnaire was checked and the final checked questionnaire was returned to the principal investigator.

Operational Definition

- A drug switch is defined as the switch from a first-line NNRTI-based ART to a second-line PI-based ARV regimen. According to treatment guidelines, drug changes are usually made after confirmation of virologic failure [20].

- Drug substitution is defined as the replacement of one or more drugs in first-line ARV therapy (NRTI or NNRTI) with another drug (NRTI or NNRTI [20]) of the same ARV class.

- Secondary ART A regimen used to treat HIV patients who have failed primary ART generally includes a Protease Inhibitor (PI) and two or three Nucleoside Reverse Transcriptase Inhibitors (NRTI) [21].

- Transfer is defined as the transfer of HIV care from a HIVDR (HIV drug resistance) facility to another identified ART administration facility for a patient who has not completed first-line ART at the time of transfer [22].

- The baseline CD4 count is the latest value measured before starting therapy.

- HAART is the combination of antiretroviral treatment with at least three drugs, including at least one Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) or protease inhibitor (PI), and/or abacavir, or a treatment regimen with a combination of an NNRTI and a boosted PI [23].

- Treatment failure is defined as a persistently detectable viral load that exceeds 1000 copies / ml (based on two consecutive measurements within a three-month interval) after at least six months of using antiretroviral drugs; defined according to the criteria of the World Health Organization and / or immunologic failure (fall of absolute CD4 below baseline or persistent absolute CD4 count levels below 100 cells/mm3 or 50% fall of absolute CD4 count from treatment peak values) after six months of therapy and clinical failure (WHO stage 3 or 4 conditions) after six months of therapy [24].

- Adherence was assessed by patient self-report of missed doses and calculated using the following formula:

% Adherence = (# of doses that should have been taken - # missed doses)* 100

# of doses that should have been taken Adherence is considered optimal when its rate is greater than or equal to 95%.

- Incomplete files: will be considered when the indicator of the dependent variable and/or 20% of the independent variable is not registered [25].

- Adverse reactions (Adverse Drug Reactions): defined as the occurrence of diarrhea, nausea, vomiting, anemia, rash, fatigue, lipodystrophy, metabolic disturbances, or other symptoms associated with antiretroviral therapy [26].

Data Quality Control

Before starting the actual data collection, pre-testing was performed on randomly selected patients to check the clarity and completeness of the overall data collection format and methods. Possible modifications and changes to the data collection format were made based on available data and a review of the previous literature. The data collector was his two BSc nurses at his ART clinic at the hospital, a supervisor was also from the clinic, and he is the pharmacy manager at his ART clinic. A one-day training session was held to familiarize both data collectors and supervisors with the data collection tools. Data were collected over 30 days. Data quality was maintained through intensive training of data collectors and supervisors on study objectives and data retrieval and extraction from patient records. The completed data collection tools were routinely verified for completeness of the information.

Data Processing and Analysis Procedures

The precision and consistency of each questionnaire was reviewed by the primary investigator and supervisor after data collection. Epi-Data version 4.6 was used to import the cleaned, modified, and coded data. From there, the data were exported to STATA version 15. To ensure that the data were distributed as expected, an exploratory data analysis was performed. We used descriptive statistics, such as mean, standard deviation, median, and interquartile range, after confirming the distribution of the data. Cohort characteristics were described in terms of frequencies and proportions. By dividing the number of individuals who altered their initial regimen throughout the follow-up period by the proportion of subject's time at risk for the entire follow-up period, the incidence of initial regimen change was estimated. To assess cumulative survival, life tables were used. The logarithmic ranking test and Kaplan-Meier survival curves were used to compare the overall survival experiences of two

or more groups and estimate mean times. After the Schoenfeld residual test and graphs validated the assumptions, the Cox proportional hazards model was modified. To find correlations between each independent variable and the dependent variable, a bivariate analysis was used. In the multivariate analysis, variables having P<0.25 values in the bivariate analysis were included. In addition, when choosing candidate variables for multivariate analysis, the history and findings of previous investigations were taken into account. 95% CI and P-values were used to determine the degree of connection and statistical significance after an inverse variable selection technique was performed to provide a list of the top predictors and adjusted hazard ratios. Each statistical test was considered significant with a P-value < 0.05.

Ethical Considerations

Ethical clearance was obtained from Jimma University, the Institute of Health, Institutional Review Board (IRB/2021). Adola and Negele General Hospital administrators were informed about the study objectives by a letter of support from the Epidemiology Department and obtained approval before data collection. Patient informed consent does not apply, as routinely available patient record data was used for the study. The confidentiality of the information obtained from each study participant was ensured by omitting names and personal identification information. Furthermore, the data collected were kept secure throughout the research work process to limit third-party access to the data.

Results

Sociodemographic Characteristics

In total, records from 854 HIV patients were selected and analyzed. The median age of the patient was 32.5 years (IQR=27–40), with the majority 345 (40.4%) in her 25-34-year group. More than half of the patients, 448 (52.5%), were women and approximately 433 (50.7%) were Orthodox Christians. Regarding the patient's educational background, about 489 (57.3) had primary education or higher. A total of 541 (63.3%) were urban residents (Table 1).

Table 1: Baseline sociodemographic characteristics of HIV-positive adults at the start of ART at Adola and Negele General Hospital from June 2010 to June 2020.

Characteristics	Categories	Total (No. (%))
Age	15-24	131(15.3)
	25-34	345(40.4)
	35-44	269(31.5)
	>45	109(12.8)
Sex	Male	406(47.4)
	Female	448(52.6)
Marital status	in a couple	493(57.3)
	single	361(43.7)
Religion	Orthodox	433(50.7)
	Muslim	68(8)
	Protestant	337(39.5)
	Catholic	16(1.9)
Educational status	No formal education	365(42.7)
	Primary education and above	489(57.3)
Occupation	Farmer	216(25.3)
	Merchant	215(25.2)
	Government employee	62(7.3)
	Daily laborer	105(12.3)
	Student	54(6.3)
	Housewife	202(23.6)
Residence	Urban	541(63.3)
	Rural	313(36.7)
Disclosure status	Yes	469(54.9)
	No	385(45.1)

Clinical, Iimmunological, Virological, and Therapeutic-Related Characteristics

The first major HAART regimen they prescribed was the combination of Tenofovir (TDF) + Lamivudine (3TC) + Efavirenz (EFV), 537 (62.9%), followed by Zidovudine (AZT) + Lamivudine (3TC) + Nevirapine (NVP) and zidovudine (AZT) + Lamivudine (3TC) + Efavirenz (EFV). Most (753 (88.2%) of the patients received CPT prophylaxis (Table 4) 398 (46.6%) were in WHO clinical stage II at the initiation of ART, which was 56.00 kg Quartile Range (IQR): 50-61. Of a total of 854 patients, 108 (12.6%) met the treatment failure criteria and only 52 (48%) patients transitioned to second-line ART therapy. The reason for not switching is not documented. The median baseline CD4 cell count at the initiation of ART was 409.50 cells/mm3 (IQR: 236.75-600.00). Most of the participants in their study, 619 (72.5%), had undetectable viral loads and more than 80% (686) recorded good adherence (Tables 2 and 3).

Table 2: Virological, Clinical and Immunological characteristics of HIV-positive adults on first-line ART at Adola and Negele General Hospital from June 2010 to June 2020.

Characteristics	Categories	Total (No. (%))
Viral load	Undetectable	619(72.5)
	150-1000	130(15.2)
	>1000	105(12.3)
Baseline WHO stage	Stage I	236(27.6)
	Stage II	398(46.6)
	Stage III	175(20.5)
	Stage IV	45(5.3)
BMI	<18.5	151(17.7)
	18.5-24.5	660(77.3)
	>24.5	43(5)
Nutritional status	Not malnourished	707(82.8)
	Moderate	120(14)
	Severe	27(3.2)
Functional status	Working	715(83.7)
	Ambulatory	102(11.9)
	Bedridden	37(4)
CD4+	<100	81(9.5)
	100-350	286(33.5)
	>350	487(57)

Table 3: Treatment-related characteristics of HIV-positive adults on first-line ART therapy at Adola and Negele General Hospital from June 2010 to June 2020.

Characteristics	Categories	Total (No. (%))
Type of initial HAART regimen	TDF-3TC-DGT	71(8.3)
	TDF-3TC-EFV	537(62.9)
	AZT-3TC-NVP	169(19.8)
	AZT-3TC-EFV	58(6.8)
	D4T-3TC-EFV	19(2.2)
Adherence level	>95%	686(80.3)
	85-94%	89(10.4)
	<85%	79(9.3)
Treatment change	Yes	293(34.3)
	No	561(65.7)
Treatment failure	Yes	105(12.3)
	No	749(87.7)
CPT prophylaxis	Yes	753(88.2)
	No	101(11.8)
History of TB	Yes	127(14.9)
	No	727(85.1)
ARVs adverse effect	Yes	152(17.8)
	No	702(82.2)

Change in the Incidence of First-Line ART Regimens to Second-Line

The median follow-up for IQR (21-59) was 44 months, with a total of 35,444 person months (2919.36 person years) of observation. The overall incidence of switching to the first ART regimen was 1.88 (95% CI: 0.88, 2.89) per 100 years of follow-up.

Overall, 55 (6.4%) people switched to second-line therapy, the most common second-line regimen to which people switched was atanavir boosted with tenofovir, lamivudine and ritonavir 28 (50.9%) followed by atanavir boosted with stavudine, lamivudine and ritonavir 18 (37.5%). Among the reasons for the switch to the regimen, virologic failure was the most common reason for the initial change to the regimen, accounting for 61.8% of cases and contributes 15.9 (95% CI: 11.33–22.2) per 100 Y (Figure 2).

The cumulative probability of survival on an initial regimen to the end of 2 years was 96%; to the end of 4 years was 83%; to the end of 6 years was 75% and to the end of 8 years was 37% (Table 4).

The general estimate of the Kaplan-Meir survival function showed that most of the initial change in the ART regimen occurred in the later months of follow-up, with a median survival of 104 months (Figure 3).

Time to Switch to Second-Line Antiretroviral Treatment

Fifty-three (50.5%) out of 105 patients who met the treatment failure criteria switched to the second line with delays of more than six months with IQR (6-11 months) from the date of confirmed treatment failure to the date of switch to second-line ART (Table 5).

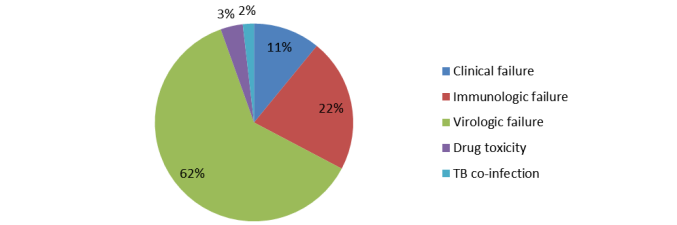

Figure 2: Reasons for switching among those patients who switched to second-line ART at Adola and Negele General Hospital from June 2010 to June 2020.

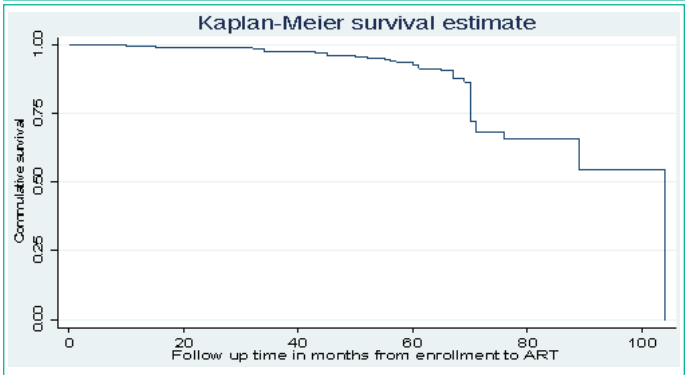

Figure 3: Kaplan-Meier curve of the first line surviving ART regimen for HIV-positive adults at Adola and Negele General Hospital, from June 2010 to June 2020.

Table 5: Time to switch to the second ART regimen from the date of treatment failure to the date of regimen change among treatment-failed patients at Adola and Negele General Hospital from June 2010 to June 2020.

Number of Total Treatment Failures = 105		
Time to Switch	**Frequency**	**Percent**
Less than 6 months	0	0
Greater than 6 months	53	50.5

Predictors of Initial First-Line ART Regimen Switch to the Second Line

Bivariate Cox regression analysis showed that marital status, residence, baseline WHO stage viral load, adhesion level, disclosure to close family member, treatment change, baseline BMI, baseline CD4 +, nutritional status, adverse effects of ARVs, functional status, prophylaxis of CPT, and history of tuberculosis are candidate variables for multivariate Cox regression. However, in the multivariate Cox regression analysis, viral load, baseline CD4 +, adhesion level, and disclosure status remained statistically significant predictors of the incidence rate of the initial regimen change (Table 6).

Comparison of Survival Probability Among Categories of Covariates

Patients with a high viral load are at greater risk of switching regimens compared to those with a low viral load. Having an adherence level below 85% is the risk of switching patients from the initial first-line ART regimen to the second-line ART regimen. Patients with baseline CD4 count below 100 cells/mm3 are at increased risk of switching their initial first-line ART regimen to a second-line ART regimen compared to those with baseline CD4 count above 350 cells/mm^3. Disclosure of HIV serostatus reduces the risk of switching from an initial first-line ART regimen to a second-line ART regimen compared to patients who do not disclose HIV status.

Discussion

In low-income countries, the choice of appropriate regimens is limited, so a well-performed first line of his ART is very important. Evaluation of the continuous switching rate of the first regimen and its predictors can help the patient maintain her first ART regimen as long as possible [27].

In this study, the incidence of switching to the first ART regimen was 1.14 per 100 years of follow-up (95% CI 0.88, 1.7), and the median follow-up was 44 months with his IQR (21-59). If all patients on first-line therapy had access to viral load tests, the conversion rate to second-line ART could be higher. The main factors that influenced the incidence of the first change in ART regimen were treatment change, viral load, CD4 + at baseline, adherence level and disclosure status.

The rate of switching to second-line ART in this study, which is 1.8 per 100 PYFU, is in line with the results of some other

Table 4: Life table on the incidence of the initial change in ART regimen and predictors among adult HIV patients on the first-line HAART regimen at Adola and Negele General Hospital from June 2010 to June 2020.

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Surviving	Cumulative Proportion Surviving at End of Interval
0	854	222	743.000	9	.99	.99
2	623	234	506.000	14	.97	.96
4	375	313	218.500	29	.87	.83
6	33	28	19.000	2	.89	.75
8	3	2	2.000	1	.50	.37

Table 6: Bivariate and Multivariate Cox regression analysis of the incidence rate of the change in the initial ART regimen among adults on first-line HAART at Adola and Negelle General Hospitals, southern Ethiopia, from June 2010 to June 2020.

Patient cohort		Number of switches	PYFU	Rate/100PY	Bivariate Analysis		Multivariate Analysis	
					Hazard ratio (95% CI)	P-Values	Adjusted HR (95% CI)	P-values
Viral load	Undetectable	0	2142.73	0	Ref.		Ref.	
	150-1000	5	423	1.2	3.4(1.8-6.34)	<0.001	3.3(1.8-6.3)	0.009
	>1000	50	387.91	12.9	9.4(5.6-15.7)	<0.001	7.3(2.6-20.3)	0.001*
Adherence level	>95%	1	2342.3	0.043	Ref.		Ref.	
	85%-95%	12	308.83	3.9	3(1.6-5.8)	0.06	2.2(1.1-4.5)	0.058
	<85%	42	302.51	12.9	6.5(3.3-12.7)	0.001	5.9(3-11.5)	0.001*
Baseline CD4+	<100	44	344.66	12.8	7.7(4-14.6)	0.001	2(1.53-4)	0.039*
	100-350	9	970.89	0.93	1.4(0.65-2.98)	0.39	7(4-14)	0.57
	>350	2	1638.09	0.12	Ref.		Ref.	
D Disclosure status	Yes	12	1644.84	0.73	Ref.		Ref.	
	No	43	1308.8	3.3	1.7(1-2.9)	0.048	1.8(1.1-3.1)	0.025*

studies, especially programs that do not routinely monitor viral load [6,19,28,29]. This is lower than a study conducted in a resource-limited setting supported by Medecins Sans Frontiers (MSF) 48/100PY [30], in Uganda, it was 49/100PY [31], in Mali, it was 3.3/100PY [27]. This lower rate could be due to the difference in the median follow-up period, which was 20 months in countries supported by Medecins Sans Frontiers (MSF) supported countries, 16.8 months in Uganda, and 15 months in Mali, but 44 months in this study, and this may be associated with decreasing the incidence rate as the observation time increases of the person. Another reason may be that physicians are reluctant to switch to ART when treatment options are limited and may also be that our study evaluated 10-year data on the time at which the second treatment was not decentralized to General Hospitals. This finding is also lower than the study conducted in another resource-limited setting with access to viral load monitoring (2.4/100PY). A possible reason may be the accessibility of the viral load to help identify more patients with treatment failure [32]. In this study, regular monitoring of viral load, which allows early detection of virologic failure and indicates the need to change the regimen, is not routine.

In this study, toxicity was one of the reasons for switching from first-line HAART therapy to second-line therapy. This can be observed in several other studies [32,27]. Tuberculosis coinfection accounts for 1.8% of patients who switched to secondary ART. Failure in treatment can cause tuberculosis. The risk of virologic suppression may also increase with his concomitant treatment with ART and tuberculosis due to impaired adherence and drug pharmacokinetic interactions [33].

Patients receiving ART for active tuberculosis should be prioritized for viral load monitoring and compliance support. It is important to strengthen interventions to prevent tuberculosis during ART. B. Isoniazid prophylaxis and infection control in healthcare settings. A possible explanation for this could be an increase in viral copies. This can adversely affect treatment response by compromising immunity and contributing to the side effects of the double burden of tuberculosis and HIV, which approved his CDC guidance on HIV treatment and strategies. [12].

In this study, in all patients who transitioned to a second-line ART regimen, there was a delay of 6 months or more in transitioning to a second-line ART regimen after documented treatment failure, consistent with reports from other institutions [31]. Delays in transitioning patients to secondary ART; highlight the lack of robust systems needed to manage chronic diseases such as HIV in public health settings.

The results of this study showed that viral loads in patients with viral loads between 150 and 1000 copies/mL and >1000 were significant predictors of the incidence of switching to the first regimen, with a 2.2-fold and 7.3-fold increased risk of 1, respectively. The 2nd administration exhibits the line ART scheme. A detectable high viral load is the result of poor disease progression. As the viral load increases, the disease is considered progressive and eventually the patient becomes more susceptible to treatment failure and declining CD4 levels in her, which eventually leads to the development of opportunistic infections. This finding is supported by studies conducted in Dakar, Senegal, and Rakai, Uganda [31,29]. Possible reasons could be patients with high viral load, advanced-stage disease, low CD4 counts, IOs, and possibly other chronic diseases. This increases the likelihood of taking additional medications and can also lead to drug interactions, the occurrence of side effects, and a poor treatment response. More extensive viral load monitoring in resource-limited areas good access should be considered a priority to guide physicians in the management of ART and optimize the use of limited treatment options.

Patients with low baseline CD4+ counts (<100 cells/mm3) on ART were more likely to switch initial therapy at any time compared to patients with high baseline CD4+ counts (>350 cells/mm3) were twice as high. It is well known that CD4 counts are inversely related to viral replication and viral load.

When the patient's immune status is compromised, the rate of viral replication increases compared to immunocompetent counterparts. In addition, immune-suppressed patients are susceptible to various opportunistic infections that maintain a vicious cycle of immunity and viral replication, and failure of immune reconstitution should also be a surrogate marker of virologic failure [34]. This finding is supported by studies conducted in Myanmar, Dakar, Senegal, Rakai, Uganda, and sub-Saharan Africa [31,19,29,35]. A possible explanation is that patients who initiate ART treatment in advanced stages are more likely to develop the worse disease, develop side effects, and are at higher risk of failure of treatment. This leads to changes in treatment regimens and drug interactions likely to be more susceptible to other forms of opportunistic infection. Virologic and immunological responses are slower than those with higher CD4 counts. Patients with <85% adherence are 5.9 times more likely to switch to a second regimen of ART than those with >95% adherence. This finding is consistent with studies conducted in southwestern Uganda and Myanmar [19,36]. There is general agreement that adherence issues are the most important concern for ART users, and therefore poor adherence increases the risk of virologic failure.

Evidence suggested that patients are more likely to acquire drug resistance and low immunity when adherence levels are below 95% and that the CD4 count significantly decreases in these individuals. High adherence rates are typically required to achieve therapeutic success, and it is possible for treatments to cause immunological failure [37]. This results in virological failure and provides the right environment for viral replication. The reason for the regimen changes could later be due to the fact that patients who skip a clinic visit, are not fully retained in care, or have poor drug adherence are more likely to have treatment failure.

The loss of care of a patient is a proxy for poor adherence and interruption of therapy, according to published evidence patients who miss a clinic visit, are not fully retained in care, or have poor drug adherence are more likely to experience failure of treatment and loss of follow-up at least once [38,39]. Social professionals or counselors need to further analyze this group of patients to understand why they are not receiving care and provide the appropriate help. The results of this study indicate that the disclosure status emerged as a significant predictor of the incidence of the first regimen switching, with patients who did not initially disclose their status more likely to switch regimens than those who did. The rate was 1.8 times higher. This is because patients who disclose their condition have the opportunity to access social networks for advice, emotional support, information, and other social resources, making them more aware of the appropriate use of ART medications. These benefits are lost in patients who do not disclose this.

Limitations of Research

The retrospective nature of this study may be a limitation as the accuracy of the analysis depends on the completeness of the records, thus information bias may have occurred due to underreporting/missing data elements. Other limitations include evaluating adherence based on records without using standardized questionnaires and excluding transfer patients. These analyzes did not include patients who lost follow-up, which may have contributed to treatment failure and ultimately led to treatment change.

Conclusion

In the current study, the incidence of early regime change is low. Viral load <150–1000 copies/mL to <1000 copies/mL, adherence level <85%, baseline CD4 count <100 cells/mm3, and non-disclosure of HIV serostatus were shown to be an independent predictor of the initial ART regimen change. Patients should inform their family and relatives of their HIV status and adhere to treatment. Providers should encourage patients initiating ART to disclose their HIV status. In addition, special caution should be exercised in patients with a baseline CD4 count <100 cells/mm3, adherence <85%, viral load 150-1000 copies / ml and viral load >1000 copies/ml/ml. It is recommended that you pay. Providers should quickly switch patients who fail initial HAART therapy. Those in a position to develop guidelines should consider decentralizing viral surveillance of HIV patients. Researchers should work with stakeholders. Prospective follow-up including socioeconomic factors, loss of follow-up, outsourced patients, and stigma-related factors is recommended to better understand the predictors of her switch from first-line to second-line ART therapy. Conducting research is recommended.

Author Statements

Availability of Data and Materials

The data essential for the conclusion are included in this manuscript. Additional data can be obtained from the corresponding author in a reasonable request time.

Competing Interest

We declare that we have no conflicts of interest in all activities pertaining to this research work."

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