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Predictive Factors Associated with Therapeutic Failure of First-Line Antiretroviral Therapy in People Living with HIV Monitored at Seven Large Cohort Sites in Conakry, Guinea (2019-2024)

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Abstract

Background: This study aimed to evaluate the incidence of first-line antiretroviral therapy (ART) failure and identify associated predictive factors among people living with HIV in Conakry, Guinea. **Methods:** A retrospective cohort analysis was conducted across seven major HIV care sites. Eligible participants were ART-naive at treatment initiation, aged 15 years or older, and had received ART for at least six months by March 30, 2024. The study included 19,464 patients enrolled between April 1, 2019, and March 30, 2024, with follow-up until September 30, 2024. Data was extracted from medical records, pharmacy logs, and SMR databases. Statistical analyses included descriptive summaries, chi-square, Fisher's exact, and Wilcoxon tests. Kaplan-Meier curves estimated treatment failure incidence over time, and the log-rank test compared survival distributions. Cox regression with backward stepwise selection was used to identify factors independently associated with first-line ART failure. **Results:** The median follow-up duration was 36.20 months (about 3 years). The overall incidence of first-line ART failure was 14.83% (95% CI: 13.67 - 16.93), corresponding to 4.92 failures per 100 person-years. Virological failure accounted for 9.87% and immunological failure accounted for 4.96% of the total. ART failure increased significantly with time on treatment, from 1.49% at six months to 47.82% at 60 months. Multivariate analysis revealed three key predictors of

treatment failure: lack of formal education (adjusted Hazard Ratio [HR]: 1.482), a baseline CD4 count below 100 cells/mm^3 (adjusted HR: 4.049), and HIV-tuberculosis co-infection at ART initiation (adjusted HR: 4.223). **Conclusion:** This study reveals a high incidence of antiretroviral therapy (ART) failure in Conakry, largely attributed to advanced immunosuppression, co-infections, and limited health literacy. To enhance treatment outcomes, the authors recommend strategies including early HIV diagnosis, timely initiation of ART, patient-centered health education, community-based support systems, and integrated, tailored TB/HIV services. Future research should investigate antiretroviral resistance patterns and additional risk factors to better inform national HIV response strategies.

Keywords

First-Line Antiretroviral Therapy Failure, HIV/AIDS, Incidence, Associated Factors, Conakry

1. Introduction

The global expansion of combined antiretroviral therapy has extended the lives of people living with HIV and reduced the risk of HIV transmission. However, therapeutic resistance, which causes therapeutic failure in people living with HIV, undermines the beneficial effects of antiretrovirals [1] [2].

Therapeutic failure of antiretroviral treatment can be clinical, immunological, and virological. Clinical failure is the reappearance of opportunistic infections after six months of antiretroviral treatment. Immunological failure is the return to a CD4 count similar to or lower than that preceding treatment and/or the persistence of a CD4 count below 100/mm^3. As for virological failure, it is defined by a plasma viral load greater than or equal to 1000 copies/ml, based on two consecutive viral load measurements three months apart, after reinforcing adherence [3].

Antiretroviral treatment failure may result from various factors, including adherence issues, socioeconomic conditions, and patients' clinical characteristics. Strict adherence to the prescribed treatment regimen is essential, as research has shown that inconsistent intake of antiretroviral therapy can lead to viral rebound, thereby compromising treatment efficacy and viral suppression [4]. Additionally, socioeconomic conditions play a crucial role in treatment outcomes. Individuals from disadvantaged backgrounds may encounter barriers such as limited access to healthcare facilities and medications, which further hinder adherence to therapy [5].

Clinical factors, including baseline viral load, CD4 cell count, and the presence of comorbidities, significantly influence the success of antiretroviral therapy. Studies have shown that patients with a high viral load prior to initiating treatment are more likely to experience treatment failure compared to those with a lower viral load. Additionally, other parameters—such as the patient's overall health status,

immune response, and adherence to treatment—play a crucial role in the effectiveness of antiretroviral therapy [6].

It is worth recalling that the fight against HIV/AIDS remains a global public health priority and is among the Millennium Development Goals, particularly through the expansion of access to antiretroviral therapy. However, the alarming rise in treatment failures in recent years poses a major challenge. In 2017, the World Health Organization (WHO) published a concerning report highlighting the increasing prevalence of viral resistance to antiretrovirals in Africa—a threat that could jeopardize the goal of eliminating the epidemic within the next decade **[7]** [8]. Although viral load testing is essential for the early detection of treatment failures, its use remains limited due to restricted access to equipment, frequent stockouts of reagents, and weak logistical systems for transporting samples and delivering results **[9]**.

Globally, it is estimated that between two and four million people living with HIV may have experienced treatment failure in 2020 [10]. In sub-Saharan Africa, first-line antiretroviral therapy (ART) failure rates are high, ranging from 11.1% to 24% within the first 12 months of treatment initiation. Approximately 71% to 90% of patients experiencing ART failure show signs of drug resistance [1] [11]. In Cameroon, a national study conducted in 2018 found that 30% of individuals on ART were experiencing treatment failure [12].

In Guinea, the HIV epidemic has a generalized profile within the population, with a national prevalence estimated at 1.5%. This prevalence of HIV is slightly higher among women (1.6%) than men (1.3%), with a peak at ages 30 - 34 for women (2.5%) and 35 - 39 for men (2.2%). The HIV rate is higher in urban areas (2.0%) than in rural areas (1.1%), increasing with the household's economic level [13]. However, certain key populations exhibit alarmingly high prevalence rates, reaching up to 10% [14]. In 2023, Guinea had approximately 130,000 people living with HIV, including 11,000 children aged 0 to 14 and 74,000 women aged 15 and older. During the same year, the country recorded 4600 new HIV infections and 3200 deaths related to HIV/AIDS. As far as access to treatment is concerned, 88,000 people were receiving antiretroviral therapy in 2023, representing a treatment coverage rate of 70%. However, this coverage was only 59% among children aged 0 to 14 [15]. This situation is further complicated by structural and epidemiological challenges that hinder the effectiveness of antiretroviral therapy (ART). A study conducted in 2014 in Senegal, Mali, and Guinea-Conakry revealed that the virological failure rate among HIV patients undergoing antiretroviral treatment was 24% (95% CI, 17 - 32) in Guinea-Conakry [16]. A study conducted among 50,598 people living with HIV, monitored across eight care sites in Guinea, estimated the failure rate of first-line antiretroviral (ARV) treatment at approximately 10.3%, while 26% of patients were lost to follow-up [17]. It appears that published data on antiretroviral treatment failure in Guinea are limited and provide insufficient insight into the predictive factors associated with these failures. Furthermore, the available data are outdated, which limits their relevance for informing

current decision-making in the management of antiretroviral treatment programs in Guinea. As we approach the UNAIDS "95-95-95" targets [18], it is crucial to establish a clear and accurate assessment of first-line antiretroviral therapy (ART) failure in Guinea. This analysis is vital to optimize treatment strategies, improve adherence, and enhance the effectiveness of interventions aimed at controlling the HIV epidemic. Investigating first-line ART failure in Guinea is a key research priority that addresses a major public health concern. Although antiretroviral therapy has significantly improved the prognosis of people living with HIV, treatment failure remains a major challenge in managing the epidemic. In Guinea, where HIV continues to be a significant public health issue, analyzing the factors associated with treatment failure is essential for designing tailored interventions and improving patient outcomes.

Moreover, the emergence of drug-resistance mutations remains a growing concern in antiretroviral therapy (ART) failure, as these mutations can significantly limit future treatment options and worsen health outcomes [19]. Studies have shown that monitoring resistance mutations in patients experiencing treatment failure is essential for guiding subsequent therapeutic strategies [20]. In Guinea, the available data are insufficient to provide a comprehensive understanding of the extent of this issue or to accurately identify the predictive factors of treatment failure within HIV care facilities. Therefore, identifying the factors associated with first-line ART failure in Guinea requires an approach that integrates biological, social, economic, and healthcare-related dimensions. The findings from such research can inform public health initiatives and policy decisions aimed at improving treatment protocols and patient education efforts, thereby enhancing the effectiveness of ART programs in Guinea. This study aims to estimate the incidence of first-line treatment failure among people living with HIV followed in large-cohort sites in Conakry and to identify the associated predictive factors.

2. Methods

2.1. Types and Duration of Study

We conducted a retrospective analytical cohort study involving people living with HIV who were receiving antiretroviral therapy and were followed at seven large HIV care cohort sites in Conakry. Patient enrollment in the study spanned a five-year period, from April 1, 2019, to March 30, 2024, with follow-up scheduled to end on September 30, 2024.

2.2. Study Setting

General Setting

The Republic of Guinea, located in West Africa, covers an area of 245,857 square kilometers. As of 2025, it has an estimated population of 14,363,931, with an annual growth rate of 2.9%, reflecting strong demographic dynamics. This growth is driven by a fertility rate of 4.8 children per woman and an infant mortality rate of 67 per 1000 live births. Guinea's population is predominantly young, with 43%

under the age of 15 and a median age of 19 years. The sex distribution shows a slight female majority, with women accounting for 51.7% of the population. The life expectancy at birth is 59 years. Administratively, the country is divided into eight regions comprising 38 health districts. Rich in natural resources, Guinea boasts diverse ecosystems favorable for agriculture, livestock, and tourism. Its subsoil is abundant in bauxite, gold, and diamonds, positioning Guinea as a major player in the global mining sector. However, the country faces significant socioeconomic challenges, with a poverty rate of 43.7% [21].

In terms of health, Guinea experiences a high prevalence of communicable and epidemic-prone diseases, many of which are preventable through vaccination, along with high maternal and infant mortality rates. In 2018, malaria prevalence was 15%, accounting for 40.8% of outpatient consultations, 45.3% of hospital admissions, and 36% of hospital deaths, making it the leading cause of morbidity and mortality. Tuberculosis and HIV also remain prevalent, particularly among high-risk groups [13].

Guinea's health policy is based on a primary health care approach, introduced in 1988, which includes a minimum package of activities focused on maternal and child health, notably through the Expanded Program on Immunization (EPI) and the provision of essential medicines. To enhance service quality and accessibility, this strategy has been complemented by health financing reforms and a hospital reform program [22].

The fight against HIV/AIDS in Guinea is coordinated by the National Program for the Fight Against AIDS and Hepatitis (PNLSH) under the Ministry of Health and the National Committee for the Fight Against AIDS (CNLS) under the Prime Minister's Office. The PNLSH is responsible for implementing strategies for the prevention and management of STIs/HIV/AIDS/Hepatitis, while the CNLS develops and implements national policy, mobilizes necessary resources, and coordinates development partners [23] [24].

The national protocol for HIV care in Guinea recommends initiating antiretroviral therapy (ART) for all HIV-positive patients, regardless of immune status. Fixed-dose combinations are preferred to improve adherence and reduce costs. However, a significant proportion of patients are on second- or third-line treatments, highlighting ongoing challenges related to treatment failure and the management of complex cases [25].

Specific Setting

The study was conducted in healthcare facilities across the city of Conakry. Located on the Kaloum Peninsula and bordered by the Atlantic Ocean, Conakry is the capital and principal urban center of Guinea. As of 2025, it has an estimated population of 2,269,898 inhabitants. Its distinctive geographic position gives it a northeast-southwest orientation, extending from Tombo Island to the Kaloum Peninsula. The city's landscape features a rocky promontory rising to an altitude of 146 meters, surrounded by forests and mangroves. Conakry's width does not exceed 6.5 kilometers, and its predominantly lateritic soil stretches northward to-

ward Mount Kakoulima, which peaks at 1011 meters. The mangroves surrounding Conakry play a critical role in local agriculture, particularly for rice cultivation and market gardening, activities that support approximately 8.5% of the population. However, the rapid expansion of urban fabric increasingly threatens these cultivable lands, jeopardizing the city's food security and reducing areas available for peri-urban farming.

Like many rapidly growing metropolitan areas, the Conakry faces major challenges related to urbanization and housing. The concentration of economic activities on the Kaloum Peninsula generates intense daily migratory flows, exacerbating traffic congestion and urban mobility issues. Additionally, the city's autonomous port serves as a key driver of the national economy, facilitating the importation of food, industrial, and energy goods, as well as the export of the country's mineral resources [21].

In terms of healthcare, Conakry concentrates on the country's most important medical infrastructure. The Donka National Hospital, the main public healthcare facility in Guinea, serves as a referral center while also fulfilling teaching and research missions. The city is also home to other major hospital institutions, including Ignace Deen Hospital and the Sino-Guinean Hospital, further strengthening its role as the nation's leading medical hub [21].

In terms of HIV care, Conakry hosts 15 of the country's 32 large-cohort HIV care sites, accounting for approximately 50%. It is important to note that these 32 large-cohort sites manage over 90% of the national cohort of people living with HIV in Guinea. Currently, the country has 142 HIV care sites. A large-cohort site is defined as a site managing 250 or more people living with HIV. Our study focused on 7 large-cohort sites in Conakry. These sites were selected based on the availability of a digital database capable of providing longitudinal follow-up data for patients enrolled in the antiretroviral treatment program over a 5-year period [26].

2.3. Study Population

In this study, we included patients aged 15 years and older with confirmed HIV infection who had been receiving antiretroviral therapy (ART) for at least six months by the end of the study period. These were ART-naïve patients prior to initiation, followed at seven (7) large-cohort HIV care sites in Conakry.

The exclusion criteria were patients younger than 15 years; those without a CD4 cell count measurement obtained within three months of initiating their first ART regimen; patients who initiated treatment at other sites without documented initiation dates; and those with missing essential baseline data (weight, height, or initial treatment regimen).

2.4. Data Collection

Data Sources

Data were collected from primary monitoring tools used for patients receiving

antiretroviral therapy, including medical records, prescription logs, patient follow-up registers, enrollment registers, and pharmacy records. Databases from the seven (7) high-volume HIV care sites were also utilized for study data collection, notably the SMR (Simplified Monitoring and Reporting) databases for annual patient follow-up under antiretroviral treatment.

Data collection was carried out by final-year medical students from Gamal Abdel Nasser University of Conakry, under the supervision of site managers. Individual patient data were entered into a pre-designed file created specifically for the study.

Prior to the start of field data collection, investigators received specific training on the data collection tools and procedures provided by supervisors from the Chair of Public Health at the Faculty of Health Sciences and Techniques of Gamal Abdel Nasser University of Conakry.

Cohort Formation

We conducted a retrospective cohort study. Patient enrollment began on April 1, 2019, corresponding to the initiation date of antiretroviral therapy based on triple-drug regimens. The enrollment period extended from April 1, 2019, to March 30, 2024. The study closure date (data cutoff) was set for September 30, 2024, to ensure a minimum follow-up duration of six months for the last patient enrolled.

2.5. Study Variables

Dependent Variable

The dependent variable (or event of interest) in our study was therapeutic failure following the initiation of a first-line antiretroviral therapy (ART) regimen. To assess therapeutic failure, we used both immunological and virological criteria.

- ***Immunological failure***: From an immunological perspective, therapeutic failure was defined as the absence of a significant increase in CD4 count despite optimal antiretroviral treatment for at least six months. Specifically, it was characterized by a CD4 count below 250 cells/mm^3 accompanied by clinical manifestations, or by the persistence of a CD4 count below 100 cells/mm^3.
- ***Virological failure***: From a virological perspective, therapeutic failure was defined either as an insufficient reduction in plasma viral load (viral RNA > 1000 copies/mL) six months after ART initiation, or as a rebound in viral load after initially achieving an undetectable level.

In this study, a patient was considered to have first-line therapeutic failure if they exhibited immunological and/or virological failure during the defined follow-up period. Patients experiencing therapeutic failure were coded as "0," while those without therapeutic failure were coded as "1."

To further characterize first-line therapeutic failure, the following parameters were assessed:

- **Cumulative incidence of therapeutic failure**: the ratio of the total number of

patients who experienced therapeutic failure to the total number of patients included in the cohort, expressed as a percentage.

- **Incidence rate of therapeutic failure**: the ratio of the total number of therapeutic failures to the total person-months of follow-up accumulated across all study participants.
- **Follow-up time**: the duration, expressed in months, between the date of ART initiation and the date of therapeutic failure, the last follow-up visit, or the study endpoint.
- **Initiation date**: the date when first-line ART (triple therapy) was started.
- **Event date**: the date on which therapeutic failure was confirmed based on immunological and/or virological criteria.
- **Censoring date**: the date marking the end of follow-up or observation, set on September 30, 2024.

Independent or Explanatory Variables

The independent variables, also referred to as explanatory variables, included the baseline characteristics of the patients included in the study:

- Sociodemographic characteristics: age (in years), sex, marital status, education level, employment status or profession.
- Clinical characteristics: weight, height, body mass index (BMI), stage of infection according to the World Health Organization (WHO) classification, presence of active tuberculosis or a tuberculosis/HIV co-infection.
- Biological characteristics: CD4 count (expressed in cells per mm^3).
- Therapeutic characteristics: antiretroviral treatment regimen based on a three-drug therapy.

It is important to note that the tuberculosis cases reported in this study, in the context of TB/HIV co-infection, were exclusively derived from data collected at HIV care and treatment sites. Tuberculosis diagnosis was primarily based on clinical evaluation and confirmed through bacteriological analyses, particularly sputum smear microscopy for the detection of acid-fast bacilli (AFB). When bacteriological results were negative or extrapulmonary tuberculosis was suspected, chest radiography was performed. In certain health facilities, the GeneXpert MTB/RIF assay was used for rapid diagnosis—within approximately two hours—enabling the detection of Mycobacterium tuberculosis and rifampicin resistance. Additional investigations were conducted as needed, depending on the disease site, including lymph node aspiration with histological examination and/or GeneXpert testing, as well as cerebrospinal fluid analysis in cases of suspected tuberculous meningitis. In some cases, pleural, abdominal, or bone biopsies were required for definitive diagnostic confirmation.

2.6. Data Analysis

Descriptive analysis was conducted by summarizing quantitative variables using means and standard deviations, or medians and interquartile ranges, depending on the distribution of the data. Qualitative variables were presented as proportions

with their corresponding 95% confidence intervals.

To compare characteristics between the two groups of participants (patients with treatment failure versus those without treatment failure), Pearson's chi-square test was used for parametric data. When the assumptions for parametric testing were not met (normal distribution, sufficient sample size), non-parametric tests such as Fisher's exact test and the Wilcoxon test were applied. A significant level of 0.05 was used throughout.

Kaplan-Meier survival methods were generated to estimate the incidence or probability of treatment failure over time during antiretroviral therapy.

Factors associated with first-line treatment failure were identified through multivariate analysis using a Cox proportional hazards regression model. Results were reported as adjusted Hazard Ratios (aHR) with their corresponding 95% confidence intervals. A stepwise backward selection approach was employed to identify significant predictive factors. Potential confounding factors were controlled. The association between a predictive factor and treatment failure was considered statistically significant when the p-value was less than or equal to 0.05. All statistical analyses were performed using SPSS software, version 25.

3. Results

3.1. Flow of Patient's Selection Included in the Study

The total number of patients living with HIV enrolled for antiretroviral treatment follow-up at the study sites since their inception was 47,321. During our study period, 26,783 were registered for care. We excluded 7319 patients who did not meet our inclusion criteria. For this study, 19,464 patients aged 15 and older were included. By the end of the study, 2887 (14.83%) patients had experienced first-line antiretroviral treatment failure. Among these, 1921 experienced virological failure and 966 experienced immunological failure (**Figure 1**).

3.2. Characteristics of the Patients Included in the Study

During the study period, we included 19,464 patients living with HIV and receiving antiretroviral treatment at seven sites in the Conakry health region. Among them, 62.78% were women and 37.22% were men aged 15 years and older. The median age was 45 years (IQR: 31 - 72). Patients aged 15 to 24 years accounted for 8.01%, while those aged 35 and older accounted for 66.05%. A significant proportion (29.58%) of the patients had no formal education. In 32.34% of cases, patients started antiretroviral treatment with a CD4 count below 100 cells/mm^3. We also observed that patients who began treatment at stages 3 and 4 of HIV infection represented 10.52% and 27.99%, respectively. Additionally, the study revealed that 18.99% of patients were underweight (malnutrition) at the start of antiretroviral treatment. Furthermore, 26.99% of patients had tuberculosis/HIV co-infection when initiating antiretroviral treatment. The most common initial antiretroviral regimen was the combination of AZT + 3TC + EFV (57.59%), followed by TDF + 3TC + DTG (35.06%).

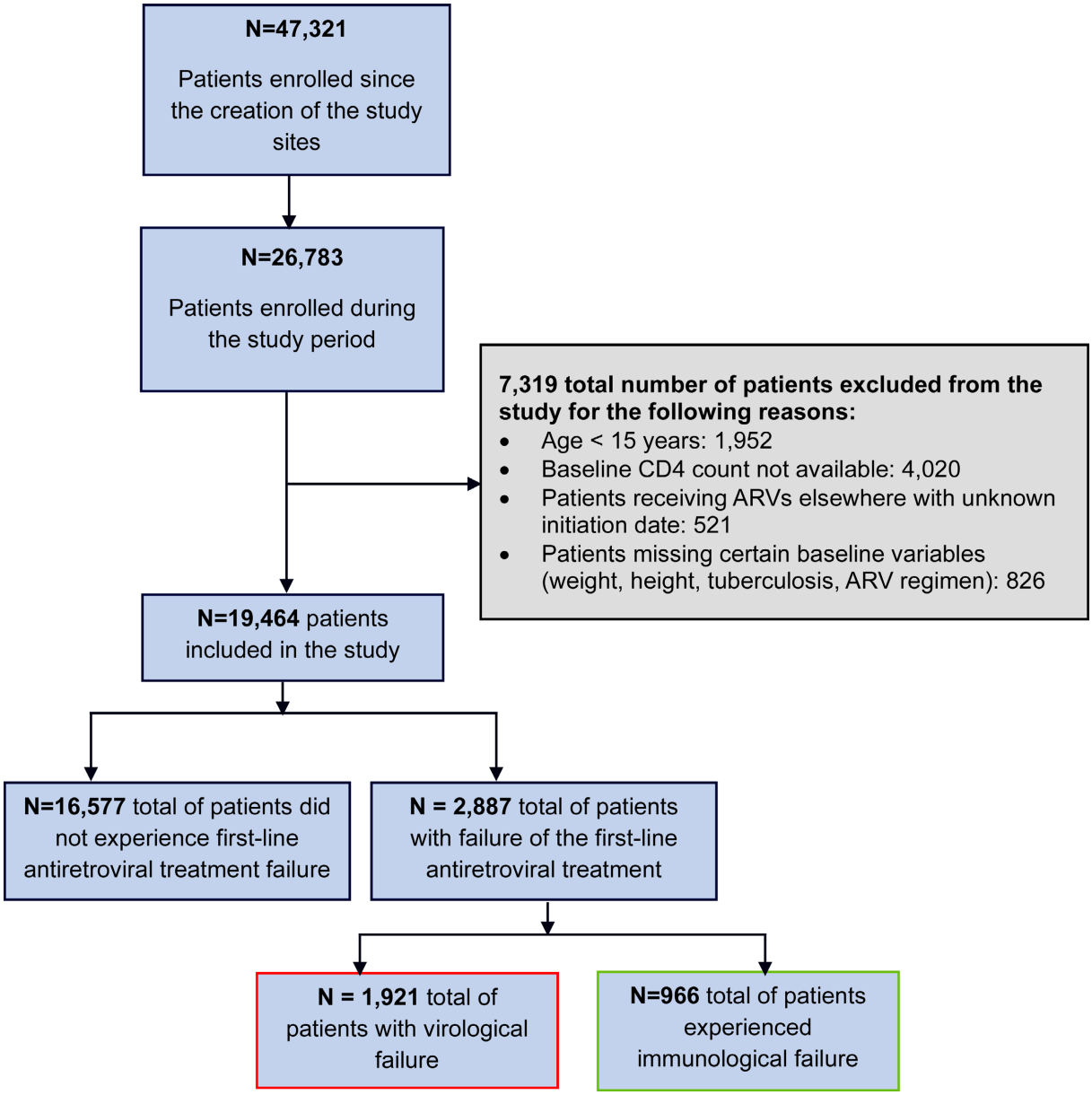

Figure 1. Flow diagram of the selection of the 19,464 included in the study on the incidence of first-line antiretroviral treatment failure monitored between 2019 and 2024 in seven large cohort sites in Conakry (Guinea).

In terms of comparison, we found that the baseline characteristics of patients who experienced therapeutic failure of the first-line treatment and those who did not were similar, except for characteristics related to CD4 count in cells/mm^3, body mass index, WHO clinical stage of HIV infection, educational level achieved by the patient, and tuberculosis/HIV co-infection, which were different (p-value < 0.05) (**Table 1**).

In terms of survival, we observed that at the end of the study, 70.54% of patients were still being monitored and receiving antiretroviral treatment at the study sites. Conversely, we noted that 15.50% of patients were lost to follow-up and 6.88% had died (**Figure 2**).

Table 1. Characteristics of the 19,464 patients living with HIV followed between 2019 and 2024 in seven sites of the large cohort of Conakry (Guinea), according to the therapeutic failure of the first line of antiretroviral treatment.

Variables	Sample description		Failure of first-line antiretroviral therapy		
	Number	%	Yes (%)	No (%)	p-value
Total	19,464	100	2886 (14.83)	16578 (85.17)	
Medical care site					
Dabompa Health Center	1798	9.24	243 (13.52)	1555 (86.48)	
Coleah Municipal Medical Center	1520	7.81	204 (13.42)	1316 (86.58)	
Tombolia Health Center	2508	12.89	370 (14.75)	2138 (85.25)	
Matam Municipal Medical Center	6927	35.59	1025 (14.80)	5902 (85.20)	0.1226
Ratoma Municipal Medical Center	2358	12.11	352 (14.93)	2006 (85.07)	
Flamboyants Municipal Medical Center	2821	14.49	436 (15.46)	2385 (84.54)	
Gbessia Port 1 Health Center	1532	7.87	256 (16.71)	1276 (83.29)	
Sex of patient					
Male	7245	37.22	1053 (14.53)	6192 (85.47)	0.3868
Female	12219	62.78	1833 (15.00)	10386 (85.00)	
Body Mass Index					
Normal	8449	43.41	999 (11.82)	7450 (88.18)	
Obesity	4063	20.87	640 (15.75)	3423 (84.25)	0.000
Overweight	3256	16.73	544 (16.71)	2712 (83.29)	
Underweight	3696	18.99	703 (19.02)	2993 (80.98)	
WHO infection stage					
Stage 1	6972	35.82	371 (5.32)	6601 (94.68)	
Stage 2	4996	25.67	386 (7.73)	4610 (92.27)	0.000
Stage 3	2048	10.52	264 (12.89)	1784 (87.11)	
Stage 4	5448	27.99	1865 (34.23)	3583 (65.77)	
Education Level					
College/University	4070	20.91	460 (11.30)	3610 (88.70)	
High School	4241	21.79	592 (13.96)	3649 (86.04)	0.000
Elementary school	5395	27.72	795 (14.74)	4600 (85.26)	
No formal education	5758	29.58	1039 (18.04)	4719 (81.96)	
Marital status					
Divorced	1957	10.05	258 (13.18)	1699 (86.82)	
Widowed	3300	16.95	478 (14.48)	2822 (85.52)	0.1023
Married	7793	40.04	1164 (14.94)	6629 (85.06)	
Single	6414	32.95	986 (15.37)	5428 (84.63)	

Continued

Employment					
Unemployed	13111	67.36	1905 (14.53)	11206 (85.47)	0.0942
Employed	6353	32.64	981 (15.44)	5372 (84.56)	
Group Age					
25 - 34 years old	5048	25.94	748 (14.82)	4300 (85.18)	
15 - 24 years old	1560	8.01	232 (14.87)	1328 (85.13)	0.9986
35 years old and above	12856	66.05	1906 (14.83)	10950 (85.17)	
CD4 count (cells/mm³)					
≥350	5335	27.41	348 (6.52)	4987 (93.48)	
250 - 350	3716	19.09	325 (8.75)	3391 (91.25)	0.0000
100 - 250	4119	21.16	777 (18.86)	3342 (81.14)	
<100	6294	32.34	1436 (22.82)	4858 (77.18)	
Antiretroviral regimen					
AZT + 3TC + LPV/r	329	1.69	42 (12.77)	287 (87.23)	
TDF + 3TC + DTG	6824	35.06	994 (14.57)	5830 (85.43)	0.5061
AZT + 3TC + EFV	11209	57.59	1677 (14.96)	9532 (85.04)	
AZT + 3TC + NVP	1102	5.66	173 (15.70)	929 (84.30)	
Tuberculosis					
No	14210	73.01	1691 (11.90)	12519 (88.10)	0.0000
Yes	5254	26.99	1195 (22.74)	4059 (77.26)	

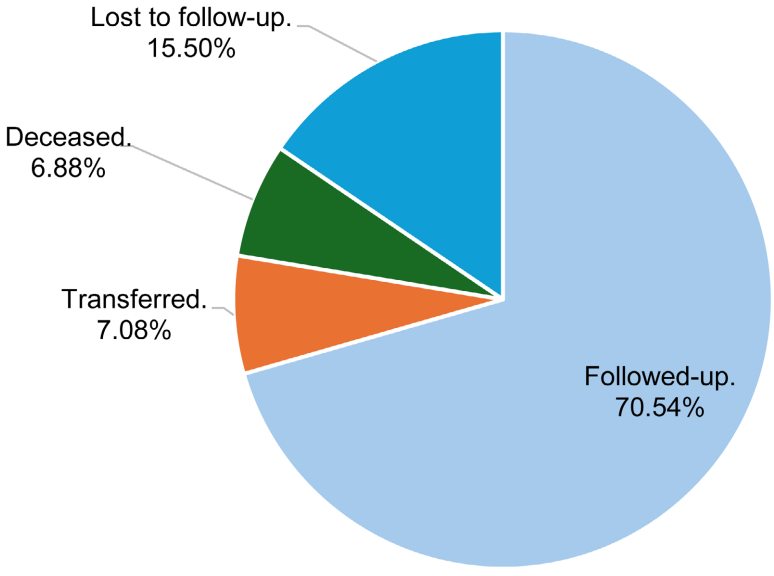

Figure 2. Outcomes at the End-of-Study Follow-Up of 19,464 People Living with HIV Monitored Between 2019 and 2024 in Seven Large Cohort Sites in Conakry (Guinea).

3.3. Incidence of First-Line Antiretroviral Therapy Failure

The patients included in this study were followed for a median duration of 36.20 months, or approximately 3.017 years. At the end of the study, we noted that the overall incidence of first-line antiretroviral treatment failure was 14.83% (95% CI: 13.67 - 16.93), with an incidence rate of 4.92 per 100 person-years (Table 3). According to Figure 3, the cumulative incidence of virological failure was 9.87% and that of immunological failure was 4.96%.

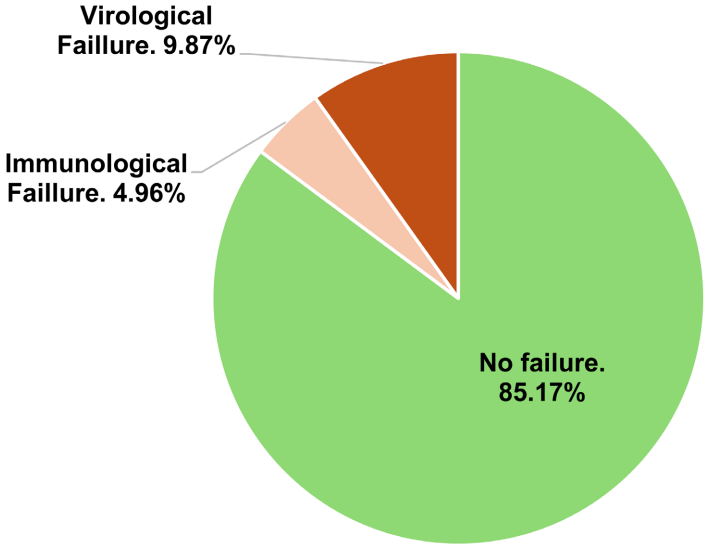

Figure 3. Types of first-line antiretroviral therapy failure at the end-of-study follow-up of 19,464 people living with HIV monitored between 2019 and 2024 in seven large cohort sites in Conakry (Guinea).

Table 2. Incidence of first-line antiretroviral treatment failure over time among 19,464 people living with HIV monitored between 2019 and 2024 in seven large cohort sites in Conakry (Guinea).

Follow-up time in months	Number of people at risk	Number of terminal events	Cumulative risk of therapeutic failure		Incidence of therapeutic failure (per 100 person-years)
			%	CI 95%	
0	19,464	-			
6	18,626	277	1.49	1.35 - 2.33	2.97
12	16,654	295	3.23	3.12 - 3.87	3.23
18	14,667	287	5.13	4.78 - 5.66	3.42
24	12,717	274	7.17	6.87 - 7.84	3.58
30	10,832	261	9.41	9.11 - 9.54	3.76
36	8941	324	12.69	11.86 - 13.01	4.23
42	6949	294	16.38	15.67 - 16.89	4.68
48	4984	284	21.15	20.45 - 21.68	5.29
54	3029	296	28.86	27.56 - 29.10	6.41
60	1103	294	47.82	47.11 - 48.12	9.56

Table 3. Incidence of first-line antiretroviral treatment failure according to the characteristics of 19,464 people living with HIV monitored between 2019 and 2024 in seven large cohort sites in Conakry (Guinea).

Variables	Total number	Person-years	Failure of first-line antiretroviral therapy		
			number	%	Incidence per 100 person-years
Total	19464	58716	2886	14.83	4.92
Medical care site					
Dabompa Health Center	1798	5424	243	13.52	4.48
Coleah Municipal Medical Center	1520	4585	204	13.42	4.45
Tombolia Health Center	2508	7566	370	14.75	4.89
Matam Municipal Medical Center	6927	20,896	1025	14.80	4.91
Ratoma Municipal Medical Center	2358	7113	352	14.93	4.95
Flamboyants Municipal Medical Center	2821	8510	436	15.46	5.12
Gbessia Port 1 Health Center	1532	4622	256	16.71	5.54
Sex of patient					
Male	7245	21,856	1053	14.53	4.82
Female	12,219	36,861	1833	15.00	4.97
Body Mass Index					
Normal	8449	25,488	999	11.82	3.92
Obesity	4063	12,257	640	15.75	5.22
Overweight	3256	9822	544	16.71	5.54
Underweight	3696	11,150	703	19.02	6.30
WHO infection stage					
Stage 1	6972	21,032	371	5.32	1.76
Stage 2	4996	15,071	386	7.73	2.56
Stage 3	2048	6178	264	12.89	4.27
Stage 4	5448	16,435	1865	34.23	11.35
Education Level					
College/University	4070	12,278	460	11.30	3.75
High School	4241	12,794	592	13.96	4.63
Elementary school	5395	16,275	795	14.74	4.88
No formal education	5758	17,370	1039	18.04	5.98
Marital status					
Divorced	1957	5904	258	13.18	4.37
Widowed	3300	9955	478	14.48	4.80
Married	7793	2,3509	1164	14.94	4.95
Single	6414	19,349	986	15.37	5.10

Continued

Employment					
Unemployed	13,111	39,552	1905	14.53	4.82
Employed	6353	19,165	981	15.44	5.12
Group Age					
25 - 34 years old	5048	15,228	748	14.82	4.91
15 - 24 years old	1560	4706	232	14.87	4.93
35 years old and above	12,856	38,782	1906	14.83	4.91
CD4 count (cells/mm³)					
≥350	5335	16,094	348	6.52	2.16
250 - 350	3716	11,210	325	8.75	2.90
100 - 250	4119	12,426	777	18.86	6.25
<100	6294	18,987	1436	22.82	7.56
Antiretroviral regimen					
AZT + 3TC + LPV/r	329	992	42	12.77	4.23
TDF + 3TC + DTG	6824	20,586	994	14.57	4.83
AZT + 3TC + EFV	11,209	33,814	1677	14.96	4.96
AZT + 3TC + NVP	1102	3324	173	15.70	5.20
Tuberculosis					
No	14,210	42,867	1691	11.90	3.94
Yes	5254	15,850	1195	22.74	7.54

Table 2 shows that the incidence of first-line antiretroviral treatment failure increases significantly over time, from 1.49% (2.97 person-years) at 6 months to 47.82% (9.56 person-years) at 60 months. Moreover, Table 3 reveals that the incidence of first-line antiretroviral treatment failure varies according to patient characteristics. Hence, this incidence is high among patients who initiated treatment with a nutritional status of thinness (19.02%), patients who started treatment at stage 4 of the infection (34.23%), those with no level of education (18.04%), patients who initiated treatment with a CD4 count below 100 cells/mm³ (22.82%), and patients co-infected with HIV and tuberculosis (22.74%).

3.4. Associated Factors of First-Line Antiretroviral Therapy Failure

After a multivariate Cox analysis, we identified that education level, CD4 count, and tuberculosis-HIV co-infection were the main predictive factors associated with first-line antiretroviral therapy failure. Table 4 shows that patients with no education had an increased risk of treatment failure (adjusted HR: 1.482; 95% CI: 1.027 - 1.983) compared to those with a university education. Additionally, individuals with elementary education at the start of treatment had a higher risk of

Table 4. Factors associated with first-line antiretroviral treatment failure according to the characteristics of 19,464 people living with HIV monitored between 2019 and 2024 in seven large cohort sites in Conakry (Guinea).

Variables	Number	Failure of first-line antiretroviral therapy Yes (%)	HR adjusted	CI 95%
Medical care site				
Dabompa Health Center	1798	243 (13.52)	*Ref.*	
Coleah Municipal Medical Center	1520	204 (13.42)	0.787	0.66 - 0.939
Tombolia Health Center	2508	370 (14.75)	0.804	0.669 - 0.966
Matam Municipal Medical Center	6927	1025 (14.80)	0.855	0.729 - 1.003
Ratoma Municipal Medical Center	2358	352 (14.93)	0.882	0.769 - 1.011
Flamboyants Municipal Medical Center	2821	436 (15.46)	0.838	0.713 - 0.985
Gbessia Port 1 Health Center	1532	256 (16.71)	0.992	0.85 - 1.158
Body Mass Index				
Normal	8449	999 (11.82)	*Ref.*	
Obesity	4063	640 (15.75)	0.99	0.894 - 1.097
Overweight	3256	544 (16.71)	0.675	0.599 - 0.759
Underweight	3696	703 (19.02)	0.659	0.584 - 0.744
WHO infection stage				
Stage 1	6972	371 (5.32)	*Ref.*	
Stage 2	4996	386 (7.73)	0.06	0.051 - 0.071
Stage 3	2048	264 (12.89)	0.085	0.074 - 0.097
Stage 4	5448	1865 (34.23)	0.234	0.204 - 0.268
Education Level				
College/University	4070	460 (11.30)	*Ref.*	
High School	4241	592 (13.96)	1.148	1.022 - 1.29
Elementary school	5395	795 (14.74)	1.206	1.084 - 1.341
No formal education	5758	1039 (18.04)	1.482	1.027 - 1.983
Marital status				
Divorced	1957	258 (13.18)	Ref.	
Widowed	3300	478 (14.48)	0.85	0.739 - 0.977
Married	7793	1164 (14.94)	0.969	0.868 - 1.082
Single	6414	986 (15.37)	1.027	0.941 - 1.12
CD4 count (cells/mm^3)				
≥350	5335	348 (6.52)	*Ref.*	
250 - 350	3716	325 (8.75)	3.061	2.577 - 3.637
100 - 250	4119	777 (18.86)	3.534	2.999 - 4.165

Continued

<100	6294	1436 (22.82)	4.049	3.623 - 4.525
Tuberculosis				
No	14210	1691 (11.90)	*Ref.*	
Yes	5254	1195 (22.74)	4.223	3.727 - 4.858

failure (adjusted HR: 1.206; 95% CI: 1.084 - 1.341) compared to those with university-level education.

Regarding CD4 count, patients who started treatment with less than 100 cells/mm^3 had a 4.05 times higher risk of failure (adjusted HR: 4.049; 95% CI: 3.623 - 4.525) compared to those with a count of 350 cells/mm^3 or higher. Similarly, those with CD4 counts between 100 and 250 cells/mm^3 and between 250 and 350 cells/mm^3 were 3.53 times (adjusted HR: 3.53; 95% CI: 2.999 - 4.165) and 3.06 times (adjusted HR: 3.06; 95% CI: 2.577 - 3.637) more likely to experience failure than those with counts of 350 cells/mm^3 or higher. Lastly, patients co-infected with tuberculosis and HIV at the start of treatment showed a 4.22 times higher risk of treatment failure (adjusted HR: 4.223; 95% CI: 3.727 - 4.858) compared to those who were not co-infected (Table 4).

These results highlight the importance of considering these factors when initiating and monitoring antiretroviral therapy to improve therapeutic effectiveness and reduce the rate of failure.

4. Discussion

This retrospective cohort study analyzed data from 19,464 HIV-positive patients aged 15 years and older who initiated first-line antiretroviral therapy (ART) between 2019 and 2023 across seven major cohort sites in the Conakry health region. Patients included had been on ART for at least six months prior to data collection, with an average follow-up duration of 36.02 months (approximately 3.017 years). The primary objective was to estimate the incidence of first-line ART failure and identify key predictive factors associated with such failures. Data were retrospectively extracted from health facility databases and data management tools. A multivariate Cox proportional hazards model was employed to determine the main predictive factors associated with first-line ART failure. The study revealed that 14.83% of patients experienced first-line antiretroviral treatment failure (4.92 per 100 person-years). Multivariate Cox regression analysis identified low educational attainment, low CD4 count, and co-infection with tuberculosis as significant predictors of treatment failure.

The findings of this study reveal a considerable burden of first-line antiretroviral therapy (ART) failure in the Conakry Health region, with an overall incidence of 14.83%, equivalent to 4.92 failures per 100 person-years. This figure aligns with previous reports from sub-Saharan Africa, where ART failure rates have ranged between 11% and 22%, depending on the study population and duration of follow-

up [27] [28]. Also, this figure is comparable to findings from other sub-Saharan African countries, where incidence rates of first-line ART failure range from 3.0 to 6.0 per 100 person-years, depending on the population characteristics and monitoring strategies employed [29]. The high rate of first-line treatment failure observed during our study period can be attributed to several factors. The main contributors include: a) poor adherence to treatment, often due to forgetfulness or voluntary discontinuation related to inadequate psychosocial support, side effects, or sociocultural beliefs; b) stigma and fear of social rejection, which discourage some patients from consistently taking their medication; c) delayed diagnosis or initiation of HIV care; d) the use of traditional medicine, sometimes in place of antiretroviral therapy (ART), thereby compromising treatment effectiveness; e) intermittent stock-outs of ARVs, which may lead to the development of drug resistance; f) insufficient virological monitoring, limiting the early detection of treatment failure; g) financial barriers that hinder regular access to healthcare services; h) the lack of routine screening for primary drug resistance, which can render certain first-line regimens ineffective from the outset; and i) frequent HIV-tuberculosis co-infection, which may worsen clinical outcomes and negatively impact the response to ART.

The cumulative incidence of virological failure at 9.87% is particularly important, as viral load is the most sensitive and reliable indicator of ART efficacy and the early detection of treatment failure [29]. Virological failure often precedes immunological and clinical failure, thus acting as an early warning signal for the need to switch to second-line therapy. In many low- and middle-income countries, limited access to routine viral load monitoring contributes to delays in detecting virological failure, resulting in prolonged exposure to ineffective regimens and the emergence of drug-resistant strains [30].

Virological failure, the main treatment failure in this study, is concerned due to its link with higher disease progression risk and transmission of resistant HIV strains [31]. This reinforces the importance of routine viral load testing as the gold standard for treatment monitoring, as recommended by the World Health Organization (WHO) [32]. However, in many resource-limited settings, such testing remains inconsistently implemented, resulting in reliance on less sensitive clinical and immunological indicators.

The relatively lower rate of immunological failure may reflect the limited sensitivity of CD4 count criteria to detect virological rebound, especially in patients with immune recovery despite ongoing viral replication. This discrepancy has been widely reported and supports the shift towards viral load-centered monitoring [28] [32].

Moreover, the sharp rise in failure after 24 months calls attention to long-term adherence challenges and the potential development of drug resistance. Several studies have demonstrated that adherence tends to decline over time, particularly in the absence of robust psychosocial support, adequate counseling, and effective health system interventions [31] [33]. The high and increasing incidence of first-

line ART failure over time in this study calls for urgent attention to strengthening ART monitoring systems, ensuring regular viral load testing, improving adherence support mechanisms, and scaling up timely switching to second-line regimens when needed.

The progressive increase in treatment failure rates, from 1.49% at 6 months to 47.82% at 60 months, underscores the need for sustained treatment monitoring and early intervention strategies. Similar temporal trends have been observed in longitudinal studies, suggesting that prolonged exposure to suboptimal regimens, poor adherence, and drug resistance mutations contribute to increased failure rates over time [33] [34].

Patients with lower educational levels, particularly those without formal education or with only elementary schooling, were found to have a higher likelihood of treatment failure compared to those with a university education. Specifically, the risk was 48.2% higher for individuals with no education and 20.6% higher for those with only elementary education.

This study showed that education significantly influences health outcomes, including ART adherence and retention in care. A retrospective cohort analysis in Guinea highlighted that lower educational attainment is associated with higher rates of loss to follow-up (LTFU), a key contributor to treatment failure. Similarly, a study in Southeast Ethiopia found that patients with no formal education or only primary education had higher rates of virological and immunological treatment failure [35] [36].

The mechanisms underlying this association include limited health literacy, which can impede understanding of treatment regimens and the importance of adherence. Additionally, individuals with lower education levels may face socioeconomic challenges, such as poverty and limited access to healthcare resources, further hindering consistent treatment adherence [37]. It's important to note that even in settings with universal healthcare, educational disparities can lead to differences in health outcomes. For instance, a study in Spain demonstrated that individuals with lower education levels had delayed HIV diagnoses and poorer responses to ART, despite equal access to healthcare services [37]. These findings underscore the need for targeted interventions that address educational disparities. Strategies may include tailored health education programs, community-based support initiatives, and efforts to improve overall health literacy among populations with lower educational attainments.

Our findings reveal that patients initiating ART with CD4 counts below 350 cells/mm^3 faced significantly higher risks of treatment failure. Specifically, individuals with CD4 counts under 100 cells/mm^3 exhibited over four times the risk, while those with counts between 100 - 250 and 250 - 350 cells/mm^3 had 3.53 and 3.06 times greater risk, respectively, compared to patients with CD4 levels of 350 cells/mm^3 or more.

These results align with existing literature emphasizing the importance of early ART initiation. A study by Moore et al. demonstrated that initiating ART at higher CD4 counts is associated with improved immune recovery and reduced mortality.

Patients who began treatment with CD4 counts above 200 cells/mm^3 were more likely to achieve CD4 counts exceeding 750 cells/mm^3, leading to better long-term outcomes [38].

Furthermore, research indicates that delayed ART initiation can lead to prolonged immune suppression, increasing the risk of both AIDS-related and non-AIDS-related complications. Mocroft et al. found that patients with lower baseline CD4 counts had higher incidences of non-AIDS diseases, such as liver and cardiovascular conditions, highlighting the broader health implications of late treatment initiation [39].

In the Conakry Health region, these findings are particularly pertinent. Studies have shown that patients initiating ART at higher CD4 counts experience reduced follow-up and better adherence to treatment protocols. For instance, a study in South Africa reported that initiating ART at CD4 counts above 200 cells/mm^3 was associated with improved treatment outcomes and reduced mortality [40].

Our study's findings reinforce the necessity of early HIV diagnosis and prompt initiation of ART to enhance treatment efficacy and patient survival rates. Implementing strategies to increase early testing and treatment initiation could significantly improve health outcomes for individuals living with HIV in Guinea and similar settings.

This study also revealed that patients co-infected with tuberculosis (TB) and human immunodeficiency virus (HIV) at the initiation of treatment had a significantly higher risk—over fourfold—of first-line treatment failure compared to those without co-infection (adjusted hazard ratio: 4.22). This finding aligns with existing literature that underscores the detrimental impact of TB/HIV co-infection on treatment outcomes. The immunosuppressive nature of HIV compromises the body's ability to combat TB, leading to increased susceptibility and severity of TB infections. Conversely, TB can accelerate the progression of HIV by enhancing viral replication and dissemination, thereby creating a synergistic effect that exacerbates patient outcomes [41].

Moreover, co-infected patients often face challenges such as drug-drug interactions between antiretroviral therapy (ART) and anti-TB medications, overlapping toxicities, and the risk of immune reconstitution inflammatory syndrome (IRIS) upon initiation of ART. These factors can complicate treatment regimens and adherence, further increasing the risk of treatment failure [41] [42].

The high prevalence of multidrug-resistant TB (MDR-TB) among patients experiencing first-line treatment failure is another concern. In high HIV prevalence settings, studies have reported a significant association between first-line treatment failure and the emergence of drug-resistant TB strains. This underscores the need for prompt and accurate drug susceptibility testing (DST) to guide effective treatment strategies [43].

Additionally, the timing of ART initiation in TB/HIV co-infected patients is critical. Early initiation of ART has been associated with improved survival rates; however, it also increases the risk of IRIS, which can complicate the clinical course.

Therefore, individualized treatment plans that consider the patient's immunological status and potential risks are essential [42] [44].

TB/HIV co-infection significantly increases the risk of first-line treatment failure. Addressing this issue requires a multifaceted approach that includes early diagnosis, careful management of co-infections, consideration of drug interactions, and robust healthcare infrastructure to support integrated care services. In the context of Guinea, where healthcare resources are limited, these findings highlight the importance of integrated TB and HIV services. Strengthening collaborative efforts between TB and HIV programs can facilitate early detection, timely initiation of appropriate therapies, and improved patient education, all of which are vital for reducing treatment failure rates.

5. Strengths and Limitations of the Study

Strengths

This study presents the following strengths:

- Large Sample Size: With 19,464 participants, this study provides robust data, enhancing the reliability of its findings.
- Extended Follow-Up: An average follow-up of over three years allows for the observation of long-term treatment outcomes.
- Multicenter Design: Data from seven cohort sites improves the generalizability of results within the Conakry region.

Limitations

Despite these strengths, this study presents the following limitations:

- Retrospective design: The study's retrospective nature may introduce biases related to data completeness and accuracy.
- Lack of adherence data: The absence of detailed adherence information limits the ability to assess its impact on treatment failure.
- Potential confounding variables: Factors such as socioeconomic status, mental health, and substance use were not accounted for, which could influence treatment outcomes.
- The study also did not include an assessment of antiretroviral treatment resistance in patients with therapeutic failure, particularly through genotypic tests that identify potential resistance mutations.
- The study was limited to HIV care sites in Conakry; therefore, its findings cannot be generalized to the entire country, particularly to inland regions, which may have distinct epidemiological, organizational, and socio-economic characteristics.

Despite these limitations, this study provides crucial reference information for the Ministry of Health and Hygiene, as well as the National Program for the Fight against AIDS and Hepatitis in the Conakry Health region. However, the findings of this study can provide key guidance to the Ministry of Health for considering the development and implementation of innovative strategies aimed at reducing first-line antiretroviral treatment failures nationwide. The aim is to establish an

effective and accessible monitoring system for therapeutic failures of first-line antiretroviral treatment in people living with HIV. This will help ensure better treatment success for individuals infected and affected by HIV/AIDS.

6. Conclusions

This study highlights the persistent challenge of first-line antiretroviral therapy (ART) failure in enhancing HIV care quality. Over a median follow-up of approximately 3 years, the cumulative incidence of ART failure reached 14.83%, with an incidence rate of 4.92 per person-years—rising as treatment progressed. Key predictors of failure included low education, low CD4 count, and tuberculosis-HIV co-infection at treatment initiation.

These findings emphasize the critical importance of early HIV diagnosis and prompt ART initiation to improve outcomes and survival. Limited health literacy, often linked to low educational attainment, can hinder treatment adherence and comprehension. Thus, addressing educational disparities is crucial. Interventions should incorporate tailored health education, community-based support, and efforts to boost health literacy. Moreover, integrated TB-HIV programs can promote early detection, timely care, and better patient guidance, helping to reduce failure rates. Future research should explore a broader set of variables through mixed-method studies and investigate antiretroviral resistance to strengthen HIV treatment strategies, especially in Guinea.

Ethical Considerations

Prior to the commencement of this study, the research protocol was reviewed and approved by the medical scientific committee of Gamal Abdel Nasser University of Conakry and registered under the number (272/UGANC/RECT/VRE/2024). Permission to use the data was obtained from the coordination of the National AIDS and Hepatitis Control Program (PNLSH) and from the administrators of the study sites. To maintain confidentiality, all patient-identifying information was excluded during data collection.

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Author Contributions

N. N. L.: Study design, supervision of data collection, data analysis, manuscript

writing.

T. S. D.: Supervision of data collection, data analysis, and manuscript writing.

M. F. K.: Data analysis, manuscript review.

S. P. K.: Supervision of data collection, data analysis, and manuscript review.

A. M. C.: Data analysis, manuscript review.

S. S.: Study design, results validation, manuscript review.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral therapy
CD4	Cluster of Differentiation 4
HIV	Human immunodeficiency virus
PNLSH	National AIDS and Hepatitis Control Progra
WHO	World Health Organization