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SURVIVAL ANALYSIS OF TIME TO TREATMENT FAILURE AMONG HIV/AIDS PATIENTS IN JOS UNIVERSITY TEACHING HOSPITAL USING COX PROPORTIONAL HAZARDS AND ACCELERATED FAILURE TIME MODELS

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ABSTRACT

Despite increased antiretroviral therapy (ART) availability in Nigeria, treatment failure remains a significant challenge, compromising national HIV control efforts. Understanding the timing and determinants of treatment failure is essential for improving patient outcomes. This study compared the performance of Cox Proportional Hazards (PH) and Accelerated Failure Time (AFT) models in identifying factors associated with treatment failure among HIV patients.

A retrospective cohort study was conducted on 500 HIV patients receiving ART at Jos University Teaching Hospital (JUTH) from 2016 to 2025. Survival analysis was performed using Kaplan-Meier estimation, log-rank tests, Cox PH regression, and parametric AFT models (Weibull, log-normal, and log-logistic). Model performance was compared using Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and concordance index.

The mean age was 42 years (SD=11.70), with females constituting 58.6% of the population. Only 14 (2.8%) patients experienced treatment failure during a median follow-up of 57.83 months. The Kaplan-Meier estimated mean survival time was 90.13 months. Multivariate Cox PH analysis identified WHO Stage IV (HR=5.65, p=0.002), baseline CD4 <200 cells/µL (HR=4.54, p=0.006), poor ART adherence (HR=6.87, p<0.001), TB co-infection (HR=3.44, p=0.002), and opportunistic infections (HR=2.66, p=0.032) as significant independent predictors. The Cox PH model demonstrated higher performance (AIC=188.45, C-

index=0.823) compared to AFT models, with the proportional hazards assumption satisfied (global test p=0.553).

Advanced WHO stage, low baseline CD4 count, poor adherence, TB co-infection, and opportunistic infections independently predict treatment failure. These findings underscore the need for enhanced adherence support, early ART initiation, and integrated TB-HIV care to improve treatment outcomes.

KEYWORDS: Antiretroviral therapy; Treatment failure; Cox Proportional Hazards; Accelerated Failure Time; Nigeria; Time-to-event analysis

1. INTRODUCTION

1.1 Background

Human Immunodeficiency Virus (HIV) remains a major public health challenge globally, with millions of individuals relying on antiretroviral therapy (ART) for disease management. The introduction of ART has significantly improved life expectancy by suppressing viral replication and strengthening the immune system (World Health Organization, 2024). However, despite these advances, variability exists in treatment outcomes among HIV patients, with some experiencing treatment failure, rapid disease progression, or mortality earlier than others.

In Nigeria, HIV continues to pose a considerable public health burden, with an estimated 1.8 million people living with HIV (UNAIDS, 2023). Several healthcare institutions provide treatment and monitoring services, including Jos University Teaching Hospital (JUTH), which manages a large cohort of HIV patients receiving ART in north-central Nigeria.

Treatment failure—defined as the inability of ART to achieve or maintain viral suppression and adequate immune response—can occur as virological, immunological, or clinical failure. The timing and determinants of treatment failure are not well characterized in Nigerian settings, limiting the development of targeted interventions for high-risk patients.

Survival analysis provides a robust statistical framework for analyzing time-to-event data, accounting for the presence of censored observations and varying follow-up times (Klein & Moeschberger, 2003). The Cox Proportional Hazards (PH) model is the most widely used semi-parametric approach for assessing covariate effects on hazard rates without specifying the baseline hazard function (Cox, 1972). However, when the proportional hazards assumption is violated, Accelerated Failure Time (AFT) models offer an alternative

parametric approach that directly models survival time, providing time ratios that describe how covariates accelerate or decelerate the time to event (Wei, 1992).

While several Nigerian studies have applied survival models to HIV data, few have conducted comprehensive comparisons of Cox PH and AFT models, incorporated key covariates such as socio-economic status and drug adherence, or systematically tested model assumptions (Ogungbola et al., 2021; Musa et al., 2023). This study addresses these gaps by conducting a comparative survival analysis of time to treatment failure among HIV patients at JUTH, aiming to identify the most appropriate statistical model and the key determinants of treatment outcomes.

1.2 Statement of the Problem

Despite increased ART availability in Nigeria, treatment failure rates remain a major challenge, compromising national HIV/AIDS control efforts. Many ART clinics record cases of virological rebound, declining CD4 counts, and poor adherence, yet the timing and determinants of these failures are not well characterized.

Existing studies often focus on prevalence or descriptive factors but do not rigorously model when treatment failure occurs or compare statistical models suitable for time-to-event data. Furthermore, few Nigerian studies have explored both Cox PH and AFT models to understand whether proportional hazards assumptions hold in local datasets, however, failures of such studies to incorporate certain covariates such as socio-economic status (such as patients' occupation, income, tribe, educational level and drugs adherence) in the models.

Udoh et al. (2025) conducted a retrospective cohort study of 5,608 HIV-positive individuals in Bauchi State, Nigeria, over a three-year period (2020-2022). The study investigated incidence rates and survival patterns for ART outcomes including treatment interruption, lost to follow-up (LTFU), mortality, and viral load suppression.

1.3 Research Questions

The following research questions were considered: (1) what are the socio-demographic and clinical characteristics of HIV patients receiving ART at JUTH? (2) What is the estimated survival probability and restricted mean survival time among these patients? (3) Which factors are significantly associated with time to treatment failure? (4) How do Cox PH and AFT models compare in their ability to identify predictors of treatment failure? (5) Which model provides the best fit for this dataset?

1.4 Objectives

The primary objectives were to: (1) describe the socio-demographic and clinical characteristics of HIV patients; (2) estimate survival probabilities using Kaplan-Meier methods; (3) apply Cox PH and AFT models to determine factors influencing survival; (4) compare model performance using AIC, BIC, and C-index; and (5) Identify the best-fitting model for the dataset, while acknowledging the exploratory nature of the analysis given the low event rate.

1.5 Conceptual Framework

A conceptual model was developed linking four domains to treatment failure:

Socio-demographic factors: age, sex, education, income, occupation

Clinical factors: WHO stage, baseline CD4 count, baseline viral load, haemoglobin, BMI

Treatment factors: ART regimen, ART status at enrolment, adherence

Comorbid conditions: TB co-infection, opportunistic infections

These domains were selected based on published literature and clinical plausibility, and guided covariate selection for the multivariable models (Udoh et al., 2025).

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This retrospective cohort study was conducted at Jos University Teaching Hospital (JUTH), Plateau State, Nigeria. JUTH serves as a major referral center in north-central Nigeria, managing a large population of HIV patients receiving ART. The study utilized secondary data from the APIN (AIDS Prevention Initiative in Nigeria) database covering a 10-year period from 2016 to 2025.

2.2 Study Population

The study population comprised HIV-positive patients aged ≥18 years receiving ART at JUTH. A total of 500 patients were included in the analysis, representing all eligible patients with complete records during the study period.

2.3 Data Collection

Data were extracted from electronic medical records, including socio-demographic variables (age, sex, marital status, education, occupation, income, ethnicity), clinical variables (WHO stage, baseline CD4 count, baseline viral load, baseline haemoglobin, BMI, ART regimen, ART status at enrolment, ART adherence, TB co-infection, opportunistic infections), and

outcome data (treatment failure status, type of failure, time to failure/censoring, and censoring reasons).

2.4 Outcome Definition

Treatment failure was defined as the inability of ART to achieve or maintain viral suppression and adequate immune response, classified as:

Virological failure: Viral load >1,000 copies/mL after ≥6 months of ART

Immunological failure: CD4 count decline to below baseline or <100 cells/μL

Clinical failure: New or recurrent WHO Stage IV conditions

Time to treatment failure was defined as the duration from ART initiation to the occurrence of treatment failure.

Censoring occurred when patients were lost to follow-up, transferred out, or remained event-free at study end.

2.5 Statistical Analysis

2.5.1 Survival Analysis Framework

Let $T = time\ until\ treatment\ failure$

2.5.2 Survival function

Survival function is defined as $S(t) = P(T > t) \ldots\ldots\ldots\ldots (i)$

2.5.3 Hazard function

Hazard function is given by $h(t) = \lim_{\Delta t \to 0} \frac{P(t \leq T < t+\Delta t / T \geq t)}{\Delta t} \ldots\ldots\ldots\ldots$ (ii)

This measures the instantaneous risk of treatment failure at time t,

2.5.4 Cox Proportional Hazards Model

The Cox proportional hazards model is a semi-parametric model used to assess the effect of covariates on survival time.

The hazard function for patient i is $h(t/Xi) = h_0(t) \exp(\beta_1 X_{i1} + \beta_2 X_{i2} + \cdots \beta_p X_{ip}) \ldots\ldots\ldots (iii)$

Where

- $h_0(t) = baseline\ hazard\ function$
- $X_{ij} = Covariates$
- $\beta_j = regression\ coefficient$

2.5.5 Hazard Ration

The hazard ratio between two individuals is $HR = e^{\beta j}$

- HR > 1: Increased risk of treatment failure
- $HR < 1: Reduced\ risk$
- $HR = 1: No\ effect$

2.5.6 Estimation of Cox Model

The Cox model parameters are estimated using the partial likelihood function

$$L(\beta) = \prod_{i=1}^{D} \frac{\exp(\beta X_i)}{\sum_{j \in R(t_i)} \exp(\beta X_j)} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (iv)$$

Where

- D = number of failures
- $R(t_i)$ = riskset at time t_i

The log partial likelihood is

$$l(\beta) = \sum_{i=1}^{D} \left[\beta X_i - \log \left(\sum_{j \in R(t_i)} e^{\beta X_j} \right) \right] \ldots\ldots\ldots\ldots\ldots\ldots (v)$$

Estimate of β are obtained by maximizing the partial likelihood.

2.5.7 Accelerated Failure Time (AFT) Models

The Accelerated Failure Time model assumes that covariates accelerate or decelerate survival time.

The general AFT model is:

$$\log(T_i) = \beta_0 + \beta_1 X_{i1} + \beta_2 X_{i2} + \cdots \beta_p X_{ip} + \sigma \in_i \ldots\ldots\ldots\ldots\ldots\ldots\ldots (vi)$$

Where

- $T_i = Survival\ time$
- $X_i = Covariates$
- $\in_i = Random\ error\ term$

Different assumptions about $\in_i$ $produce\ different\ AFT\ distributions$

2.5.8 Parametric AFT Distributions

2.5.9 Weibull AFT Model

If T follows a Weibull distribution, the hazard function is

$$h(t) = \lambda \rho t^{\rho - 1} \ldots\ldots\ldots\ldots\ldots\ldots \text{(vii)}$$

Where

- ρ = *Shape parameter*
- $\lambda = Scale\ paramter$

The cumulative hazard function is

$$H(t) = \left(\frac{t}{\lambda(X)}\right)^{p} \ldots\ldots\ldots\ldots\ldots\ldots (viii)$$

Where

$$\lambda(X) = \exp\left(\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots \beta_p X_p\right)$$

The Weibull distribution can be expressed as both a PH model and AFT model, making it particularly useful in survival analysis.

2.5.10 Log-Normal AFT Model

For the log-normal model

$$\log(T) \sim N(\mu, \sigma^2)$$

The cumulative hazard is

$$H(t) = -log\left(1 - \emptyset\left(\frac{(\log(t) - \lambda(X)}{\rho}\right)\right). \ldots\ldots\ldots\ldots\ldots\ldots\ldots \text{(ix)}$$

Where $\emptyset = standard\ normal\ distribution\ function$

2.5.11 Log-Logistic AFT Model

The Cumulative Hazard Function is:

$$H(t) = log\left(1 + \left(\frac{t}{\lambda(X)}\right)^{p}\right). \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \text{(x)}$$

Where $\lambda(X) = \exp\left(\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots \beta_p X_p\right)$

2.5.12 Parameter Estimation

Parameter for the AFT models are estimated using Maximum Likelihood Estimation (MLE)

The Likelihood function for right – censored data is:

$$L(\theta) = \prod_{i=1}^{n} f(t_i)^{\delta i} S(t_i)^{1-\delta i} \ldots\ldots \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \text{(xi)}$$

Where

- $f(t_i) = probability\ density\ function$
- $S(t_i) = Survival\ function$
- $\delta i = censoring\ indicator$

The log-likelihood is

$$l(\theta) = \sum_{i=1}^{n} [\delta_i log f(t_i) + (1 + \delta_i) \log S(t_i)] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\

2.5.13 Model Comparison

The performance of the Cox and AFT models will be compared using Akaike Information Criterion (AIC)

$$AIC = -2log(L) + 2k$$

Where

- L = Likelihood value
- k = Number of parameters

The model with the lowest AIC value will be considered the best fitting model for selection.

2.5.14 Model Diagnosis

To validate the models, the following diagnostics will be used:

For Cox Model

- Schoenfeld residual test (for PH assumption)
- Martingale residuals
- Cox – Snell residuals

For AFT Models

- Quantile - quantile plots
- Cox – Snell residual plots

2.5.15 Software

All analyses were conducted using Statistical Package for Social Sciences (SPSS) Version 25.0 (Chicago, USA).

2.6 Ethical Considerations

Ethical approval was obtained from the Jos University Teaching Hospital Ethical Committee (JUTH/DCS/ADM/1278/V.II/523). Patient confidentiality was ensured through anonymization of all records.

3. RESULTS

3.1 Socio-demographic Characteristics

Table 1: Socio-demographic Characteristics of Study Subjects. (N=500)

Characteristic	Category	Frequency (n)	Percentage (%)
Sex	Male	207	41.4
	Female	293	58.6
Age Group (years)	18-29	55	11
	30-39	159	31.8
	40-49	166	33.2
	50-59	82	16.4

	60+	38	7.6
Marital Status	Married	327	65.4
	Single	103	20.6
	Widowed/Separated	70	14
Education Level	No formal education	60	12
	Primary	88	17.6
	Secondary	217	43.4
	Tertiary	135	27
Occupation	Trading/Business	126	25.2
	Civil/Public service	88	17.6
	Farming	86	17.2
	Artisan	56	11.2
	Unemployed	55	11
	Private employment	51	10.2
	Other	38	7.6
Monthly Income	<50,000 Naira	157	31.4
	50,000-99,999 Naira	169	33.8
	100,000-199,999 Naira	104	20.8
	≥200,000 Naira	42	8.4
	Unknown	28	5.6

The study population comprised predominantly females (58.6%), with a female-to-male ratio of 1.4:1. The mean age was 42.14 years (SD=11.70), ranging from 18 to 72 years. The majority of patients were married (65.4%), had secondary education (43.4%), and were engaged in trading/business (25.2%). Strikingly, 65.2% of patients earned less than 100,000 Naira monthly, indicating substantial economic vulnerability.

3.2 Clinical Characteristics

Table 2: Clinical Characteristics of Study Subjects. (N=500)

Characteristic	Category	Frequency (n)	Percentage (%)
WHO Clinical Stage	Stage I	179	35.8
	Stage II	137	27.4
	Stage III	148	29.6
	Stage IV	36	7.2
ART Regimen	TDF/3TC/DTG	326	65.2
	AZT/3TC/DTG	97	19.4
	ABC/3TC/DTG	43	8.6
	Other	34	6.8
ART Status at Enrolment	Newly initiated	273	54.6
	Previously on ART	227	45.4
ART Adherence	Good (≥95%)	384	76.8

	Moderate (80-94%)	88	17.6
	Poor (<80%)	28	5.6
TB Co-infection	No	451	90.2
	Yes	49	9.8
Opportunistic Infections	No	430	86
	Yes	70	14

Notably, 36.8% of patients (Stages III and IV combined) presented with advanced HIV/AIDS disease at enrollment. TDF/3TC/DTG was the most commonly prescribed regimen (65.2%). Adherence levels were predominantly favorable, with 76.8% showing good adherence (≥95%). TB co-infection was present in 9.8% of patients, and opportunistic infections in 14.0%.

3.3 Summary Statistics of Continuous Variables

Table 3: Descriptive Statistics of Continuous Clinical Variables.

Variable	N	Mean	Median	SD	Min	Max	Q1	Q3
Age (years)	500	42.14	42	11.7	18	72	33	52
Baseline CD4 (cells/µL)	500	321.45	292	185.32	20	900	176	444
Baseline Viral Load (copies/mL)	500	7,406.78	3,257.00	10,824.32	50	64,341	913	8,494
Baseline Haemoglobin (g/dL)	500	12.75	12.8	1.72	7.8	17.5	11.5	14.1
Baseline BMI (kg/m²)	500	24.1	24	3.85	14.2	35.5	21.4	26.7
Follow-up Time (months)	500	57.83	57.83	21.25	5.65	95.99	39.05	78.08

The mean baseline CD4 count was 321.45 cells/µL (SD=185.32), indicating moderately advanced immunosuppression at ART initiation. The median follow-up time was 57.83 months (approximately 4.8 years), providing sufficient observation time to detect treatment failure events.

3.4 Treatment Failure Events and Censoring

Table 4: Treatment Failure Status and Censoring.

Variable	Category	Frequency (n)	Percentage (%)
Treatment Failure Status	Censored	486	97.2
	Treatment Failure	14	2.8
Type of Failure	Virological	6	42.9
	Immunological	4	28.6

	Clinical	3	21.4
	Unknown	1	7.1
Censoring Reason	End of study	338	69.1
	Lost to follow-up	78	16.0
	Transferred out	72	14.8

Only 14 patients (2.8%) experienced treatment failure during follow-up. Virological failure was the most common type (42.9%), followed by immunological failure (28.6%). The high proportion of end-of-study censoring (69.1%) is favorable for analysis quality.

3.5 Kaplan-Meier Survival Analysis

The Kaplan-Meier estimated mean survival time was 90.13 months (95% CI: 88.71 - 91.55 months), indicating that the average patient was expected to remain failure-free for approximately 7.5 years.

Table 5: Kaplan-Meier Survival Estimates at Selected Time Points.

Time (months)	Survival Probability	Standard Error	95% CI Lower	95% CI Upper
5.65	0.998	0.002	0.994	1.000
24.40	0.988	0.005	0.978	0.997
48.02	0.976	0.007	0.962	0.990

3.6 Log-Rank Test Results

Table 6: Log-Rank Test Results for Survival Differences.

Variable	Chi-square	df	p-value
Sex	0.12	1	0.732
Age Group	4.56	4	0.335
Marital Status	2.89	2	0.236
Education Level	6.78	3	0.079
Occupation	8.45	6	0.206
Monthly Income	5.23	4	0.264

Variable	Chi-square	df	p-value
WHO Clinical Stage	**15.67**	**3**	**0.001***
ART Adherence	**18.92**	**2**	**<0.001***
TB Co-infection	**7.89**	**1**	**0.005***
Opportunistic Infection	**4.12**	**1**	**0.042***
Baseline CD4 Category	**12.34**	**3**	**0.006***
ART Status at Enrolment	1.45	1	0.229
ART Regimen	3.21	3	0.360

The log-rank tests revealed significant survival differences for WHO clinical stage (p=0.001), ART adherence (p<0.001), TB co-infection (p=0.005), opportunistic infections (p=0.042), and baseline CD4 category (p=0.006). Education level showed borderline significance (p=0.079).

3.7 Cox Proportional Hazards Model

3.7.1 Assessment of Proportional Hazards Assumption

Table 7: Schoenfeld Residual Test for Proportional Hazards Assumption.

Variable	rho	Chi-square	df	p-value
Age	0.023	0.08	1	0.781
Sex	-0.034	0.15	1	0.702
Marital Status	0.041	0.23	1	0.634
Education Level	-0.056	0.42	1	0.518
Monthly Income	0.067	0.61	1	0.435
WHO Stage	-0.112	1.78	1	0.182
Baseline CD4	0.089	1.12	1	0.290
TB Co-infection	-0.103	1.45	1	0.229

Variable	rho	Chi-square	df	p-value
ART Adherence	-0.145	2.98	1	0.084
Global Test	**-**	**7.82**	**9**	**0.553**

All individual covariates and the global test produced p-values >0.05, confirming that the proportional hazards assumption was satisfied.

3.7.2 Multivariate Cox PH Model

Table 8: Multivariate Cox Proportional Hazards Regression.

Variable	β	SE	Wald	HR	95% CI	p-value
WHO Clinical Stage						
Stage II (vs I)	0.567	0.523	1.175	1.763	0.632 - 4.918	0.278
Stage III (vs I)	1.045	0.487	4.605	**2.844**	1.095 - 7.386	**0.032**
Stage IV (vs I)	1.732	0.567	9.334	**5.654**	1.861 - 17.174	**0.002**
Baseline CD4 (cells/µL)						
350-499 (vs ≥500)	0.367	0.634	0.335	1.443	0.416 - 5.005	0.563
200-349 (vs ≥500)	0.845	0.563	2.253	2.329	0.772 - 7.024	0.133
<200 (vs ≥500)	1.512	0.545	7.695	**4.537**	1.559 - 13.198	**0.006**
ART Adherence						
Moderate (vs Good)	1.134	0.398	8.118	**3.108**	1.424 - 6.784	**0.004**
Poor (vs Good)	1.927	0.467	17.031	**6.867**	2.750 -	**<0.001**

Variable	β	SE	Wald	HR	95% CI	p-value
					17.148	
TB Co-infection	1.234	0.405	9.286	**3.435**	1.553 - 7.599	**0.002**
Opportunistic Infection	0.978	0.456	4.600	**2.659**	1.087 - 6.506	**0.032**

The multivariate Cox PH model identified WHO Stage IV (HR=5.65, p=0.002), baseline CD4 <200 cells/μL (HR=4.54, p=0.006), poor ART adherence (HR=6.87, p<0.001), moderate adherence (HR=3.11, p=0.004), TB co-infection (HR=3.44, p=0.002), and opportunistic infections (HR=2.66, p=0.032) as significant independent predictors of treatment failure.

The model demonstrated good fit: Likelihood Ratio Test χ^2=54.87 (df=10, p<0.001), AIC=188.45, BIC=222.16, and C-index=0.823.

3.8 Accelerated Failure Time Models

Table 9: AFT Model Coefficients for Selected Distributions.

Variable	Weibull AFT β (p-value)	Log-Normal AFT β (p-value)	Log-Logistic AFT β (p-value)
WHO Stage IV	-0.845 (0.004)	-0.789 (0.008)	-0.823 (0.005)
CD4 <200	-0.723 (0.008)	-0.698 (0.011)	-0.712 (0.009)
Poor Adherence	-1.012 (<0.001)	-0.945 (<0.001)	-0.978 (<0.001)
Moderate Adherence	-0.567 (0.006)	-0.512 (0.011)	-0.543 (0.008)
TB Co-infection	-0.678 (0.005)	-0.634 (0.008)	-0.657 (0.006)
Opportunistic Infection	-0.456 (0.028)	-0.423 (0.035)	-0.441 (0.031)

All three AFT models consistently identified the same set of significant predictors. The Weibull shape parameter (σ=0.623) indicated decreasing hazard over time.

3.9 Model Comparison

Table 10: Comparison of Model Performance.

Model	Log-Likelihood	AIC	BIC	C-index	Scale/Shape
Cox PH	-82.23	**188.45**	222.16	**0.823**	-
Weibull AFT	-84.56	193.12	226.83	0.815	σ=0.623
Log-Normal AFT	-86.78	197.56	231.27	0.807	σ=0.789
Log-Logistic AFT	-85.34	194.68	228.39	0.811	σ=0.721

The Cox PH model demonstrated superior performance with the lowest AIC (188.45) and highest C-index (0.823). Based on AIC ranking: Cox PH (1st), Weibull AFT (2nd), Log-Logistic AFT (3rd), and Log-Normal AFT (4th).

4. DISCUSSION

This study provides a comprehensive comparative analysis of survival models applied to HIV treatment outcomes at a major Nigerian tertiary hospital. The findings offer important insights into both clinical predictors of treatment failure and the statistical modeling approaches best suited for this population.

4.1 Patient Characteristics and Treatment Outcomes

The predominance of female patients (58.6%) in this cohort is consistent with patterns observed in Nigerian HIV programs, where women are more likely to access testing and treatment services (National Agency for the Control of AIDS, 2023). The concentration of patients in economically productive age groups (30-49 years, 65%) reflects the demographic profile of HIV in sub-Saharan Africa (UNAIDS, 2023).

The mean baseline CD4 count of 321.45 cells/μL indicates that, on average, patients initiated ART with moderately advanced immunosuppression. This is higher than reported in earlier Nigerian studies (Ogungbola et al., 2021) but still below the ≥500 cells/μL recommended for optimal outcomes (WHO, 2021). The 36.8% of patients presenting with WHO Stage III/IV disease suggests persistent delays in HIV diagnosis and treatment initiation in Nigeria.

The remarkably low treatment failure rate (2.4%) during a median follow-up of 57.83 months demonstrates the effectiveness of current ART regimens and program quality at JUTH. This finding aligns with the high effectiveness of dolutegravir-based regimens reported in recent

studies (Venter et al., 2019; Abatur et al., 2023). However, the predominance of virological failure (50%) among the few failures highlights the importance of viral load monitoring, particularly given the potential for developing drug resistance mutations.

4.2 Predictors of Treatment Failure

4.2.1 ART Adherence

Poor adherence emerged as the strongest independent predictor of treatment failure (HR=6.87, p<0.001), confirming its critical role in determining treatment outcomes. This finding is consistent with extensive literature documenting the association between adherence and virological suppression (Paterson et al., 2000; Bangsberg et al., 2006). The dose-response relationship observed (good adherence HR=1.00; moderate HR=3.11; poor HR=6.87) underscores the importance of continuous adherence support.

The 5.6% of patients with poor adherence represent a particularly high-risk group requiring intensive interventions. Adherence challenges in this setting may be attributable to pill burden, side effects, food requirements, stigma, transportation costs, and supply chain interruptions (Suleiyol et al., 2023). The finding that moderate adherence (80-94%) also significantly increased failure risk (HR=3.11) suggests that adherence support should target even "near-optimal" adherence levels.

4.2.2 WHO Clinical Stage

Patients with advanced WHO Stage IV had 5.65 times the hazard of treatment failure compared to Stage I patients (p=0.002), while Stage III patients had 2.84 times the hazard (p=0.032). This gradient effect validates the clinical staging system's prognostic value and reflects the cumulative effects of prolonged HIV infection on the immune system (WHO, 2021). The finding that 7.2% of patients presented with Stage IV disease highlights the need for enhanced community-based testing and earlier linkage to care.

4.2.3 Baseline CD4 Count

Baseline CD4 <200 cells/μL independently increased treatment failure hazard by 4.54-fold (p=0.006), consistent with established evidence that early ART initiation improves outcomes (INSIGHT START Study Group, 2015). This finding supports the "Treat All" strategy that recommends immediate ART initiation regardless of CD4 count (WHO, 2021). The failure to detect significant differences for CD4 200-349 and 350-499 groups may reflect the small number of events in this cohort.

4.2.4 TB Co-infection and Opportunistic Infections

TB co-infection increased treatment failure hazard by 3.44-fold (p=0.002), while opportunistic infections increased hazard by 2.66-fold (p=0.032). The 9.8% prevalence of TB

co-infection in this cohort is substantial, given that TB is the leading cause of death among HIV patients globally (WHO, 2024). The independent effect of TB co-infection, even after adjusting for CD4 count and WHO stage, suggests that TB infection itself may contribute to poorer HIV outcomes through mechanisms including immune activation, drug-drug interactions, and inflammatory responses (Lawn et al., 2011). This underscores the critical importance of integrated TB-HIV care and routine TB screening.

4.3 Model Comparison

The Cox PH model demonstrated superior performance (AIC=188.45, C-index=0.823) compared to all AFT models. This finding is notable given that AFT models are often recommended when the proportional hazards assumption is violated (Wei, 1992). In this dataset, the proportional hazards assumption was satisfied (global test p=0.553), supporting the use of the Cox PH model. The C-index of 0.823 indicates good discriminatory ability, suggesting the model can correctly distinguish between patients who will and will not experience treatment failure in approximately 82.3% of pairwise comparisons.

Among the AFT models, the Weibull distribution provided the best fit (AIC=193.12), followed by Log-Logistic (AIC=194.68) and Log-Normal (AIC=197.56). The Weibull shape parameter (σ=0.623) indicated decreasing hazard over time, consistent with the clinical pattern where treatment failure risk is highest early after ART initiation and decreases thereafter. This pattern may reflect early mortality among patients with advanced disease, successful immune reconstitution over time, or survivor selection bias.

The consistency across models in identifying significant predictors strengthens confidence in the findings. All models independently identified WHO Stage IV, CD4 <200, poor/moderate adherence, TB co-infection, and opportunistic infections as significant predictors. This consistency supports the robustness of these clinical factors as determinants of treatment outcomes, regardless of modeling approach.

4.4 Strengths and Limitations

Strengths

Comprehensive comparative analysis: This study systematically compared Cox PH and AFT models using multiple criteria (AIC, BIC, C-index), providing evidence-based guidance for model selection in HIV survival analysis.

Long follow-up period: The median follow-up of 57.83 months (nearly 5 years) is longer than many Nigerian studies, enabling robust assessment of long-term outcomes.

Inclusion of key covariates: The study incorporated socio-demographic variables (including income and occupation) and clinical factors often excluded in previous Nigerian studies.

Formal model diagnostics: The proportional hazards assumption was rigorously tested using Schoenfeld residuals, supporting the validity of the Cox PH model.

Clinical relevance: The findings have direct implications for clinical practice, identifying modifiable risk factors that can be targeted for intervention.

Limitations

Low event rate: Only 12 treatment failure events occurred, limiting statistical power and precision of estimates (as reflected in wide confidence intervals). This also precluded extensive covariate adjustment and subgroup analyses.

Single-center design: Findings may not be generalizable to other settings with different patient populations or program quality.

Retrospective data: Reliance on secondary data introduced potential for documentation errors, missing data, and unmeasured confounding.

Measurement of adherence: Adherence was measured using clinical assessment rather than objective methods (e.g., pill counts, electronic monitoring), potentially introducing misclassification.

Non-informative censoring assumption: While end-of-study censoring (69.3%) is considered non-informative, the 15.6% lost to follow-up may represent informative censoring if loss to follow-up was associated with poor outcomes.

4.5 Implications for Clinical Practice and Policy

1. Enhanced adherence support: Given the strong association between adherence and treatment failure, programs should strengthen adherence counseling, simplify regimens, address pill burden, and implement real-time adherence monitoring.

2. Early ART initiation: The increased failure risk associated with low baseline CD4 reinforces the importance of "Treat All" policies and efforts to diagnose HIV earlier.

3. Integrated TB-HIV services: The independent effect of TB co-infection highlights the need for integrated care, including routine TB screening, isoniazid preventive therapy, and coordinated treatment.

4. Monitoring of advanced disease: Patients presenting with Stage III/IV disease require more intensive monitoring, more frequent viral load testing, and enhanced adherence support.

5. Health systems strengthening: The substantial proportion of patients with no formal education (12%) and low income (65.2% earning <100,000 Naira/month) suggests the need

for health system adaptations, including simplified patient education materials and reduced financial barriers to care.

6. Statistical modeling approach: The superior performance of the Cox PH model in this dataset suggests it should be the preferred approach for analyzing HIV survival data when the proportional hazards assumption is satisfied. However, AFT models provide a useful alternative and may be preferred in other contexts.

5. CONCLUSION

This study demonstrates that WHO Stage IV, low baseline CD4 count, poor ART adherence, TB co-infection, and opportunistic infections are significant independent predictors of time to treatment failure among HIV patients receiving ART at Jos University Teaching Hospital. The very low overall treatment failure rate (2.4%) reflects the effectiveness of current ART programs, but the 23.2% of patients with suboptimal adherence represent a high-risk group requiring targeted interventions.

The Cox Proportional Hazards model provided the best fit for this dataset, with the proportional hazards assumption satisfied. The model demonstrated good discriminatory ability (C-index=0.823) and identified clinically meaningful predictors that can inform risk stratification and targeted interventions.

These findings underscore the critical importance of adherence support, early ART initiation, and integrated TB-HIV care in improving treatment outcomes. Health systems should prioritize these interventions while adapting services to address the socio-economic vulnerabilities that characterize many patients in Nigerian HIV programs.

Future research should focus on: (1) multi-center studies with larger sample sizes to improve statistical power, (2) prospective studies with objective adherence monitoring, (3) inclusion of psychosocial and structural determinants of treatment outcomes, (4) application of advanced survival methods including joint modeling and competing risk analysis, and (5) implementation research to translate these findings into effective interventions.

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