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TREATMENT FAILURE AMONG YOUTH AGED 10-24 YEARS ON ANTIRETROVIRAL THERAPY ATA LEVEL TWO TEACHING HOSPITAL IN RWANDA

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Abstract: **Introduction Treatment failure among youth aged 10–24 years receiving antiretroviral therapy (ART) remains a critical challenge to achieving the UNAIDS 95-95-95 targets in sub-Saharan Africa. In Rwanda, where HIV prevalence is approximately 3.0% nationally, adolescents and young adults face disproportionate adherence barriers and poorer treatment outcomes relative to older adults. Evidence on the magnitude and determinants of ART failure in this age group from decentralized Rwandan facilities is limited. This study aimed to quantify the prevalence and identify socio-demographic and clinical determinants of treatment failure among youth on ART at Rwamagana Level Two Teaching Hospital. Methods We conducted a retrospective cross-sectional study using secondary data extracted from 385 medical records of youth aged 10–24 years enrolled in HIV care and on ART for at least 12 months at Rwamagana Level Two Teaching Hospital, Rwanda (March–June 2024). Treatment failure was defined according to WHO 2023 criteria and classified as virological (viral load ≥1,000 copies/mL on two consecutive measurements following enhanced adherence counselling), immunological, or clinical failure. Socio-demographic and clinical variables were extracted using a structured data abstraction form. Data were analyzed using SPSS v26.0; descriptive statistics, chi-square tests, and multivariable logistic regression were performed. This study adheres to STROBE reporting guidelines. Results : Of 385 youth (53.8% female; median age group 20–24 years), 97 (25.2%) experienced treatment failure. Virological failure predominated (62.9%), followed by immunological (23.7%) and clinical (13.4%) failure. In the multivariable model, older youth aged 20–24 years had more than double the odds of treatment failure compared with those aged 10–14 years (AOR = 2.1; 95% CI: 1.2–3.8; p = 0.009). Female sex (AOR = 1.6; 95% CI: 1.0–2.6; p = 0.047), advanced WHO clinical stage III–IV (AOR = 3.8; 95% CI: 2.1–6.9; p < 0.001), presence of opportunistic infections (AOR = 2.2; 95% CI: 1.3–3.9; p = 0.004), and ART duration exceeding five years (AOR = 2.4; 95% CI: 1.3–4.1; p = 0.002) were independently associated with treatment failure. Conclusions: One in four youth on ART at Rwamagana Level Two Teaching Hospital experienced treatment failure, predominantly virological. Clinical disease burden, older adolescent age, female sex, and long ART duration are key risk factors. Targeted interventions including intensified viral load monitoring, gender-responsive adherence support, and early initiation of ART are urgently required. These findings inform national strategies for adolescent and youth-friendly HIV services in Rwanda and comparable settings.**

Keywords: **HIV; antiretroviral therapy; treatment failure; virological failure; adolescents; youth; Rwanda; sub-Saharan Africa.**

1. INTRODUCTION

Globally, an estimated 1.74 million adolescents aged 10–19 years and approximately five million young people aged 15–24 years are living with HIV, with 89% concentrated in sub-Saharan Africa (SSA)[1]. Despite the transformative impact of antiretroviral therapy (ART) in reducing HIV-related morbidity and mortality, adolescents and young adults consistently exhibit the lowest rates of viral suppression across all age groups[2]. The UNAIDS 2030 goal of ending AIDS as a public

health threat is contingent upon achieving the 95-95-95 targets, that 95% of people living with HIV (PLHIV) know their status, 95% of those who know are on ART, and 95% of those on ART are virally suppressed yet youth remain the age group furthest from these benchmarks[3].

Treatment failure occurs when ART fails to achieve or sustain viral suppression, and is categorized clinically, immunologically, or virologically. Virological failure, defined as plasma viral load ≥1,000 copies/mL on two consecutive measurements, is the earliest and most objective indicator, and its detection is critical to preventing onward transmission and the emergence of drug resistance[4]. Among adolescents in SSA, pooled estimates of unsuppressed viral load range from 24% to 30%, substantially exceeding the <5% threshold implicit in the third 95[5].

Rwanda has made substantial progress in its HIV response achieving near-universal health insurance through Mutuelle de Santé, deploying a dense community health worker network, and sustaining commendable antiretroviral coverage yet national surveillance data indicate that youth aged 10–24 years continue to experience suboptimal ART outcomes[6]. Reported virological failure rates in Rwandan pediatric and adolescent cohorts range between 13.9% and 25.1%[7]. Factors contributing to this gap include psychosocial stressors inherent to adolescent development, stigma, inadequate HIV status disclosure, treatment fatigue, and structural barriers to youth-friendly service delivery[8,9].

Despite this recognized burden, empirical data on the magnitude and independent determinants of treatment failure among youth specifically at decentralized Rwandan facilities which bear the majority of the national HIV caseload remain sparse. This study therefore aimed to: (i) quantify the prevalence of treatment failure (and its sub-types) among youth aged 10–24 years on ART at Rwamagana Level Two Teaching Hospital; and (ii) identify socio-demographic and clinical factors independently associated with treatment failure, to inform evidence-based, age- and gender-responsive interventions.

2. METHODS

Study design and setting

We conducted a retrospective cross-sectional study using secondary data from medical records at Rwamagana Level Two Teaching Hospital, a public referral facility with 220 beds located approximately 60 km east of Kigali, Rwanda. The hospital operates an active HIV clinic providing ART, viral load monitoring, and adherence counselling, and supervises 16 health centres within its catchment area. HIV prevalence in Rwamagana District is estimated at 1.7%[10].

Participants and eligibility

The study population comprised youth aged 10–24 years who were HIV-positive and enrolled in the HIV clinic for at least 12 months, with at least two consecutive viral load results recorded in their treatment files. Medical records were reviewed retrospectively for the period March–June 2024. Records with incomplete data on the primary outcome or key covariates were excluded.

Sample size and sampling

The sample size was determined using the Fisher formula for estimating a population proportion, assuming a treatment failure prevalence of 50% (conservative estimate), 95% confidence level, and 5% margin of error, yielding n = 384, rounded to 385. A stratified sampling approach was used, with stratification by sex and age group, to ensure proportional representation across strata.

Outcome variable

Treatment failure was the primary outcome, defined according to WHO 2023 consolidated HIV guidelines as follows:

1. Virological failure: plasma viral load ≥1,000 RNA copies/mL on two consecutive measurements three months apart, following enhanced adherence counselling (EAC).
2. Immunological failure: failure of CD4 count to rise above 200 cells/mm³ or a fall to pre-ART baseline despite being on ART.
3. Clinical failure: occurrence of new or recurrent WHO Stage III–IV events despite at least six months on ART.

Independent variables

Variables were extracted using a structured data abstraction form, organized across three domains: (a) socio-demographic: age group (10–14, 15–19, 20–24 years), sex (male/female), caregiver relationship, and parental survival status; (b) clinical: WHO clinical stage at ART initiation, opportunistic infection history, and ART regimen type; and (c) treatment-related: ART duration (≤5 years, >5 years) and history of regimen change.

Data analysis

Data were entered into and analyzed using IBM SPSS Statistics version 26.0. Frequencies and proportions characterized the study population and treatment failure by sub-type. Chi-square (χ^2) tests assessed bivariate associations between each independent variable and treatment failure (significance threshold: $p < 0.05$). Variables achieving $p < 0.20$ in bivariate analysis, plus clinically important covariates, were entered into multivariable logistic regression. Results are reported as crude odds ratios (COR) and adjusted odds ratios (AOR) with 95% confidence intervals. The Hosmer–Lemeshow goodness-of-fit test confirmed model adequacy.

Ethical considerations

Ethical approval was obtained from the Institutional Review Board of Mount Kenya University and from Rwamagana Level Two Teaching Hospital administration. As this was a retrospective secondary data analysis of de-identified patient records, a waiver of individual informed consent was granted. No personal identifiers were recorded; unique study codes were assigned to each record. Data were stored in password-protected files in accordance with Rwanda's Data Protection and Privacy Law (No. 058/2021). This study adheres to the STROBE checklist for reporting observational research.

3. RESULTS

Socio-demographic and clinical characteristics

A total of 385 youth medical records were reviewed. Females comprised 53.8% (n = 207) of the sample. The majority were in the oldest age stratum (20–24 years: 44.7%, n = 172), followed by 15–19 years (31.4%, n = 121) and 10–14 years (23.9%, n = 92). Most youth (62.6%) were cared for by biological parents; 24.9% by relatives, and 12.5% by guardians or peers. Parental loss was substantial: 29.1% had one parent deceased and 14.3% were double orphans. Detailed characteristics are presented in Table 1.

Regarding clinical profile, 71.7% were classified at WHO Stage I–II at initiation, with 28.3% presenting at advanced Stage III–IV. One-third (34.3%) had a documented opportunistic infection. The majority (81.0%) were on first-line ART; 59.0% had been on ART for five years or less, and 23.1% had experienced at least one regimen change (Table 2).

Table 1. Socio-demographic characteristics of youth on ART at Rwamagana Level Two Teaching Hospital (n = 385).

Variable	Category	Frequency, n (%)
Sex		
	Male	178 (46.2)
	Female	207 (53.8)
Age group (years)		
	10–14	92 (23.9)
	15–19	121 (31.4)
	20–24	172 (44.7)
Caregiver relationship		
	Biological parent	241 (62.6)
	Relative	96 (24.9)
	Guardian / Peer	48 (12.5)
Parental survival status		
	Both parents alive	218 (56.6)
	One parent alive	112 (29.1)
	Both parents deceased	55 (14.3)

Table 2. Clinical and treatment characteristics of youth on ART (n = 385).

Variable	Category	Frequency, n (%)
WHO clinical stage		
	Stage I–II	276 (71.7)
	Stage III–IV	109 (28.3)
Opportunistic infection history		
	Yes	132 (34.3)
	No	253 (65.7)
ART duration		
	≤5 years	227 (59.0)
	>5 years	158 (41.0)
ART regimen type		
	First-line	312 (81.0)
	Second-line	73 (19.0)
History of regimen change		
	Yes	89 (23.1)
	No	296 (76.9)

Prevalence and sub-types of treatment failure

Overall, 97 of 385 youth (25.2%) met criteria for treatment failure; 288 (74.8%) achieved treatment success. Virological failure was the predominant sub-type (n = 61; 62.9%), followed by immunological failure (n = 23; 23.7%) and clinical failure (n = 13; 13.4%). Treatment failure rates were notably higher among females (28.0%) than males (21.9%) and increased progressively with age: 16.3% (10–14 years), 22.3% (15–19 years), and 32.0% (20–24 years). Table 3 presents prevalence by sub-type.

Table 3. Prevalence of treatment failure and sub-types among youth on ART at Rwamagana Level Two Teaching Hospital.

Outcome	n (%)
Overall treatment failure	97 (25.2)
Virological failure	61 (62.9% of failures)
Immunological failure	23 (23.7% of failures)
Clinical failure	13 (13.4% of failures)
Treatment success	288 (74.8)

Bivariate analysis

Variables significantly associated with treatment failure in bivariate analysis included: age group ($\chi^2 = 12.84$, $p = 0.002$), sex ($\chi^2 = 4.12$, $p = 0.042$), WHO clinical stage ($\chi^2 = 31.56$, $p < 0.001$), opportunistic infection history ($\chi^2 = 18.91$, $p < 0.001$), and ART duration ($\chi^2 = 14.27$, $p < 0.001$). Youth in WHO Stage III–IV had a treatment failure prevalence of 46.8%, compared with 16.7% among those in Stage I–II. Those on ART for more than five years had a failure prevalence of 36.7%, versus 17.2% for those on treatment for five years or less. Full bivariate results are presented in Table 4.

Table 4. Bivariate analysis: association between selected variables and treatment failure among youth on ART (n = 385).

Variable	n (Total)	Treatment Failure, n (%)	χ^2	p-value
Sex			**4.12**	**0.042***
Male	178	39 (21.9)		
Female	207	58 (28.0)		
Age group (years)			**12.84**	**0.002****
10–14	92	15 (16.3)		
15–19	121	27 (22.3)		
20–24	172	55 (32.0)		
WHO clinical stage			**31.56**	**<0.001*****
Stage I–II	276	46 (16.7)		
Stage III–IV	109	51 (46.8)		
Opportunistic infections			**18.91**	**<0.001*****
Yes	132	49 (37.1)		
No	253	48 (19.0)		
ART duration			**14.27**	**<0.001*****
≤5 years	227	39 (17.2)		
>5 years	158	58 (36.7)		

**p < 0.05; **p < 0.01; ***p < 0.001.*

Multivariable logistic regression

Table 5 presents the results of multivariable logistic regression. After adjustment for all covariates, five factors remained independently associated with treatment failure:

Female sex was associated with 60% higher odds of treatment failure compared with male sex (AOR = 1.6; 95% CI: 1.0–2.6; p = 0.047), an association that persisted after controlling for clinical stage and ART duration.

Older adolescent age (20–24 years) was associated with more than twice the odds of treatment failure compared with the youngest group (10–14 years) (AOR = 2.1; 95% CI: 1.2–3.8; p = 0.009), consistent with the well-documented adherence challenges of the transitional adolescence period.

Advanced WHO clinical stage (III–IV) conferred the greatest odds of treatment failure (AOR = 3.8; 95% CI: 2.1–6.9; p < 0.001), underscoring the role of late presentation and immune compromise in undermining ART effectiveness.

Opportunistic infection history more than doubled the odds of treatment failure (AOR = 2.2; 95% CI: 1.3–3.9; p = 0.004), likely reflecting the reciprocal relationship between immune suppression and treatment efficacy.

ART duration exceeding five years was associated with 2.4-fold higher odds of treatment failure (AOR = 2.4; 95% CI: 1.3–4.1; p = 0.002), consistent with the phenomena of treatment fatigue, accumulated drug resistance, and waning adherence over prolonged therapy.

Table 5. Multivariable logistic regression: crude and adjusted odds ratios for factors associated with treatment failure among youth on ART (n = 385).

Variable	COR (95% CI)	p	AOR (95% CI)	p	
Sex (Ref: Male)					
Female	1.4 (0.9–2.2)	0.061	**1.6 (1.0–2.6)**	0.047*	†
Age group (Ref: 10–14 years)					
15–19 years	1.5 (0.8–3.0)	0.211	**1.4 (0.7–2.8)**	0.281	
20–24 years	2.3 (1.3–4.0)	0.003	**2.1 (1.2–3.8)**	0.009**	†
WHO stage (Ref: Stage I–II)					
Stage III–IV	4.4 (2.6–7.5)	<0.001	**3.8 (2.1–6.9)**	<0.001***	†
Opportunistic infections (Ref: No)					
Yes	2.5 (1.5–4.2)	<0.001	**2.2 (1.3–3.9)**	0.004**	†
ART duration (Ref: ≤5 years)					
>5 years	2.8 (1.7–4.7)	<0.001	**2.4 (1.3–4.1)**	0.002**	†

**p < 0.05; **p < 0.01; ***p < 0.001. COR, crude odds ratio; AOR, adjusted odds ratio; CI, confidence interval. † Indicates independent statistical significance retained in the adjusted model. Model fit confirmed by Hosmer–Lemeshow goodness-of-fit test (p = 0.74).*

4. DISCUSSION

This retrospective cross-sectional study documents a 25.2% prevalence of treatment failure predominantly virologicalamong youth aged 10–24 years on ART at Rwamagana Level Two Teaching Hospital. Five independent risk factors were identified: female sex, older adolescent age (20–24 years), advanced WHO clinical stage, opportunistic infection history, and ART duration exceeding five years. These findings are consistent with, and contribute to, a growing evidence base documenting the vulnerability of adolescents and young adults in SSA to suboptimal ART outcomes.

Treatment failure prevalence in context

The 25.2% treatment failure prevalence observed in this study aligns closely with pooled estimates from meta-analyses of adolescent cohorts in SSA: Hlophe et al. (2023) reported a pooled unsuppressed viral load prevalence of 24.76% among 10–19-year-olds across multiple SSA settings[5]. The Rwandan national range of 13.9–25.1% reported from prior cohorts is also broadly consistent[7]. The predominance of virological failure (62.9% of all failures) reflects the international consensus that virological indicators precede immunological and clinical deterioration and must be prioritized in monitoring protocols[4]. Viral load testing now mandated within Rwanda's ART monitoring framework is the cornerstone of early failure detection, and its routine application at facilities such as Rwamagana is critical.

Age and sex as determinants

The significantly higher odds of failure among older youth (20–24 years, AOR = 2.1) is consistent with the well-documented 'transition gap' in HIV care: as adolescents acquire greater autonomy, psychosocial stressors, peer pressure, and disengagement from pediatric care models erode adherence[11]. This age group faces simultaneous transitions in schooling, employment, and social relationships that may deprioritize daily ART adherence. Youth-specific services that bridge pediatric and adult care including structured transition programs and peer-support networks are therefore essential.

Female sex was independently associated with 60% higher odds of failure (AOR = 1.6). This contrasts with some regional studies that identify male sex as the higher-risk category but aligns with evidence from Rwanda and similar settings where young women bear disproportionate social burdens: stigma associated with HIV disclosure, domestic responsibilities, and gendered barriers to consistent clinic attendance[12]. The finding reinforces JIAS and UNAIDS guidance that HIV services must be gender-responsive, addressing not merely biological but also structural dimensions of vulnerability.

Clinical disease burden

Advanced WHO clinical stage at ART initiation was the strongest predictor of treatment failure (AOR = 3.8), a finding replicated across multiple SSA cohorts[5,13]. Late presentation reflects both delayed diagnosis and inadequate HIV testing uptake persistent problems among youth who may not self-identify as at-risk. Early diagnosis through targeted community testing for youth and systematic HIV testing within schools and youth health services would reduce late presentation and improve treatment initiation conditions. The associated role of opportunistic infections (AOR = 2.2) further confirms that immune compromise at initiation creates a poor substrate for durable viral suppression, reinforcing the priority of early ART initiation per current WHO treat-all guidelines[4].

Treatment duration and fatigue

Youth on ART for more than five years had 2.4-fold higher odds of failure a finding consistent with treatment fatigue as a longitudinal phenomenon. As ART becomes part of daily routine over years, sustained psychological engagement with treatment diminishes, particularly when youth perceive themselves as clinically well[8]. Longitudinal adherence interventions including digital reminders, peer mentorship, and psychosocial support must be designed for durability and evolve with the patient's life stage. The 23.1% regimen change rate in this cohort further suggests accumulated drug resistance and prior treatment failure episodes that complicate management over time.

Limitations

Several limitations warrant acknowledgement. First, the retrospective design and reliance on medical records introduce potential misclassification bias if documentation was incomplete. Second, the single-facility setting limits generalizability to other Rwandan districts with different patient profiles or service environments. Third, key adherence variables pill count ratios, pharmacy refill records, and patient-reported adherence were not systematically available in records, constraining the ability to model adherence directly as a mediator. Fourth, the cross-sectional outcome measure precludes inference about temporal sequence between predictors and treatment failure. Fifth, psychosocial variables including stigma, mental health, and disclosure status known adherence drivers among youth could not be extracted from routine records. Future prospective studies incorporating these dimensions are recommended.

5. CONCLUSIONS

One in four youth on ART at Rwamagana Level Two Teaching Hospital experienced treatment failure, with virological failure predominating. Five independent determinants were identified: female sex, older adolescent age, advanced WHO clinical stage at initiation, opportunistic infection history, and long ART duration. These findings demand a multi-pronged response: accelerated viral load monitoring to enable early failure detection; gender-responsive and age-stratified adherence support; systematic early diagnosis to prevent late presentation; and sustained psychosocial services for long-term ART recipients. Rwanda's strong health system infrastructure including its community health worker network and health insurance coverage provides the foundation for implementing such targeted interventions. Addressing the disproportionate burden of treatment failure among youth is not only a clinical imperative, but essential to achieving national and global HIV elimination goals.

Authors' contributions

M.Y. conceived the study, designed the data abstraction tool, conducted data collection, performed statistical analysis, and drafted the manuscript. J.O. provided methodological guidance, supervised the research design, and critically reviewed the manuscript. M.M. provided supervisory oversight and reviewed the manuscript for intellectual content. All authors approved the final version.

Competing interests

All authors declare no competing interests.

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Ethics approval

Ethical approval was obtained from the Institutional Review Board of Mount Kenya University and from Rwamagana Level Two Teaching Hospital. A waiver of individual informed consent was granted given the retrospective, secondary data design. Data handling complied with Rwanda's Data Protection and Privacy Law (No. 058/2021).

Data availability

De-identified aggregate data supporting this study's findings are available from the corresponding author upon reasonable request, subject to institutional data-sharing agreements.

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