

Clinical Outcomes and Retention Among HIV-Infected Adolescents and Adults Initiated on Protease Inhibitors Antiretroviral Therapy Regimen in Dar ES Salaam; A Longitudinal Retrospective Descriptive Study

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Abstract

Background: Globally antiretroviral therapy access has increased and significantly changed HIV morbidity and mortality patterns. In sub-Saharan Africa there are reports of increasing rates of failure to second-line antiretroviral treatment (ART) hence, assessment for clinical outcomes is critical.

Objectives: To assess clinical outcomes and retention using programmatic indicators among HIV-infected adolescents and adults receiving second-line ART in Tanzania. **Methods:** In this longitudinal retrospective cohort study, we enrolled HIV-infected individuals aged 15 years and above who were initiated on second-line ART (Protease Inhibitor based regimen) due to documented failure of first-line ART between July 2012 and September 2015. We evaluated mean change in CD4 cell count, HIV viral load and retention using survival analysis.

Results : A total of 1446 participants were enrolled, the mean duration of second-line therapy was 37.0 months \pm SD 26.50 and the median CD4 cell count at initiation of the second line was 290 cells/mm³. Virologic suppression <50 copies/ml was increasing over time and reached 58% at 36 months. Six months after switching, 80% of patients were retained and thereafter. Predictors of retention were male gender with hazard ratio (HR) 1.04; 95% CI 1.0-1.1 P-value 0.037 and younger age (25 -39 years) with HR 1.1; 95% CI 1.0-1.2 P-value 0.006. Additionally, adherence > 90% increased the likelihood of retention with a strong correlation HR 1.4; 95% CI 1.1-1.7 P-value 0.00. Clinical stage III and IV at switch were less likely to be retained HR 0.6; 95% CI 0.5-0.6 P-value 0.000 and higher CD4 cell count was associated with less retention HR <1; 95 % CI 0.4-0.6 P-value 0.000.

Conclusion: There was a low rate of viral suppression (<50copies/ml) 58% 36 months after switch however, more than 87% of participants were retained to care after switch. Predictors of retention were male gender, younger age (25-39 years) and adherence > 90%. Therefore, improving viral suppression after switching to second-line requires further interventions.

Introduction

Sub-Saharan Africa carries the major portion of the global burden of HIV infection accounting for more than 80% of the global population of people living with HIV (PLHIV) [1, 2]. In 2017 about 75% of deaths and 65% of new infections were reported to occur in sub-Saharan Africa (SSA) [1]. There is country variation in the prevalence across the SSA region, the Tanzania HIV Impact Survey (THIS) reported a prevalence of 5% among HIV-infected individuals aged between 15-64 years [3] with the number of people living with HIV (PLHIV) estimated to be 1.4 million; out of these, 90.9% of adults were on antiretroviral therapy (ART) [3]. Despite expanding coverage of ART, in 2017 there were about 81,000 new cases of HIV among adults aged 15 to 64 years [3]. However, there has been a reduction of about 49% for HIV related deaths from 48 000 in 2010 to 24 000 deaths (age \geq 15) in 2018 [4]. The number of new HIV infections has also decreased, from 83 000 to 72 000 in the same period [4].

In recent years, virological monitoring has been scaled up in most resource-limited countries especially in SSA. There have also been growing efforts for an early switch to a Protease Inhibitor (PI) based regimen which is the preferred and the only available option for second-line ART after the failure of first-line. This makes monitoring of PI therapy of paramount importance to guarantee good outcomes. However, there is limited existing literature showing the progress and outcomes of patients using PI therapy in our setting. The reported increase in rates of switching to second-line ART in SSA due to the failure of first-line ART regimens [5-10] could be associated with increased access to viral load testing services. Despite the improvement in switching patients to appropriate second-line ART, there is substantial number of eligible patients who are delayed to switch to second-line ART [6-8]. Delaying patients to start second-line ART has been associated with increased risk for developing drug resistance, morbidity and mortality [7, 8, 10]. High levels of viral load (more than 5000 copies/ml) at the time of switch to second-line ART increase the risk of treatment failure [7, 11]. In Tanzania, the proportion of patients who accessed viral load testing and achieved viral suppression among those aged between 15-64 years was 52% in 2018 [3].

Retention of patients on second-line ART is critical for better health outcomes among HIV-infected individuals. There are regional as well as a country variation of rates of retention on HIV care. In SSA a finding from 39 cohorts of PLHIV showed that one-third of HIV-infected patients are lost to follow-up (LTFU) 36 months after initiation of ART which corresponds to about 60% of cases enrolled in care [12]. In Ethiopia, ART retention was 80.5% among patients on second-line ART with a median follow up of 22.2 months [13]. On the other hand, LTFU (defined as missing a scheduled HIV clinic appointment by 90 days or more) was found to be associated with low thresholds of CD4 cell count of <100 cells/mm³ among adolescents and adults initiated on second-line ART [13]. In addition, the CD4 cell count <100 cells/mm³ at the time of second-line ART initiation and first-line ART failure that was not confirmed by HIV viral load testing was reported to be notably associated with increased rates of second-line ART failure [7,13].

Patients on second-line ART require close programmatic monitoring in order to optimize HIV care and maximize health benefits especially after the failure of first-line ART. The limited resources and few available choices of second-line ART regimens make it critical to guarantee optimal adherence for positive clinical outcomes. Additionally, it is equally important to study outcomes of patients on PI-based second-line ART regimen and provide findings that are key to develop practical recommendations to further improve the delivery of HIV care services in SSA. In this study, we analyzed a cohort of patients who were switched to second-line ART to understand their clinical, immunologic, virologic outcomes and associated factors and retention in HIV care.

Methods

Study design, site, and population

This was a follow-up cohort study conducted among adolescents and adult (15 years and above) patients enrolled in two HIV Care and Treatment Clinics (CTCs) in Dar es Salaam (Mnazi Mmoja and Muhimbili Hospitals). All HIV-infected adolescents and adults switched to second-line ART between July

2012 and September 2015 were included in this study. Patients were considered eligible for second-line ART if they were classified as having virologic failure (two consecutive viral load measurements ≥ 1000 copies after 3 months, with adherence support) and/or immunological failure (50% drop in CD4 cell counts from peak value) according to national guidelines for the management of HIV and AIDS [14].

Clinical procedures

Clinical care of all HIV-infected patients on second-line ART was provided based on the national guidelines for HIV care and treatment services (14). HIV-infected patients on second-line ART were examined monthly by clinical providers, they also received ART adherence counseling, nutrition support, and drug refills. Laboratory tests including haemoglobin, CD4 T cell count, viral loads, and blood chemistries were performed every 6 months. Before switching to second-line ART, patients were assessed for treatment readiness, which included a review of their risk reduction behaviors, and their general understanding of second ART.

Data collection and management

Patient demographic, clinical, laboratory and therapeutic data were collected using the National Care and Treatment Center forms (CTC 2), which were entered into a secured computerized database. Data collected for this study included gender, marital status, age, district, BMI, WHO stage, self-reported adherence, dates of all clinic visits, facility level, history of past or current TB, co-trimoxazole use, ART regimen at initiation and follow-up, ART duration and date of loss to follow-up and/or death. Laboratory data included hemoglobin (g/dL), CD4 T cell count (/mm³), ALT (IU/L) and HIV RNA (copies /mL).

Data collected by health providers and trackers were reviewed for quality checks at different stages. Data supervisors located at each facility were responsible to review and print a daily data report, which contained a number of clients seen and a summary of key data quality metrics such as completeness. Data managers performed additional quarterly data quality assessment in each clinic, and it focused on reviewing patient's cards, and accuracy-entering data from patient's forms to the electronic database.

Study outcomes

The study outcomes were viral suppression, immunological recovery, and retention in HIV care. Viral load suppression was defined as a person's viral load (HIV RNA) to an undetectable level <50 copies/ml [14]. We defined retention when a patient attended a clinical appointment within three months (90 days) since the last visit [12]. There existed a network of community-based trackers to trace the defaulters and provided feedback on the status of tracked patients on whether the patient was alive, dead, attending another clinic or opted out.

Statistical analysis

We used descriptive statistics to summarize the baseline characteristics of the study populations. In this analysis, continuous baseline variables were presented as means and standard deviations, and binary

variables as proportions. Expert knowledge and evidence from previously published findings were used to select individual risk factors for inclusion in the model. Individual-level characteristics included in multivariate models included sex, baseline CD4 T-cell counts (<50, 51-100, 101-200, >200 cells/ μ L), age at enrollment (<30, 30-39, 40-49, \geq 50 years), BMI at enrollment (<18.5, 18.5-<25, 25-<30, 30+ kg/m²), WHO clinical stage (I, II, III and IV), self-reported adherence, and tuberculosis. We also controlled for the calendar year as patient's outcomes may have changed over the years due to other unmeasured factors.

We conducted two regression models to examine the association of study outcomes and patients' characteristics. In the first model, we used Cox proportional hazard modeling to assess predictors of retention and patients characteristics. In the second model we used a generalized regression equation to assess the association of patient characteristics and two study outcomes (viral suppression and retention). Missing data for risk factors were retained in the analysis by using the missing indicator method. Hazard ratios and GEE estimates were presented with their 95% confidence intervals (CI). P values less than 0.05 were considered statistically significant. All statistical analysis was done using STATA version 15.

Ethics

Data used for this study was obtained from the HIV clinic databases with no names of the patients or other identifiers. Ethical review of this study was approved by National Institute for Medical Research and Muhimbili National Hospital Institutional Review Boards.

Results

Patient characteristics

A total of 1446 PLHIV aged 15 years and above receiving second-line PI-based ART were enrolled for this study at two urban clinics in Dar es Salaam. Table 1 shows patient characteristics whereby for both clinics, women were the majority accounting for 64.5% and 63.6% at Mnazi Mmoja and Muhimbili National Hospital (MNH) respectively. About 66.9% (791) PLHIV presented with WHO stage III at the time of switch to second-line ART at Mnazi Mmoja and 53.8% (86) at MNH. At the end of the study follow-up, 99.6% (1205) were alive at Mnazi Mmoja and 94.5% at MNH. The mean duration of second-line therapy was 37.0 months \pm SD 26.50. The mean age and body weight were 36.8 years \pm SD 13.9 and 55.6 \pm SD 17.4 kgs respectively. The median CD4 cell count at the start of second-line therapy was 290 cells/mm³ IQR: 157-443 and overall, the rate of retention was 92%.

Clinical outcomes during second-line ART

Six months after switching to second-line ART, we found increasing body weight at an average of 0.6kg at 6months, 1kg at 12 months, 2kgs at 24 months and 4kgs at 36 months (table 2). Viral load suppression <50copies/ml was increasing overtime at a proportion of 44% at 6 months, but reduced to 33% at 12 months later increased to 47% at 24 months and reached 58% at 36 months. In figure 1, we observe that 45% of patients achieved viral suppression <50cp/ml at 6months however, the proportion dropped to <40% at 12 months. But as patients continued on second-line regimen beyond 12 months, viral suppression increased to about 50% with a further increase to 58% at 36 months. The rate of retention 6 months after switching to the second line was 94%, reduced to 87% at 12 months, slightly increased to 89% at 24 months and reached 92% at 36 months.

Table 2: Trend of patients' change in weight, viral suppression and retention after initiation of second line ART (n=1446)

	06-months	12-months	24-months	36-months
Outcome	% (95 CI) / Mean (SD)			
Weight change in Kgs, (mean, SD)	0.6 10	1 9	2 9	4 10
Viral suppression (%)	44 31 58	33 26 42	47 39 54	58 51 65
Retention (%)	94 83 98	87 79 91	89 83 93	92 87 95

**Virologic suppression Plasma viral load <50copies/ml

**Retention defined as percentage of patients known to be alive and on ART at 6, 12 and 36 months after initiation of second line ART

Predictors of viral suppression

After accounting for other factors, increasing age from 25-39 years and 40-59 years were predictors of viral suppression (< 50copies/ml) HR 0.36 ; 95% CI 0.01-0.70 P value 0.040 and HR 0.46; 95% CI 0.14-0.77 P value 0.005 respectively (table 3).

Predictors of retention to care

Six months after switching to second-line ART more than 85% of patients were retained to care and this was maintained between 12 and 36 months (figure 1). Table 4 shows predictors of retention, men were found to have increased likelihood retention with a hazard ratio (HR) 1.04; 95% CI 1.0-1.1 P-value 0.037. Increasing age from younger age between 25 and 39 years to those aged 40-59 years were more likely to be retained to care with HR 1.1; 95% CI 1.05-1.18 P-value 0.000; HR 1.09; 95% CI 1.03-1.15 P-value 0.001 respectively. Also, patients with good adherence > 90% (self-reported) were found to increase the likelihood of retention to care with a strong correlation HR 1.73; 95% CI 1.42-2.10 P-value 0.000.

PLHIV who presented with WHO clinical stage III & IV at the time of switching to the second line were less likely to be retained to care HR 0.71; 95% CI 0.67-0.75 P-value 0.000. In addition, PLHIV who experienced a high body mass index (BMI) were associated with less retention HR 0.84; 95% CI 0.79- 0.90 P-value 0.000 and having a higher CD4 cell count ≥ 200 was associated with less retention to care HR 0.93;95 % CI 0.90-0.96 P-value 0.000.

Moreover, history of using Isoniazid prevention therapy (IPT) and treatment of tuberculosis were more likely to reduce retention with HR 0.77 95% CI; 0.60-0.99 P-value 0.048 and HR 0.48 95% CI 0.44-0.51 P-value 0.000 respectively.

Discussion

In this study, we aimed to assess the outcomes of adolescents and adults on second-line ART. We observed virologic suppression increasing over time from 44% six months after switching to second-line ART to 47% at 24 months and 58% at 36 months. Studies have shown that viral suppression is commonly achieved within 6 months after using effective ART and maintain undetectable viral load thereafter [15,16]. Fifty-eight percent of viral suppression in this study is below the 2020 UNAIDS third target [17]. Contrary to our study, a recent study from South Africa a country with the largest HIV epidemic in the world, found that HIV-infected patients initiated on the second line with > 90% adherence achieved moderate to high rate of viral suppression; 73% at 6 months which later increased to over 97% at 24 months [18]. In India, 78% of patients on the second line achieved viral suppression at 12 months [19]. Other areas like Cambodia have reported viral suppression in 85.7% at 24 weeks among patients on the second line [20] and Rwanda 83% [2]. The difference found in our study could be explained by the delay to initiate the second line after the failure of the first line, which was a prevalent practice in the years before scale-up of viral load monitoring in 2014, and this demonstrates the challenge of using a clinical and immunologic status for ART failure [21, 22]. Second-line comprises of Protease Inhibitor (PI) based ART regimen which is more effective than the Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) used in first-line [23, 24]. The high genetic barrier to resistance of the PI drugs provides room for improvement after the failure of first-line [25]. Enhanced adherence intervention was introduced along with HIV viral load monitoring has played a significant role to improve virologic outcomes in patients who have high viral loads >1000copies/ml and adherence issues [18, 19]. WHO guidelines recommend that

patients with HVL > 1000 copies/ml be subjected to an enhanced adherence support intervention, after which a second viral load test should be performed prior to the decision on confirmed virologic failure and the subsequent ARV regimen [26,27].

We found increasing age from the age group 25-39 years and 40-59 years as a predictor of viral suppression (viral load < 50 copies/ml) relatively similar to findings in the USA that older age (18-39 years) was significantly associated with viral suppression, as they sustained higher ART adherence as they get older [28]. Similarly, other studies have reported that increasing age reduced the odds of non-viral suppression [29].

Retention to HIV care is key to a successful ART programme. Our study found that six months after switching to second-line ART more than 80% of patients were retained and this was maintained between 12 and 36 months. In addition, increasing age from younger age between 25 and 39 years to those aged 40-59 years were more likely to be retained to care, similar to a study in Kenya [30]. This is impressive and should be maintained throughout the cascade of HIV care because retention has been considered as a predictor of viral suppression. Our findings are similar to a recent national programme analysis of routinely collected data in Tanzania, which reported the overall rate of retention after enrollment in HIV care was 80.9% at 12 [31]. In this report, it appeared that the highest level of retention was observed in young adults PLHIV aged between 35 and 49 years and those with lower and higher age groups had decreased retention [31]. However, reported findings in South Africa and Uganda found that older age \geq 45 years was protective of loss to follow up [32, 33]. This difference could be attributed to a possibility of the older PLHV have multiple co-morbidities which warrants them to maintain clinic visits [30].

Additionally, we found that male gender was a predictor of retention while in previous studies, men enrolled in HIV care and on treatment were found to have worse retention than females [34-36]. In East Africa, a qualitative study reported that men had a desire of maintaining improved health and this was a motivating factor for them to remain engaged in care [36]. Also, African men receive more support from their spouses than females and this underscores the importance of family support to maintain retention to care [36]. Furthermore, we found that good adherence increased the likelihood of retention to care similar to other studies [37] and retention has been reported to facilitate ART adherence [30]. The younger adults 25 years and above up plus those up to 59 years were found to be more retained to care. In our setting these (15-49 years) are the most affected group with HIV infection [3] therefore, retaining them to care is key for improving ART adherence hence good clinical outcomes and gain the benefit of reducing HIV transmission to their peers.

On the other hand, PLHIV who presented with WHO clinical stage III & IV at the time of switching to the second line were less likely to be retained to care similar to other studies reporting poor retention among sicker patients [38] who may be too sick to attend to HIV clinics or may have died and the death not reported at the attending clinic. Some patients with advanced HIV disease are more likely to seek alternative traditional health practitioners and leave medical care in an African setting [39, 40], some may be returned to their domicile places waiting to die there as it was found in West Africa [41].

Furthermore, patients who experienced an increase in body mass index, using Isoniazid prevention therapy (IPT), history of tuberculosis treatment and having a higher CD4 cell count were associated with less retention to care. This could be due to the fact that when PLHIV gain weight and achieve higher CD4 cell counts it translates to getting healthier. Thus weight gain gives a thought of being a marker of ART success and these individuals may not comply better with their clinic appointments than those who are underweight who will most likely keep close follow up of their care desiring for weight gain [4]. Likewise, there are reports that feeling better, pill burden, and treatment fatigue are some individual risk factors for LTFU [34]. Isoniazid Preventive Therapy (IPT) is an evidence-based intervention with the proven effectiveness of reducing the risk of TB in PLHIV by 33%–62% [43]. Despite this evidence, the integration of IPT services has been sub-optimal due to reasons of pill burden to PLHIV and fear of side effects among the patient and also rumors and misconceptions about IPT among the HIV–infected patients [43].

In this study, we observed that retention was increasing over time and patients who were switched to second-line in the recent years from 2015 had a higher proportion of patients retained to care and achieved viral suppression. This can also be explained by the introduction of tracking interventions introduced in recent years underscoring the strategies to prevent loss to follow up. Also, ARV regimens that were introduced in recent years have enhanced drug efficacy and reduced side effects, promoting more optimal treatment response.

Therefore, retention in care is important for all HIV-infected patients and central to achieving optimal virologic outcomes emphasizing that viral suppression is more strongly associated with retention in care [28]. Despite that viral load is the preferred way to monitor treatment efficacy because of the poor accuracy of CD4 monitoring in predicting viral suppression [21], less retention among patients with higher CD4 cell counts should be of concern among clinicians regarding the delay in detecting unsuppressed viral load among people failing second-line ART rendering a chance to an accumulation of drug resistance and increased risk of mortality and morbidity [44]. Patients with higher CD4 cell counts are most likely to be asymptomatic and thus less motivated to be in care.

Our study limitation involved assessing variables that were available in the clinic data from routine care, which could be faced with incomplete and missing variables. However, it could be assumed that this happens randomly within our patients and thus did not introduce a systematic bias in the results.

Low coverage of viral load testing especially in early years (2012-2014), could lead to missing prior measurements among patients switched to second ART in early years, however, we controlled for calendar years to account for some of the facility practices that were not measured and not modeled in the regression. We only included patients in urban health facilities, this could represent different types of patients and facility practices when compared to rural ones and could limit generalization of the results.

In conclusion, we found a low rate of viral suppression (<50copies/ml) about 58% at 36 months after switching to second-line ART. This suggests that earlier second line initiation or switching before HIV disease progresses to an advanced level is paramount to improve treatment outcomes. In addition, more than 87% of individuals were retained in care at 6, 12, 24 and 36 months after switch. Male gender,

having younger age (25-39years) and good adherence > 90% were predictors of retention. However, WHO stage III-IV, using IPT and higher CD4 cell count were associated with less retention. Therefore, improving viral suppression after switching to second-line requires stringent HIV viral load monitoring especially for adolescents to improve viral suppression and maximize the durability of the second-line regimens.

Declarations

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Conflict of Interests

The authors have declared that they have no conflicts of interest.

Authors' Contributions

This work was carried out in collaboration with all authors. JR conceived the presented study idea, performed the study and wrote the manuscript with support from SK. AS was involved in protocol development, theoretical framework and directed study implementation. SM performed and supervised data collection at the two study sites. DS designed a data analysis plan and performed data analysis. All authors have read and reviewed the content of the final manuscript and have approved the manuscript for submission.

Declarations

Ethics approval

Ethics approval to conduct this study was obtained from the ethics review board from National Institute for Medical Research (NIMR) and Muhimbili National Hospital. A Waiver of consent for study participants' was approved by the ethics committee for this retrospective study. Consent for publication has been provided by NIMR.

Data Availability Statement

The data sets derived from Care and treatment clinics at Amtullabhai Karimjee clinic and Muhimbili National Hospital and analyzed during the current study supporting the findings are available from the corresponding author JR on request.

Competing interests

The authors declare that they have no competing interests

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Tables

Table 1: Baseline characteristics of study participants aged ≥ 15 years initiated on Second line ART (n=1446)

Characteristics	No.	%
Sex		
Women	931	64.4
Men	515	35.6
Age category		
15-24	153	12.3
25-39	451	36.1
40-59	600	48.1
>=60	44	03.5
Patient severity at the start of second-line ART		
Not severe	236	17.6
Severe	1106	82.4
CD count category (n=626)		
<200	193	30.8
200-500	299	47.8
>500	134	21.4
Adherence		
Poor (<80%)	25	02.1
Good	1171	97.9
BMI		
Low	248	17.2
Normal	485	33.5
High	713	49.3
History of TB treatment		
No history of TB RX	1434	99.2
History of TB RX	5	0.30
History of IPT	7	0.50
Visit		
Baseline	1446	100
6-months	1372	94.9
12-months	1314	90.8
24-months	1290	89.2
Study site		
Mnazi Mmoja	1210	83.7
Muhimbili	236	16.3
Year Started 2nd Line ART		
2012	101	7
2013	157	10.9

2014	187	12.9
2015	170	11.8

Table 3: Predictors of Viral Suppression (<50copies/ml) among patients initiated on Second line ART (n=1238)

Characteristics	Coefficient	95% CI	P	Coefficient	95% CI	P value
Sex						
Women	REF			REF		
Men	-0.09 0.280	-0.25 0.77		-0.015 0.875	-0.21 0.17	
Age (years)						
15-24	REF			REF		
25-39	0.03 0.030	0.17 0.62		0.36 0.040	0.01 0.70	
40-59	0.43 0.000	0.14 0.72		0.46 0.005	0.14 0.77	
>60	0.62 0.020	0.06 0.11		0.62 0.042	0.02 1.22	
BMI						
Low	REF			REF		
Normal	0.29	-0.04 0.62	0.089	0.14 0.464	-0.23 0.49	
High	0.51 0.000	0.17 0.84		0.02 0.863	-0.31 0.36	
Disease severity						
Non severe (WHO stage I &II)	REF			REF		
Severe (WHO stage III &IV)	0.04	-0.28 -0.37	0.792	0.04 0.776	-0.26 0.35	
CD4 cell count						
<200	REF			REF		
200-500	-0.22	-0.50 0.04	0.101	0.13 0.345	-0.14 0.41	
>500	0.25 0.113	-0.05 0.57		0.33 0.058	-0.00 0.67	

TB History						
No history of TB treatment	REF					REF
History TB treatment	-0.31	-1.65	1.01	0.641	0.903	-0.08 -1.43 1.27
History of using IPT	0.21	-0.25	0.68	0.374	0.215	0.32 -0.18 0.83

Table 4: Predictors of retention among study participants initiated on second-line ART(n=1452)

Characteristics	Univariate			Multivariate		
	HR value	95% CI	P-	HR value	95% CI	P-
Sex						
Women	REF			REF		
Men	0.99 1.01	0.790	0.97	1.04 0.005	1.01 1.08	
Age						
15-24	REF			REF		
25-39	0.91 0.95	0.000	0.88	1.11 1.18	1.05	
40-59	0.93 0.96	0.000	0.89	1.09 1.15	1.03	
>60	0.99 1.06	0.900	0.92	1.04 1.16	0.94	
BMI						
Low	REF			REF		
Normal	0.88 0.91	0.000	0.85	1.00 1.08	0.93	
High	0.80 0.82	0.000	0.77	0.84 0.90	0.79	
Disease Severity						
Non severe (WHO stage I & II)	REF			REF		
Severe (WHO stage III & IV)	0.62 0.78	0.000	0.64	0.71 0.000	0.67 0.75	
CD4 Cell Count						
<200	REF			REF		
200-500	0.94 0.001	0.91 0.97		0.93 0.000	0.90 0.96	
>500	0.77 0.000	0.74 0.80		0.91 0.000	0.88 0.96	
TB History						
No history of TB treatment	REF			REF		
History of IPT	0.87 0.052	0.76 1.00		0.77 0.048	0.60 0.99	
History of TB Treatment	0.64 0.67	0.000	0.61	0.48 0.000	0.44 0.51	
Adherence to ART						
Poor	REF			REF		
Good	1.45		1.33	1.73	1.42	

	1.66	0.000		2.10	0.000
Year Started 2 nd Line ART					
2011	REF		REF		
2012-2014	1.48		1.44	1.39	1.33
	1.52	0.000		1.45	0.000
2015-2019	2.97		2.89	2.28	2.18
	3.05	0.000		2.38	0.000

Figures

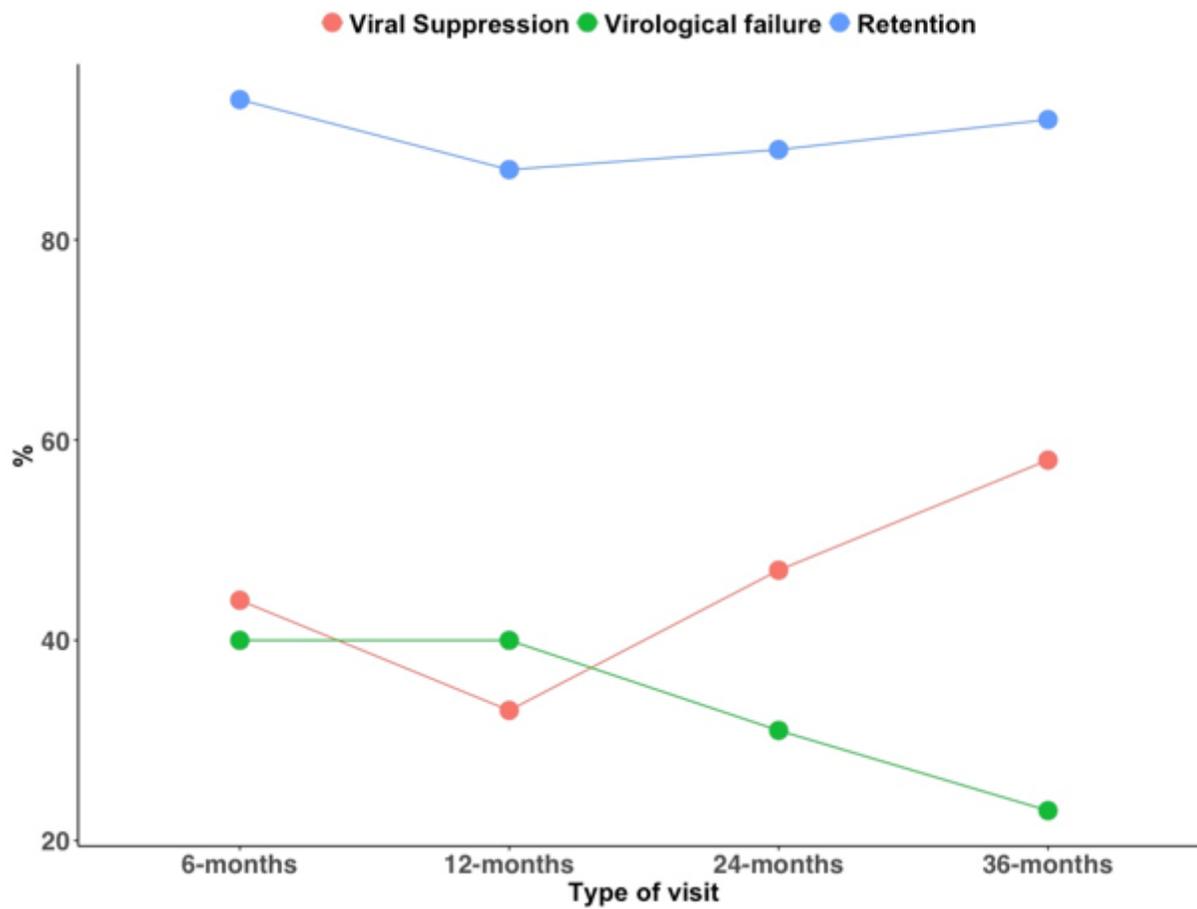


Figure 1

study participants' trend of viral suppression and retention after initiation of second line ART