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Incidence and Determinants of Lost to Follow Up Among Adults Living with HIV/AIDS on Antiretroviral Therapy in Iringa Region, Tanzania.

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Abstract

- ***Background:***

Globally, HIV/ AIDS continues to be a public health problem and as of June 2023 Iringa has a total of 81,852 clients receiving Care and treatment from DHIS2 source. Antiretroviral therapy (ART) is the backbone of management of HIV and clients need to have high adherence (≥ 95%) for ART treatment outcome to be positive. Most previous studies have identified that Lost to follow up (LTFU) from ART treatment programs is the main challenge faced by most ART treatment programs in resource constrained countries. Tanzania is reported to have high rate of LTFU among PLHIV on ART, and factors associated with LTFU in areas with high prevalence of HIV/AIDs like Iringa region are not well known and documented

- ***Objectives:***

This study intends to estimate the incidence rate of LTFU among PLHIV on ART and to identify factors associated with LTFU in Iringa region, Tanzania.

- ***Method and Materials:***

The Study design was a retrospective cohort design among PLHIV initiated in treatment from 2017 to 2020 in Iringa region. The regional HIV treatment dataset was retrieved from CTC2 electron database in excel format, cleaned, coded and imported into IBM SPSS STATISTICS version 26 for analysis. Numerical variables were summarized using median (IQR) while categorical variables were analyzed and reported as proportions. Incidence rates were calculated and used as measure of magnitude of the problem, while survival analysis and log-rank tests were used to compare rate of LTFU among adult living with HIV on ART with different level of initial exposures. Any variable associated with LTFU at significant level of P < 0.2 in univariate analysis was subjected to multivariate Cox proportion regression analysis in order to control potential confounders. Any variable which showed association with LTFU at significant level of p value < 0.05 in multivariate Cox regression analysis was regarded as independently associated with LTFU

- ***Results:***

A total of 36,043 participants were included in the analysis, the overall incidence rate of lost to follow up among adult PLHIV initiated ARV is 2.80, 95% CI (2.68 – 2.93) per 100-person years. This incidence rate was observed to vary based on duration of follow up (time), age, sex and residence. LTFU increased with increasing time of follow, it was 0.34, 95% CI (0.26 – 0.44) per 100 person-years at initial 6 months of follow up, then increased to 1.59, 95% CI (1.40 – 1.81) per 100 person-years at 6 – 12 months of follow up, which increased further to 2.56, 95% CI (2.35 – 2.78) per 100 person-years at 12 – 24 months of follow up, and the highest incidence was 4.45, 95% CI (4.08 – 4.85) per 100 person-years, which was observed at the 24 – 36 months of follow up. In terms of factors associated with LTFU, young age (aged 18 – 24 years) at the time of ARV initiation (adjusted HR = 3.95, 95% CI 2.95– 5.28, P < 0.001, residents of Mufindi DC (adjusted HR = 1.39, 95% CI 1.16 – 1.66, P < 0.001), Mafinga TC (adjusted HR = 4.04, 95% CI 3.3 – 4.90, P < 0.001), and Kilolo DC (adjusted HR = 2.11, 95% CI 1.77 – 2.53, P < 0.001), as well as PLHIV initiated NNRTI antiretroviral regimen (adjusted HR = 2.93, 95% CI 2.64 – 3.26, P < 0.001) and PLHIV at WHO clinical stage I (adjusted HR = 3.77, 95% CI 2.80 – 5.09, P < 0.001), stage II (adjusted HR = 2.59, 95% CI 1.89 – 3.53, P < 0.001) and stage III (adjusted HR = 1.62, 95% CI 1.21 – 2.17, P = 0.001) at the time of ARV initiation, were significantly associated with increased Hazard Ratio (HR) of being LTFU.

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➢ ***Conclusion and Recommendation:***

LTFU remains a challenge in care and treatment of PLHIV in the studied area. Younger age, male sex, PLHIV initiated NNRTI-regimen and PLHIV residing in Mufindi DC, Mafinga TC and Kilolo DC were factors associated with increased risk of LTFU. Moreover, Lost to Follow Up is shown to decrease with increasing WHO stage at recruitment. Interventions targeting these factors are important to address the problem

Keywords: *Lost to Follow Up, People Living with HIV, Anti Retro Viral Treatment.*

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I. INTRODUCTION

A. Background

Globally, HIV/ AIDS continues to be a public health problem. In 2019, approximately 38.0 million people were living with HIV (PLHIV), with East and Southern Africa region reporting to have more than half of this reported cases (1, 2). In Tanzania, the Joint United Nations Program on HIV/AID (UNAID) report estimated a total of 1,600,000 people were living with HIV in 2018 (3) whereby 72,000 people were newly infected with HIV in the same year (3). Furthermore, in the same report, Tanzania has been reported to have 24,000 AIDS related deaths (3).

In our study setting which is Iringa Region, the government is working in close association with Implementing Partners on HIV conducting USAID Boresha Afya project under Deloitte. And it is through this project that the researcher was able to acquire the needed data to complete the study.

With regards to the HIV/AIDS treatment, Antiretroviral therapy (ART) is the backbone of management. ART has proved to be lifesaving to PLHIV as it suppresses the viral replication, raises the number of CD4 count and clinically improves the condition and quality of life. The use of ART also results to decreased incidence of opportunistic infections, HIV related morbidities as well as mortality among PLHIV (4). Additionally, the HIV suppressed patients have low chances of transmitting the virus to their partners (5, 6).

Previously, the World Health Organization (WHO) had reported increase number of PLHIV accessing ART (7). As of 2020, UNAIDS reported an estimated 26.0 million people to have access to ART globally (1). In Tanzania, 72% of adults living with HIV and 65% of HIV infected children were reported to be on ART in 2018 (3). This was very far from UNAIDS global target of 90% ART treatment among those diagnosed with HIV. In addition, Tanzania was reported to have 62% HIV viral load suppression among PLHIV in 2018 (3).

With regard to ART treatment, clients need to have high adherence (≥ 95%) for desirable treatment outcome which is viral load results of less than 1000copies per ml. Most previous studies have identified that attrition from ART treatment programs is the main challenges faced by most resource constrained countries (8, 9). The main contributor to this attrition is reported to be LTFU, with death contributing to the remaining small portion (8-10). In the study Incidence rate is defined as the rate at which new event occur which in our case it is LTFU over a specified period for the population at risk which in our study is 100 person years.

With regards to HIV treatment guidelines evolution in Tanzania, over the years there have been many additions to the management of HIV as well as removal of others. From 2012 guideline, ART initiation of newly diagnosed clients was or those with CD4 <350 and those with HIV stage 3 and 4, moreover all clients were treated the same regardless of their characteristics with one-month refills. The WHO Consolidated guideline of 2016-2017 informed the vision for Tanzania guideline that led to creation of 2019 guideline with recommendations to incorporate innovations that were incorporated in the 2019 National guidelines for the management of HIV and AIDS for instance using treatment as preventions such as Pre Exposure Prophylaxis, ARV Optimization eg Doltegravir based regimen, Differentiated Service Delivery Models including Multi Month Dispensing as well as Test and start Secular in 2017 that led to Test and Treat Policy which was incorporated in 2019 guideline. Under this policy, all new positive identified clients were to be initiated treatment within 7 days of identification. The total number of clients initiated on treatment has been varying and was 12,976 in 2019, 9673 in 2020, 6686 in 2021 and 5681 in 2022 according to DHIS 2 system.

II. METHODOLOGY

A. Study Design

We conducted a retrospective cohort study design in Iringa region on adults that were initiated ART between 1st January 2017 to 31st December 2020.

B. Study Area

Iringa region is located in the southern highlands of Tanzania. Iringa region has five councils namely Iringa District Council, Iringa Municipal council, Kilolo District council, Mafinga Town Council and Mufindi District. The region covers an area of 35503Km^2. The region has a population of approximately 941,238 as projected from the 2012 population census.

Iringa has total of 321 health facilities of which 7 are hospitals, 33 are health centers and 281 are dispensaries. This study used data from 126 facilities which constitute of over 90% of people receiving care and treatment in Iringa. Iringa

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region has prevalence of 11.3% of people living with HIV compared to 4.6% national prevalence making it the second top region with high prevalence in Tanzania after Njombe according to Tanzania ANC HIV Sentinel Surveillance Report of 2021.

The DHIS2 Data show 81,852 adults were living with HIV and were on ART as of June 2023. This makes CTC services be one of the major outpatient services offered by many health facilities in the region

C. Study Population

All adults living with HIV/AIDS aged ≥ 18 years who were initiated on ART in Iringa region between 2017 and 2020.

D. Eligibility Criteria

➢ *Inclusion Criteria:*

Adult living with HIV/AIDS who enrolled into CTC and started ART in period between January, 2017 and December 2020 in Iringa region.

➢ *Exclusion Criteria:*

Adult living with HIV on ART who were transferred in from other clinic without documentation of date of ART initiation.

E. Power of study and Sample Size Determination

Power of study was calculated from 36,043 adult living with HIV/AIDS initiated ART between 2017 and 2020 in the study area (The number represented expected sample size) and it was 100%. WHO clinical stage was used as key predictor of LTFU among adult PLHIV, with those stage III and IV treated as exposed group. Then from previous study, the proportion of exposed and unexposed together with their outcomes were estimated in our expected sample size, and then filled in the open epi (free online open software) for calculating power.

➢ *Formula for Power Calculation is (46, 47):*

$$Power = \Phi\left(\frac{\sqrt{(n'*\Delta^2)} - z_{1-\alpha/2}\sqrt{(1+1/\kappa)*p*q}}{\sqrt{(p_1*q_1)+(p_2*q_2/\kappa)}} \right)$$

Where $\mathbf{n'} = n_1 - [(\kappa+1)/(\kappa.\Delta)]$;

- *Risk ratio calculation*

$RR = (p_1/p_2)$;

The notations for the formulae are:

Δ = difference of risk of disease between exposed group and non-exposed group;

κ = ratio of sample size: non-exposed group / exposed group;

p_1 = risk of disease among exposed group;

p_2 = risk of disease among non-exposed group;

$p = (p_1*n_1+p_2*n_2)/(n_1+n_2)$;

$q = 1-p$;

n_1 = available sample size among exposed group;

F. Study Variables

➢ *Dependent Variable*

The main outcome in this study was Loss to follow up (LTFU) and it is defined as the event that occurs when PLHIV did not attend CTC to refill ART medication for a period of ≥ 28 days from the last appointment given for refill, with such Individual not documented as transferred out or dead.

➢ *Independent Variables*

Social demographic characteristics such as age, sex, marital status, place of living (district councils), Clinical characteristics at the time of ART initiation, such as baseline CD4 count, baseline WHO clinical stage and type of ART initiated.

G. Data Collection Methods

➢ *Data Acquisition:*

After obtaining Ethical clearance from MUHAS IRB, researcher sought permission to utilize data from responsible authorities, which include; Regional Medical Officer and regional implementing partners.

➢ *Data Analysis:*

CTC2 Extracted data in Excel format were cleaned, coded and imported to the IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp, where storage and analysis were conducted. Descriptive statistics were used to describe socio demographic and clinical characteristics of participants in the dataset. This included frequencies for categorical variable, and median (IQR) for numerical variable since these numerical variables were not normally distributed. Incidence rates (density) were calculated and presented in graphs and choropleth maps. Survival analysis was carried out using Kaplan Meier method and log-ranking tests were used to compare estimated time to LTFU between study participants who had different initial level of exposure (differ in baseline characteristics). Survival analysis is a model used to measure the time taken for the event to occur and in out study the time in months taken for LTFU to occur was analyzed using this model. Multivariate Cox-proportion hazards model were performed in order to control any potential confounders, and any variable which showed p-value less than 0.05 at Multivariate analysis was regarded as independently associated with LTFU.

➢ *Ethical Consideration*

Ethical clearance to conduct research was sought from Muhimbili University of Health and Allied Sciences (MUHAS) Institutional Review Board (IRB). Furthermore, permission to utilize data for research purpose were sought and obtained from NACP, the RMO of Iringa Region and development partner Deloitte. Confidentiality on the identity of the patients was maintained throughout the study, as names were omitted in the dataset

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III. RESULTS

A region HIV treatment and care dataset containing records of 39,523 PLHIV initiated ARV between 2017 and 2020 in Iringa region was retrieved. Among these subjects, 1,142 were identified as duplicates and removed from further analysis. Additionally, 2,338 subjects were also excluded in analysis, as they were aged < 18 years by the time of ART initiation 2017 - 2020 (start of the follow up). The final analysis was performed on 36,043 adult PLHIV (aged > 18 years)

A. Social Demographic and Clinical Characteristics of Participants:

Among 36,043 adult PLHIV initiated ART in study site, many participants were aged between 25-34 (35.2%) and those between 35-44 years (35%) at the time of ARV initiation, their median age was 36 years (IQR = 30, 44). The proportion of female was higher (59.8%) than the proportion of male (40.2) and many participants (88.2%) were reported in union comprising of married and cohabiting clients at the time of ARV initiation. In terms of residence, slightly high proportion of participant were from Iringa MC (25.8%) and Mufindi DC (24.4%).

INSTI-based antiretroviral were most common regimen initiated to the newly diagnosed PLHIV enrolled to the treatment in the study site at that moments (2017 – 2020), account to about 76.6% of all ART regimen initiated. Higher proportions of participants (76.3%) had started treatment when their absolute CD4 count were ≥ 200 cells/µL, with median count of 392 cells/µL (IQR = 208, 598). Many participants were in WHO clinical stage One (38.1%) and three (40.3%) at the time of ARV initiation.

Table 1 Baseline Characteristics of Participants(N=36,063).

Variable		Frequency (n)	Percent (%)
Age group at the time of ART initiation (years)			
	18 – 24	2307	6.4
	25 – 34	12682	35.2
	35 – 44	12622	35.0
	45 – 54	5696	15.8
	≥ 55	2736	7.6
Median age in years (IQR)		36 (30, 44)	
Sex			
	Male	14497	40.2
	Female	21546	59.8
Marital status at ART initiation*			
	Married	21994	65.9
	Single	7426	22.3
	Cohabiting	336	1.0
	Widowed	1929	5.8
	Divorced	1690	5.1
Council of the facility			
	Iringa DC	6582	18.2
	Iringa MC	9301	25.8
	Kilolo DC	5843	16.2
	Mafinga TC	5508	15.3
	Mufindi DC	8809	24.4
Class of ARV initiated*			
	NNRTI	8309	23.1
	PI	113	0.3
	INSTI	27597	76.6
Absolute CD4 count at ART initiation*			
	< 200	891	23.7
	≥ 200	2861	76.3
Median absolute CD4 count (IQR)		392 (208, 598)	
WHO clinical stage at ART initiation*			
	Stage 1	11396	38.1
	Stage 2	5210	17.4
	Stage3	12053	40.3
	Stage 4	1256	4.2
Weight (Kg) at ART initiation			
	< 50	5366	15.0
	≥ 50	30473	85.0
Median weight in Kg (IQR)		57 (52, 63)	
*Variables with missing values (missing data)			

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B. Incidence Rates of loss to follow Up Among PLHIV on ART

In this study, we found that the overall incidence rate of loss to follow up among adult PLHIV initiated ARV in the study site was 2.80, 95% CI (2.68 – 2.93) per 100-person years. This incidence rate was observed to vary based on duration of follow up (time), age, sex and residence. The incidence rate was found to increase as the time of follow up increased, it was 0.34, 95% CI (0.26 – 0.44) per 100 person-years at initial 6 months of follow up, then increase to 1.59, 95% CI (1.40 – 1.81) per 100 person-years at 6 – 12 months of follow up, which increase further to 2.56, 95% CI (2.35 – 2.78) per 100 person-years at 12 – 24 months of follow up, and the highest incidence was 4.45, 95% CI (4.08 – 4.85) per 100 person-years, which was observed at the 24 – 36 months of follow up.

Youth aged 18-24 years old and 25-34 years old were observed to have high incidence rate of Lost To Follow up of (5.15 95%CI (4.45-5.95) per 100 person years) and (3.69 at 95% (3.45-3.95) per 100 person years) respectively compared to young adults aged (35-44 years), adults aged (45-54 years)s and those above 55 years old who had 2.45 95% CI (2.27-2.66) per 100 person years, 1.82 95% CI (1.60-2.08) per 100 person years and 1.44 95% (1.16-1.77) per 100 person years respectively.

Likewise, Female had slightly higher incidence rate of LTFU (2.90 95% CI (2.74 – 3.07) per 100 person-years) than male whose rate was 2.65, 95% CI (2.46 – 2.85) per 100 person-years.

Participants initiated ARV in Mafinga TC and Kilolo DC was observed to have higher incidence rate 4.70 95% (4.29 – 5.14) and 4.38 95% CI (4.01 – 4.79) per 100 person-years respectively, compared to the participants who were initiated ARV in other council of Iringa region, as shown table 3.2 1.

Table 2 Incidence Rate of Loss to follow Up Among PLHIV on ART Stratified by socio-Demographic Characteristics of the Study Participants

Variable	Total N	Person time (years)	LTFU n (%)	Incidence rate/100 PLHIV on ART	95% CI
Age group (years)					
18 – 24	2300	3554.308	183	5.15	4.45 – 5.95
25 – 34	12673	22829.575	842	3.69	3.45 – 3.95
35 – 44	12616	24862.442	610	2.45	2.27 – 2.66
45 – 54	5693	11840.492	216	1.82	1.60 – 2.08
≥ 55	2735	6056.133	87	1.44	1.16 – 1.77
Sex					
Male	14497	27249.183	722 (5.0)	2.65	2.46 – 2.85
Female	21546	41893.767	1216 (5.6)	2.90	2.74 – 3.07
Councils					
Iringa DC	6582	13005.258	238 (3.6)	1.83	1.61 – 2.08
Iringa MC	9301	16223.758	257 (2.8)	1.58	1.40 – 1.79
Kilolo DC	5843	11384.425	499 (8.5)	4.38	4.01 – 4.79
Mafinga TC	5508	10026.383	471 (8.6)	4.70	4.29 – 5.14
Mufindi DC	8809	18503.125	473 (5.4)	2.56	2.34 – 2.80

C. Factors Associated with LTFU from the CTC Among Adult PLHIV on ART

Figure 1 shows comparison of rates of LTFU among participants with different baseline socio- demographic characteristics. There were variations in the rate of LTFU among participants with different age groups, those initiated at young age (18 – 24 years) had higher rate of LTFU, followed by those aged 25 – 34 years old. The rates of LTFU were found to be low among those initiated ARV at adult age (45–54 years) and elders aged (> 55 years old), the differences in rates of LTFU among participants-initiated ARV at different age groups were statistically significant, Log-rank p-value < *0.001*. Male and female had approximately equal rate of LTFU, Log-rank p-value = 0.436, and in terms of residences, participants residing in Mafinga TC and Kilolo DC were observed to have higher rate of LTFU compared to the resident of other councils of the region and the differences in rates of LTFU among participants-initiated ARV at different councils were statistically significant, Log-rank p-value < *0.001.*

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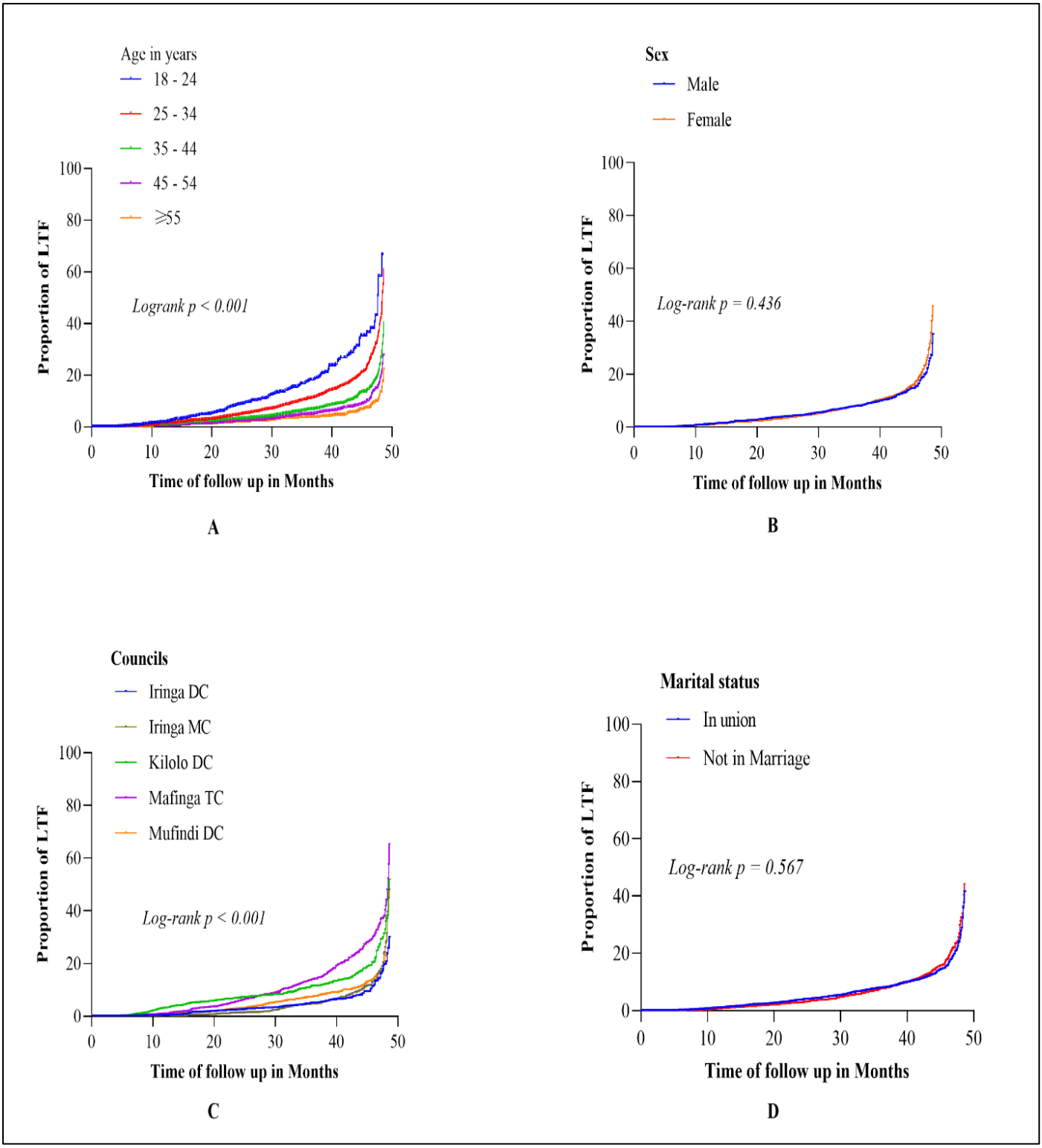

Fig 1 Rates of LTFU Among Participants with Different Baseline socio-Demographic Characteristics. A.

Figure 2 shows comparison of rates of LTFU among participants with different baseline clinical characteristics. Participants initiated NNRTI antiretroviral regimen had higher rate of LTFU compared to those initiated PI and INSTI antiretroviral; Log-rank p – value < 0.001. Additionally, those participants-initiated ARV at WHO clinical stage 1 were found to have higher rate of LTFU compared to participants initiated ART at stage 2 and 3, the lowest rate of 4.3.2

LTFU were observed among participants initiated ARV at stage 4. These differences of rate of LTFU among PLHIV initiated ARV at deferent WHO clinical stages was found to be statistically significant, Log-rank p < 0.001. The differences in rates of LTFU among participant with different absolute CD4 counts, as well as functional status were not statistically significant (Log-rank p – value = 0.095 and 0.071 respectively), as shown in figure

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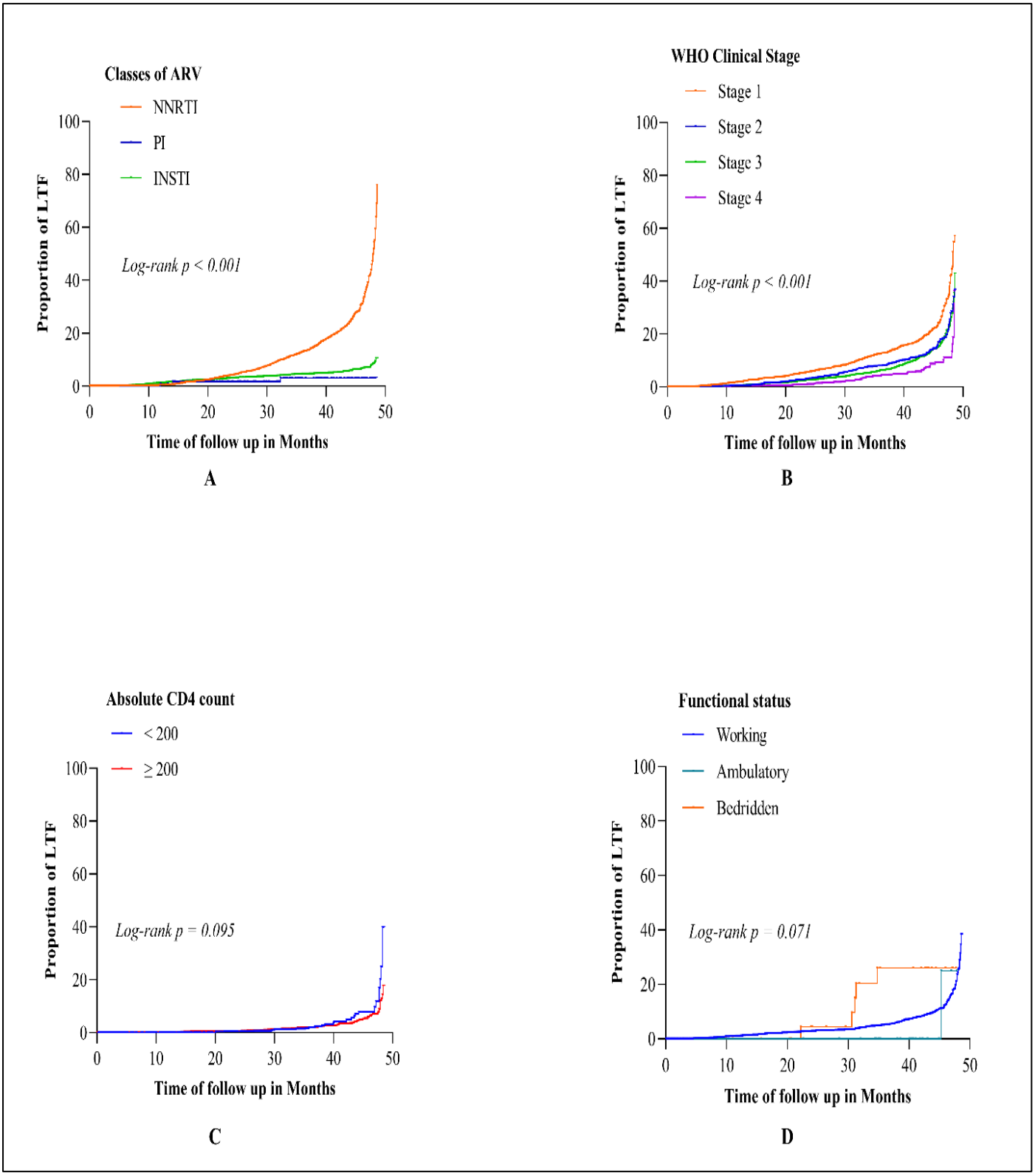

Fig 2 Rates of LTFU Among Participants with Different Baseline Clinical Characteristics

D. Univariable and Multivariable Analysis of the Factors Associated with lost to follow Up

Table 3.4 1 shows univariate and multivariate analysis of the factors associated with LTFU among adult PLHIV initiated ARV in Iringa region. At univariate analysis, age, residence (councils), Type/class of ARV initiated and WHO clinical stages were found to have association with LTFU among adult PLHIV on ART in the study sites.

Youth aged 18 – 24 were 5.4 times more likely to be LTFU compared to the elderly aged > 55 (crude HR = 5.39, 95% CI 4.17-6.97, P < 0.001), and this association persisted after adjusting for confounders HR = 3.95, 95% CI 2.95-5.28, P < 0.001 (see table 3.4). Participants from Mufindi DC were 1.3 times (crude HR = 1.31, 95% CI 1.12 – 1.53, P = 0.001), those from Mafinga TC were 2.7 times (crude HR = 2.72, 95% CI 2.33 – 3.18, P < 0.001), and Kilolo DC were 2.4 times

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(crude HR = 2.40, 95% CI 2.06 – 2.81, P < 0.001) more likely to be LTFU compared to participants from Iringa DC. Also, this association persisted after adjusting for confounders where by participants from Mufindi DC (adjusted HR = 1.40, 95% CI 1.17 – 1.68, P < 0.001), from Mafinga TC (adjusted HR = 4.26, 95% CI 3.52 – 5.17, P < 0.001), and from Kilolo DC (adjusted HR = 2.14, 95% CI 1.79 – 2.56, P < 0.001) were more likely to be LTFU compared to participants from Iringa DC. Moreover, male were found to have a high incidence rate of LTFU compared to the female counterparts after adjusting for confounders in multivariate analysis (adjusted HR 1.37 95% CI 1.23-1.52, P<0.001). Participants initiated NNRTI antiretroviral regimen were 3.2 times more likely to be LTFU compared to those initiated INSTI antiretroviral (crude HR = 3.18, 95% CI 2.90 – 3.49, P < 0.001) and such association persisted after adjusting for confounders whereby participants who were initiated NNRTI antiretroviral regimen (adjusted HR = 2.93, 95% CI 2.69 – 3.33, P < 0.001) were more likely to become LTFU compared to those initiated in INSTI. Participants initiated ARV at WHO clinical stage one were 3.5 times (crude HR = 3.45, 95% CI 2.61 – 4.58, P < 0.001), those initiated at stage two were 2 times (crude HR = 1.97, 95% CI 1.47 – 2.65, P < 0.001), and at stage three were 1.7 times (crude HR = 1.74, 95% CI 1.31 – 2.31, P < 0.001) more likely to be LTFU compared to participants initiated ARV at WHO clinical stage 4 and this association persisted after adjusting for confounders whereby being at WHO clinical stage I (adjusted HR = 3.77, 95% CI 2.8 – 5.09, P < 0.001), stage II (adjusted HR = 2.59, 95% CI 1.89 – 3.53, P < 0.001) and stage III (adjusted HR = 1.62, 95% CI 1.21 – 2.17, P = 0.001) at the time of ARV initiation, were significantly associated with increased Hazard Ratio (HR) of being LTFU.

Table 3 Univariate and Multivariate Analysis of the Factors Associated with loss to follow Up Among Adult PLHIV Receiving Treatment and care in Iringa Region.

	Univariate analysis			Multivariate analysis		
Variable	**cHR**	**95% CI of cHR**	**P -value**	**aHR**	**95% CI of aHR**	**P - Value**
Age at ARV initiation						
18 – 24	5.39	4.17 – 6.97	< 0.001	3.95	2.95 – 5.28	< 0.001
25 – 34	3.22	2.59 – 4.02	< 0.001	2.43	1.89 – 3.13	< 0.001
35 – 44	1.93	1.54 – 2.41	< 0.001	1.67	1.30 – 2.15	< 0.001
45 – 54	1.35	1.05 – 1.73	0.018	1.35	1.02 – 1.78	0.037
≥ 55	Ref					
Sex						
Male	0.96	0.88 – 1.06	0.437	1.37	1.23 – 1.52	< 0.001
Female	Ref					
Marital status						
In union	1.03	0.93 – 1.14	0.568	1.02	0.91 – 1.13	0.755
Not in marriage	Ref					
Council						
Mufindi DC	1.31	1.12 – 1.53	0.001	1.38	1.16 – 1.66	< 0.001
Mafinga TC	2.72	2.33 – 3.18	< 0.001	4.04	3.33 – 4.90	< 0.001
Kilolo DC	2.40	2.06 – 2.81	< 0.001	2.11	1.77 – 2.53	< 0.001
Iringa MC	0.96	0.80 – 1.14	0.615	1.02	0.84 – 1.25	0.828
Iringa DC	Ref					
Class of ARV						
NNRTI	3.18	2.90 – 3.49	< 0.001	2.93	2.64 – 3.26	< 0.001
PI	0.41	0.13 – 1.27	0.122	0.63	0.20 – 1.96	0.422
INSTI	Ref					
WHO clinical stage						
I	3.45	2.61 – 4.58	< 0.001	3.77	2.80 – 5.09	< 0.001
II	1.97	1.47 – 2.65	< 0.001	2.59	1.89 – 3.53	< 0.001
III	1.74	1.31 – 2.31	< 0.001	1.62	1.21 – 2.17	0.001
IV	Ref					

Key: cHR: crude Hazard Ratio, aHR: adjusted Hazard Ratio, CI: Confidence Interval, Ref: Reference group

IV. DISCUSSION

In this study, the overall incidence rate of lost to follow up among adult PLHIV (aged ≥ 18 years) on ART was found to be fair high in the study area and was further observed to increase as the time of follow up increase. Additionally; age, residence (district council), class of ART initiated and WHO clinical stages were all found to have statistically significant association with loss to follow up among these adults PLHIV on ART in the study area.

During sample description, weight was used instead of BMI because there were missing height documentation in most client data in the extracted dataset.

The high rate of lost to follow up among adult PLHIV on ART found in this study is consistent with the rate reported in most areas with resource constrained (10, 48-51). Many factors are thought to contribute on these high rates of LTFU in these areas, which include age, clinical stage, locality and type of drug (52). Increase incidence rate of LTFU among

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adults PLHIV on ART with time probably occurred because of clients being tired with long treatment schedule which demand individual PLHIV to take pill daily. There are several studies that reported similar findings, that is increase of incidence of LTFU as the time of treatment increase(21, 53). Furthermore; being tired with long term treatment has been highlighted in several studies as the reason of poor adherence and LTFU (54, 55). If the same reasons hold in our findings, then a need of strengthening retention strategies as time on ART treatment increase among PLHIV may be warranted. A periodic group specific targeted intensive counselling both on site at facility and off site at home in order to restore the awareness on the importance of treatment may reduce the problem.

In this study, it was observed that young aged PLHIV were at high risk of being lost to follow up in care and treatment compared to the older PLHIV. Young people are thought to be a difficult group for being initiated and maintained in the long-term treatment such as ART because of their lifestyle. They are constantly moving from one place of residence to another in the searching of economic opportunities or improved lives, and most of them do not like to be seen taking medication for fear of stigma and discrimination in the society. Also, disclosure to new partners that they may have acquired from time to time is an issue that they avoid when seen taking ARV and hence default from medication. The finding is similar to most studies conducted in the developing countries where young aged PLHIV on ART are reported to have increased risk of LTFU compared to elderly (21, 24, 26, 52, 56). Young PLHIV on ART should be targeted for proper intervention of this problem. Sustainable programs in their localities focusing on involving them in their economic improvement, such as provision of entrepreneurship education, together with formation of small-scale business organization in the society as well as youth awareness programs may attract them to settle and hence encouraging them to attend clinic regularly as per arranged schedule. The previous proposed approach might reduce the problem of LTFU, especially if these formed small business units are loaned capitals and capacitated to the extent of functioning. Moreover, proper client transfer systems should be placed in facilities as well as friendly services whereby a client is free to report to the facility in case of moving so that they can be transferred out with documentations. These measures might save the community from threatening of HIV epidemic as the results of having many sexually active unsuppressed PLHIV in the community.

In our study, male were found to have a high rate of LTFU compared to females. Females are known to have tendency of seeking medical care more than males, therefore they are more likely to abide with treatment schedule even if it is for long term compared to the male counterpart. Females appear to be obedient to the providers and abide to the advice given better than the male counterparts. The finding of male having high rate of LTFU compared to female was also reported in most previous studies (24, 26, 52, 53, 56). As for young aged PLHIV on ART, adult male should also be a target group for designed retention program such as community ART refills where clients are provided with ART where they reside or work. Males are thought to be busy striving in order to provide to their family and for this reason, interventions such as extended working hours in care and treatment clinics whereby refills can be done in early morning, late evening and weekends in order to reach this group of clients, incorporation of male expert clients in clinics may enable this group to be motivated to stay in treatment.

PLHIV on ART from Mufindi DC, Mafinga TC, and Kilolo were all found to have high risk of LTFU compared to the PLHIV on ART in Iringa DC. This finding may reflect different performances in terms of ART client retention among Care and Treatment Centers (CTCs) within councils they are located. In the study site, the CTC staffs are required to prepare the coming clinics with activities such as reminding their clients to attend clinic visit according to schedule via SMS reminders and phone calls, they are also responsible for early tracking as well as intense counselling any clients who shows early signs of loss to follow up in the treatment, this is because a client misses appointments before they fully mature to LTFU. Moreover, a considerable number of clients receiving care at Mafinga TC more concentrated at the township and Kilolo DC where there is a township called Ilula where Lula Hospital carries over 50% of all clients on ART in Kilolo, the places consist of clients that are constantly moving from one area to another. Most are long track drivers and workers in the hospitality and hotel business such as bar tenders and receptionists. Therefore, the observed difference in risk of LTFU among PLHIV on ART in these councils may reflect variation in abilities of these groups of clients in dealing with the problem. Alternative explanation to this finding may be high number of ART clients in comparison to the CTC staff (Number of Clients per CTC staffs) among CTCs located in councils with clients who have high risk of LTFU compared to the CTCs located in Iringa DC or TC. Facilities with the highest number of clients receiving care in the region are Usokami Health Center in Mufindi DC and Mafinga District Hospital in Mafinga TC. This high number of PLHIV on ART may lead to high workload in CTCs and further compromise the work itself including poor follow up of these clients. But this alternative explanation needs to be justified by conducting further research on quality of CTC services.

PLHIV who were initiated NNRTI anti-retroviral drugs were found to have high risk of LTFU compared to the participants who were initiated INSTI anti-retroviral drugs. Similar findings were reported in several studies conducted in the limited resource setting (56-58). The INSTI anti-retro viral drug were reported to have high ability of suppressing HIV virus load and improve the health condition of ART clients compared to the NNRTI drugs (59, 60). With such advantages, PLHIV using INSTI may appreciate the importance of the treatment and hence more motivated to continue with treatment than the PLHIV using NNRTI. Moreover, NNRTI drugs that were mostly used were TLE combination (Tenofovir, Lamivudine, Efavirenz) for adults, clients using these drugs experienced severe side effects of Efavirenz such as dizziness, trouble sleeping, unusual dreams and extreme tiredness and this is the reason Efavirenz is now

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removed as the most preferred and now the drug of preference is Dolutegravir and the preferred combination is TLD (Tenofovir, Lamivudine, Dolutegravir). However, this study did not assess if the clients had their regime changed from what they were initiated before and this calls for further studies to assess this. Furthermore, INSTI drugs are reported to have low short-term adverse events compared to the NNRTI (61).

PLHIV in WHO Clinical stages 1, 2 and 3 were found to have high risk of LTFU compared to the PLHIV in WHO clinical stage 4. This finding is contrarily to most of the studies, where they had reported advanced WHO clinical stage have increased risk of LTFU compared to the clients who were in early clinical stages (1 and 2)(21, 23, 62). And reason for advanced WHO clinical stage to have high risk of LTFU compared to the clients in early stage is thought to be bed ridden. But in our finding, the clients who were in clinical stage four might had been in hospitals for long time or regularly, treated other HIV related comorbidities, they have had life threatening conditions that have warranted them on adherence to ARV and hence appeared visible in clinic as per arranged schedule. There are few studies reported that advance clinical stage ART clients with or without TB comorbidity have reduced risk of LTFU compared to the clients who were in early WHO clinical stage (22). Alternatively, ART clients in WHO clinical stage 1 and 2 may feel well, hence no need to proceed with medication especially, medication which are taken daily for long term like ARV which manifest with a lot of side effect. This explanation may be supported by considering the current policy of Test and Start whereby clients that are tested Positive are supposed to start ART on the same day or within 7 days if delayed. This is a very short time of counselling conducted prior to the initiation of ART and clients start medication before they have truly accepted their status. This phenomenon plus the fact that they are not ill has led to LTFU for newly initiated clients on care. There are several studies which report relationship between early ART initiation and LTFU among PLHIV on ART (21).

V. CONCLUSION

LFTU remains a challenge in care and treatment of PLHIV in the studied area, especially for clients who stayed on ART for a long time. Younger age, male sex, PLHIV initiated NNRTI-regimen, start ART at early WHO clinical stage, and PLHIV resided in Mufindi DC, Mafinga TC and Kilolo DC were associated with increased risk of LTFU. Interventions focusing on the issues with the largest contribution of LTFU are important in order to address the challenge.

RECOMMENDATIONS

Formation of youth awareness program and involvement of youth to the program focusing of improving their economic status may attract them to stay in one place for long time and hence attend clinic.

Extending CTC working hours so that clients who are busy such as male may refill the pills in the morning, evening or even weekend.

Continue with ART client counselling to those initiated ART while they are at early WHO clinical stages of the diseases (stage I and II).

Intensify retention activities in Mufindi DC, Mafinga TC and Kilolo DC to identify and address gaps that may be linked to attrition of clients in care and treatment. This may reveal problems related with facilities or health systems and when addressed may lead to better retention of clients to care.

LIMITATIONS OF THE STUDY AND FURTHER STUDIES

The study used data collected in the routine clinical practices hence the obtained dataset like most secondary data did not contain all variables/factors that might affect loss to follow up. In response to this, the researcher decided to include as many available variables as possible in the analysis.

There were few variables with missing values; mostly in the “functional status” variable and this one was not included in the multivariate analysis. In the missing pattern analysis of the variable with missing data, it was found to miss randomly hence did not have effect on results.

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