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FACTORS AFFECTING ANTIRETROVIRAL TREATMENT ENTRANCE, ADHERENCE AND RETENTION AMONG HIV PATIENTS IN NIGERIA AND UGANDA

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DEDICATION

To Uchechukwu, Joshua and Daniel Okite

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Finally, I bow my knees in worship to a faithful God and Father. You held my hand all the way. I am in awe of You!

FACTORS AFFECTING ANTIRETROVIRAL TREATMENT ENTRANCE, ADHERENCE AND RETENTION AMONG HIV PATIENTS IN NIGERIA AND UGANDA

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The University of Texas
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Summary:

Introduction: The maximum benefits of antiretroviral therapy (ART) are achieved when HIV patients follow through the HIV Care Continuum. Understanding the factors that impact the Care Continuum are key in minimizing late ART uptake while increasing treatment retention and adherence in sub-Saharan Africa.

Objectives: To explore factors that impact the various phases of the HIV Care Continuum, we review trends in median CD4 cells count and presentation with HIV advanced disease stage between 2013 and 2017. We also examined treatment retention rates and the impact of food security on ART adherence.

Methods: Two datasets were reviewed. One dataset consists of data abstracted from 1100 HIV clinic records of adults aged ≥15 who initiated ART between 2013 and 2017 at a comprehensive clinic in Nigeria. The other dataset was a cross-sectional study conducted among HIV patients aged ≥18 years in Uganda.

Data analysis: We used Chi square tests to compare baseline median CD4 cell counts and HIV advanced disease stage among males and females initiating ART between 2013 and 2017. Logistic regression was used to determine retention rates over time as well as ART adherence. All data was analyzed using STATA version 15.

Results: The overall median CD4 cell count was 243.5 cells/μl. Men had a downward median CD4 cell count trend and presented late to treatment compared to females. Patients aged ≥36 and

those with TB also presented with advanced HIV disease stage at ART initiation. Nigeria National HIV policy changes had no impact in late presentation to ART uptake. ART treatment retention was 71.39%, 79.50%, 74.01% and 62.67% at 6, 12, 24 and 36 months respectively. CD4 cell count <100 was inversely predictive of retention (AOR 0.55; 95% CI, 0.37-0.82) while female gender (AOR, 2.00; 95% CI, 1.02 – 3.89), older age (AOR, 1.88; 95% CI, 1.01-3.51), TB at start (AOR, 2.21; 95% CI, 1.02-4.75). and CD4 cell count 100-199 (AOR, 2.54; 95% CI, 1.04-6.20) were significantly associated with retention. Overall food security level in Uganda was 65.5%. HIV positive males reported higher food security levels compared to females (77.60% vs 61.90). Food security (AOR, 1.76; 95% CI, 1.03-3.01), income (AOR 2.69; 95% CI, 1.14-6.34) and nutrition counseling (AOR, 1.99; 95% CI, 1.12-3.54) were associated with good adherence.

Conclusion: Various factors contribute gaps in the HIV Care Continuum and foster existing gender disparities in HIV care outcomes. Interventions targeting men for early ART uptake and treatment retention are needed. Promoting food security and treatment support programs may be effective in advancing HIV care in the sub-Saharan Africa. Further research is needed to examine the long -term impact of HIV policy and program changes.

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BACKGROUND

The Human Immunodeficiency Virus (HIV) continues to remain a key public health issue in the world (1,2). Since HIV was identified in the 1980s, an estimated 74.9 million people have become infected with the virus, and 32 million people have been reported to have died of HIV-related illnesses (2). In 2018 alone, records show about 1.7 million new HIV infections, 770,000 HIV-related deaths, and approximately 37.9 million people living with HIV across the globe (1). Notwithstanding improved HIV funding and programs, only 62% of the 29.9 million people who know their status were receiving antiretroviral treatment (ART) and only about 47% were virally suppressed in 2018 (1,2). In addition, an estimated 8.1million of people infected by HIV did not know their status by the end of 2018 (2).

At the same time, the global epidemiology of HIV has changed remarkably due to increased access to ART(3). Increased global efforts have ensured improved access to ART, particularly in resource-poor countries since early-mid 2000s (4,5). In 2018, the World Health Organization estimated 64% of the people living with HIV in Africa were receiving ART (1). Access to ART has been shown to contribute to reduced HIV-related deaths from 1.4 million in 2000 to less than one million in 2018 (5). Besides, reports of reduced new HIV infections have been associated with access to ART (3–5). The need to ensure a continuum of care for HIV patients cannot be overemphasized. Yet, treatment dropout and mortality of HIV patients starting ART in resource-poor settings have been shown to be considerably higher than those starting ART in developed countries (6). A review article estimated the treatment dropout rate of 20% after the first year on ART (7) while mortality rate ranged from 8 to 26% among HIV patients within one year of starting ART in sub-Saharan Africa (6,8). These high rates are suspected to be linked to various factors such as initial patient clinical characteristics that negatively impact early ART treatment entrance, adherence and retention in the sub-Saharan Africa (9–12). While initial patient clinical characteristics are intrinsic, socio-economic factors such as food insecurity level, social support and the effects of HIV status disclosure may also deter patients from seeking ART treatment early and impact ART adherence and retention (13,14). Moreover, some studies report that medication related factors such as drug side effects may interact with ART treatment retention as HIV patients

report drug side effects as a barrier to taking their medication (13–15). In contrast, very few studies have been conducted to examine the multiple interactions between structural factors such as care entry point, social factors such as enrollment in treatment support groups and economic factors such as food insecurity levels with HIV identification, uptake, adherence and retention in the sub-Saharan Africa (16) even as many other factors still remain unknown or inconclusive.

HIV in Sub-Saharan Africa

The HIV epidemic is known to have started in the late 1970s and early 1980s in the sub-Saharan Africa. The virus in this region has been found to present with two distinct virus types: HIV-1 and HIV- 2. The HIV-1 strain is argued to have emerged in West Central Africa in the early 20th century and diversified in the Congo River basin, where the highest viral diversity occurred (17). The HIV-1 strain presents in four groups (M, N, O, P) and group M, which, is reported to present with 9 subtypes (A-D, F-H, J, K) is responsible for the global pandemic (17,18). The HIV-2 is mostly found in the West African region and it is not easily transmitted (18).

The main mode of HIV transmission in the sub-Saharan is via heterosexual intercourse (5,18). The risk of transmission is heightened by multiple sexual partners and coexisting sexually transmitted infections such as herpes simplex type 2 (5). A large proportion of the new HIV infection in this region may be attributable to long-term heterosexual relationships and sexual behaviors whereby young women have sex with older men (5,18). This pattern may be one of the reasons why the sub-Saharan is the only region in the world with HIV infection rates higher among women than men (18).

Overall, the sub-Saharan African has been worst hit by the HIV epidemic (18). Even though only 10% of the world's population lives in sub-Saharan Africa, The adult HIV prevalence rate for East African countries in between 8-10%, West Africa about 3% and South Africa about 20% (18). Since HIV is the fifth leading cause of morbidity and mortality (3) and the vast majority (an estimated 25.7 million) of people living with HIV reside in low- and middle- income countries which includes the sub-Saharan Africa (3,5,18), there is a need to continue studying the factors

affecting ART treatment entrance, adherence and retention in these countries. This is imperative given that an estimated 70% of all HIV infected children and adults live in sub-Saharan Africa and achieving global targets towards ending the HIV epidemic is largely tied to the progress made in combating HIV in Africa (2,18).

HIV in Nigeria

Nigeria is the most populated country in the sub-Saharan Africa. Her first case of HIV was recorded in 1985 (19). The HIV-1 Group M subtype A and G are reported as the dominant strains of HIV in Nigeria (20). However, current research shows emerging dominant recombinant strains CRF02_AG in the southern part of the country(21). The southern part of Nigeria has also continued to show higher incidence rates of HIV which require further studies to understand the current trends (21).

Even though the government set up a National Expert Advisory Committee on AIDS and requested assistance from the WHO, no serious efforts to combat the virus was recorded until the return on democracy in 1999 (19). At that time, a national surveillance showed a HIV prevalence of 5.8%, which then continued to decrease to 1.5% in 2018 probably due to the increased access to ARTs. However, the fact that 3.1 million people still live with HIV in Nigeria in 2017, makes her the second largest HIV epidemic in the world (2).

Like most other African countries, heterosexual intercourse has been found to contribute greatly to HIV transmission in Nigeria and it accounted for over 80% of the infections in the nation (19). Other drivers of HIV transmission include: mother- to- child transmission, sex workers, men who have sex with men (MSM) and injection users (19,22) exacerbated by low condom usage, punitive laws against sex workers and MSM, gender inequalities and high sexual networking (19). Moreover, the government's initial slow response to tackling HIV may have added to the far-reaching adverse effects of the virus in Nigeria (19).

On the other hand, since the early 2000s, Nigeria has scaled-up HIV prevention services through concerted efforts from local and international organizations. More HIV programs and clinics have

been established to increase HIV awareness as well as access to ARTs (19). Yet, Nigeria continues to face challenges in attaining national and international benchmarks regarding early HIV treatment uptake and retention. For example, in 2018, only 53% of the adult HIV patients were reported to be receiving ART(1,2) and only 67% of the population knew their HIV status (2,23). Furthermore, only 44% of the pregnant women living with HIV received ART for prevention of mother-to-child transmission (PMTCT) in 2018 (23). While these may be attributed to weak health systems in the country, it also suggests there are barriers for people to access and/or stay in ART treatment (23) and these factors could have been further entrenched through other economic, structural and cultural barriers that affect early ART treatment uptake, treatment adherence and retention (23). Therefore, exploring the interaction of these factors would provide insights on how to ensure early detection of HIV, early ART treatment uptake and treatment adherence and retention.

HIV in Uganda

Uganda is another country in the sub-Saharan Africa with a high prevalence of HIV. The first case of HIV in Uganda was reported in 1982. The HIV-1 Group M subtype A and D are reported as the dominant strains of HIV in Uganda (17,24). Current research suggests the existence of other strains and recombinant strains in Uganda as well (25). Uganda recorded high rates of HIV infection in the 1980s and early 1990s with national prevalence of about 30% in 1989 (26). This led to a strong response by the government in the adoption of a Multi-Sectorial AIDS Control Approach as well as the establishment of the Uganda AIDS Commission in 1992 (26). As a result, by the early 2000s Uganda had implemented safer birth practices and offered about 41,000 women PMTCT services (26). By 2018, Uganda had reached 97% of HIV positive pregnant women with PMTCT services (27). Uganda is also known as the first country in the sub-Saharan to offer HIV voluntary counseling and testing (HCT) (26). HIV prevention programs in Uganda also aimed at increasing HIV awareness and testing, and condom use and treatment uptake which contributed to decreased adult HIV prevalence from 14% in the early 1990s to about 8% in mid-2000 (18). Currently, the adult HIV prevalence in Uganda is 5.7% (2).

However, despite the gains made by the government and its partners to combat HIV, Uganda, like most sub-Saharan countries, still faces various challenges in addressing the HIV burden. Some of the leading barriers include gender inequality, social stigma, and punitive laws against key populations. Additionally, unlike that in Nigeria, extreme economic factors leading to increased poverty has also increased food insecurity in the region (28,29) and studies show food insecurity is an emerging factor associated with ART adherence among HIV patients (10,30–32). There is also a dispute on the level of impact that gender differences among HIV patients may have on food insecurity and ultimately on ART treatment adherence in Uganda (28). Therefore, it is also important to explore the association between food insecurity and ART adherence in Uganda who is known to have established food-related gender differences (33,34).

AIMS

In order to examine the factors that interact with ART treatment entrance, adherence and retention, this study aims to:

1. Examine the trends of median CD4 cell count and the impact of HIV policy change on ART treatment presentation at a Nigerian clinic from October 2013 to December 2017. The hypotheses were as follows:

    a. *There is an upward trend in median CD4 cell count at baseline among females compared to males*
    b. *The odds of presenting with advanced HIV disease stage are higher among males compared to females*

2. Determine the association of patient baseline characteristics with treatment retention at 6, 12, 24 & 36 months among HIV patients who initiated ART treatment between October 2013 and December 2017 at a Nigerian clinic. The hypotheses are as follows:

    a. *The odds of treatment retention at 6, 12, 24 and 36 months post- ART initiations are lower among patients who enter HIV care with lower CD4 cell count compared to those who enter with higher CD4 cell counts.*

    b. *The odds of treatment retention at 6, 12, 24 and 36 months post- ART initiations are lower among patients who enter HIV care with a positive TB status compared to those who enter with a negative TB status.*

3. Determine the relationship between household food insecurity and ART treatment adherence among HIV patients in two Ugandan clinics and determine whether this interaction differs by gender. The hypotheses are as follows:

    a. *The odds of good ART adherence are higher among patients who are food secure as compared food insecure patients.*

b. *The odds of good ART adherence are higher among patients who received treatment support services as compared to those who did not receive treatment support services.*

METHODS

Data Sources

This study involved the use of de-identified data of HIV patients aged 15 and above from two different sub-Saharan countries with different HIV strains and responses to the HIV epidemic. The first data source was de-identified data abstracted from the clinic records of a retrospective cohort of HIV patients enrolled at a comprehensive urban hospital in Nigeria. The second data source was de-identified secondary data from a cross-sectional study involving HIV patients receiving ART at two level 3 health care centers in rural and semi-urban communities in Uganda.

Nigerian Data:

Patient records showing ART treatment enrollment between October 2013 and December 2017 (study period) were identified and marked for data abstraction. Trained data officers and the HIV clinic officers performed the data abstraction. Data abstraction was done using an excel spreadsheet developed for this study to retrieve variables of interest from patient clinic and follow-up records. Since medical record information are routinely and prospectively collected by health care providers, recall bias was reduced. The HIV clinic coordinator was asked to assist with data quality checks by randomly reviewing data entry. De-identified data was received electronically. Data was cleaned and transferred to STATA for analysis.

Ugandan Data:

De-identified patient records from a cross-sectional study involving HIV patients receiving ART at two level 3 health care centers in rural and semi-urban communities in Uganda was used. Data

was collected on a given data collection day using a one-time structured survey (with ART adherence and food security level questions) from consenting patients who attended the health center between November 2017 and February 2018. Electronic dataset with variables of interest was transferred on request. Data was cleaned and transferred to STATA for analysis.

PUBLIC HEALTH SIGNIFICANCE

The expansion of ART coverage has greatly improved survival among people living with HIV (5). Access to ART is noted as the main contributing factor in the estimated 28% decline in HIV-related deaths from 2006 to 2012 (5). However, in the sub-Saharan Africa, only an estimated 60% of people living with HIV are currently receiving ART (5).

Through exploring the relationship between HIV care entry points and ART treatment uptake, this study will inform HIV program planners of ways to increase opportunities for early HIV detection and early treatment commencement to promote retention. Identifying new strategies while addressing gender and age differences could also guide HIV program plans to increase timely gender- and age- focused HIV detection and treatment enrollment. Furthermore, this study will inform partnerships between health care providers to increase HIV care entry points thus increasing early treatment uptake and retention. This study will also contribute knowledge to the benefit of a more comprehensive HIV care approach, which includes social support from treatment support groups and patient family.

Besides, the sustainability of previous successes in HIV treatment adherence and retention is at stake as the effects of food insecurity persists due to widespread poverty in the sub-Saharan Africa (35,36), as food insecurity can compromise the long-term benefits of ART due to its interaction with treatment adherence. Assessing the relationship between food insecurity levels and ART adherence will then inform policy makers on whether there is need to incorporate regular food security assessment checks as part of the routine HIV care for sustained HIV program success across similar settings in the sub-Saharan. It will also enable health providers to identify HIV patients who may need referrals to food assistance programs as this could ultimately help improve ART adherence and treatment retention.

Additionally, understanding the role of gender in modifying food insecurity and ART adherence as well as treatment retention may serve to strengthen existing programs for sustainability. Identifying a gender difference, will support the development of interventions will be more effective in achieving program goals, improving patient health outcomes while addressing gender differences. Study results may also provide a basis to identify patients who are most at risk of ART non-adherence and treatment dropout so as to provide targeted care for long-term treatment adherence and retention.

JOURNAL ARTICLE 1

Trends and Correlates of Advanced HIV Disease Stage at Antiretroviral Therapy Initiation: The impact of changes in HIV treatment guidelines in Nigeria.

Journal: PLoS ONE

Abstract:

Background: HIV patients starting antiretroviral treatment (ART) with advanced disease stage minimize the effectiveness of ARTs, jeopardize their health outcomes and contribute to new HIV infections. We examined the trends in treatment presentation with advanced disease stage and reviewed the impact of changes in national HIV policy on treatment uptake.

Methods: A retrospective cohort study of data abstracted from 1050 HIV clinic records of adults aged ≥15 who initiated ART between 2013 and 2017 at a comprehensive clinic in Nigeria. Advanced HIV disease at ART initiation was defined as having a CD4 cell count of less than 100cells/μl or a WHO clinical stage 4 at start of ART. All data was analyzed using STATA version 15.

Results: The study population was 33.05% males and the median age was 34 years (inter quartile range [IQR], 29-40). Males had a plunging median CD4 cell count compared to females over time (219 cells/μl in 2013 to 159cells/μl in 2017 vs 262.5 cells/μl in 2013 to 274 cells/μl in 2017). Males also continued to present late to ART treatment uptake with advanced HIV disease stage compared to females (19.23 % vs 16.13% in 2013 and 44.83% vs 22.64% in 2017). In multivariate analysis, year of ART, age and documented TB at baseline were significantly associated with late presentation. Patients who had TB at baseline, enrolled in 2016 and 2017 and aged ≥36 showed higher odds of presenting with advanced HIV disease stage at ART initiation. There was no significant association between the 2015 National HIV treat all policy piloted in our study region and late presentation to ART uptake.

Conclusion: Late presentation for ART uptake is still a major challenge in Nigeria. There is a widening gap in ART treatment uptake among males compared to their female counterparts. Interventions targeting men for early ART uptake are needed. Further research is needed to examine the long -term impact of HIV policy and program changes.

Keywords: *Late ART presentation, ART treatment uptake, advanced disease stage, median CD4 cell count, TB, Gender, Resource-limited setting, HIV policy changes*.

INTRODUCTION

With the significant increase in funding for Human Immunodeficiency Virus (HIV) prevention, care, treatment and support programs worldwide, more HIV infected individuals have been able to receive the antiretroviral therapy (ART) (1,2). By the time the '3 by 5' initiative was launched in 2003, only 400,000 people were estimated to be receiving ART worldwide (3) but by the end of 2018, an estimated 23.3 million people were reported to be receiving ART worldwide (4). The sub-Saharan Africa has recorded the most tremendous increase (about 40%) in the number of people receiving ART with about 16.3 million people in 2018 from about 5 million people in 2010 (5).

However, the persistent problem of late ART initiation with advanced HIV disease stage in the sub-Saharan Africa diminishes the full potential of HIV scale-up in the region (6,7). Also, the high HIV-related mortality rates reported in sub-Saharan Africa have been associated with low CD4 cell counts at ART initiation (7). Data show trends in median CD4 cell count remained below 200cells/μl in most low- and middle- income countries as at 2010 (2). This trend suggests the need to increase efforts towards early ART initiation, which serves to increase immune response and improve patient health outcomes.

Conversely, individual country HIV treatment guidelines are an important reference point for ART initiation. In 2015, the World Health Organization (WHO) proposed the 'test and treat all' HIV treatment guidelines which seeks to increase ART initiation and prevent HIV transmission (9). In 2015, Nigeria began a pilot test of the 'test and treat all' in select local government areas before fully implementing the guidelines across the nation in December 2016 (9). Even though Nigeria has continued to scale up ART provision, there is only an estimated 53% ART coverage of the 1.9 million people currently living with HIV in the country (10,11). Furthermore, Nigeria 2018 country data show that of the 1.9 million people living with HIV in the country, about 1 million

are women aged 15 and above and only an estimated 68% of those women were reported to be receiving ART (9). Nigeria HIV data continues to show a disproportionate distribution of the HIV burden across age, gender and geographic region. Understanding how these factors contribute to advanced disease stage at ART initiation is vital to inform HIV program designs and support targeted interventions.

ART initiation with advanced disease stage results in a delay in CD4 cell count response; adding a considerable burden and cost to care, contributes missed opportunities to HIV prevention thereby increasing new infections and significant early mortality (2,6,8). Therefore, it is imperative that trends in ART treatment presentation be reviewed over time and the impact of policies aimed at driving early ART treatment be reviewed for effectiveness. Consequently, the objectives of this study were to assess the trends in median CD4 cell count and determine the extent of advanced disease stage at ART initiation across gender from 2013 to 2017 at a comprehensive hospital in Nigeria that participated in the pilot test of the 'test and treat all' policy.

METHODS

We conducted a retrospective cohort analysis of HIV infected individuals receiving ART treatment at a HIV clinic in a comprehensive hospital in south-south Nigeria from January 2013 to December 2017.

Data Source

Patient information routinely collected at HIV treatment enrollment and during subsequent clinic visit was documented by clinic staff on standard forms used nationally. Trained data clerks manually abstracted 1,050 adult (aged ≥15 years) medical records from the hospital HIV clinic records and entered then into an electronic database. Data quality assessments were carried out every month to assess for accuracy and completeness until data collection was completed. Data was de-identified for analysis.

Definitions and Outcomes

Advanced HIV disease at ART initiation was defined as having a CD4 cell count of less than 100cells/μl or a WHO clinical stage 4 at start of ART.

Data Analysis

We examined characteristics of all study eligible patients initiating ART at the clinic. We then assessed the proportion of patients with advanced HIV disease at ART initiation. We also examined trends over time in proportion with advanced disease stage at ART initiation as well as median CD4 cell count at ART initiation from 2013 to 2017 by gender. Bivariate analysis of advanced disease stage and each of the covariate was assessed and reported. All covariates were added to a multivariable model to determine any significant correlates to advanced disease stage. We adjusted for age and gender. Odds ratios, adjusted odds ratios, 95% confidence interval and a p value was calculated. Significance was set from a p value of < 0.05. Missing data were assumed as missing at random and were not included in the analysis. All statistical analysis was performed using Stata 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

Ethical Consideration

IRB approval was obtained from the research approval committee of the study clinic, and The University of Texas Health Science Center at Houston.

RESULTS

Characteristics of patients initiating ART

Characteristics of 1050 adults aged 15 and above who initiated ART between January 2013 and December 2017 are presented in Table 1. At ART initiation, about two-thirds were women. The median age was 34 years (inter quartile range [IQR], 29-40) and 35% of the patients were enrolled in 2015.

Clinical and Immunological Characteristics at ART initiation

Of all the men who initiated ART, 45% of them presented with CD4 cell counts lower than 200 cells/μl with a median of 229.5 cells/μl (Figure 1). Of the men whose WHO clinical stage was reported, 35% of them presented with disease stage III and IV. Both male (26%) and female (22%) patients presented with advanced disease stage. Female patients had a slightly higher record of documented tuberculosis compared to males (10% versus 9%).

Trend in Median CD4 cell count and Proportion initiating ART with Advance Disease Stage over time

There was an undulating pattern in the median CD4 cell count of patients initiating ART in our study over time (Figure 1). The overall median CD4 cell count decreased between 2013 and 2014 from 255cells/μl to 234cells/μl. It peaked in 2015 at 278cells/μl and dropped in 2016 (233 cells/μl). However, in 2017, the overall median CD4 cell count began to increase again. The median CD4 cell count for women showed the same pattern as the overall median CD4 cell count but the median CD4 cell count for men continued to decrease from 2015 (260 cells/μl) to 2017 (159 cells/μl). The median CD4 cell count for men was lower than the median CD4 cell count for women through the study years except in 2014 (Figure 1).

Nearly 25% of all patients presented with advanced HIV disease stage from 2013 to 2017. Women presenting with advanced disease stage was highest in 2016 (31.3%) while men presenting with advanced disease stage was highest in 2017 (44.8%) (Figure 2). There was no consistent trend for presenting with advanced disease stage across gender, however, the year of ART initiation was significantly associated with advanced disease stage for all patients (P= 0.02) but not significantly associated by the changes in the national HIV guideline to 'test and treat all' (Table 2).

Factors associated with Presenting with Advanced HIV Disease at ART initiation

In a multivariate model (Table 2), higher odds of initiating ART at advanced HIV disease were observed among patients aged 36-45 years and 46+ years compared with those aged 15-25 years (adjusted odds ratio [AOR], 1.8; 95% CI, 1.01-3.23; AOR, 2.10; 95% CI, 1.10-3.99, respectively), (b) patients who initiated ART in 2016 compared to those who initiated ART in 2013 (AOR, 2.06; 95% CI, 1.08-3.91), (c) patients who had documented tuberculosis (TB) at ART initiation compared to those who did not have a documented TB case (AOR, 1.79; 95% CI, 1.09-2.92).

DISCUSSION

Our study observed substantial increase in the proportion of patients presenting with advanced HIV disease at ART between 2013 and 2017 (from 17.05% to 30.49%). This increase was more significant among male patients compared to females (from 19.23% to 44.83% versus 16.13% to

22.64%). Patients aged 36-45 years as well as those aged 46 years and above were also more likely to present with advanced HIV disease stage at ART initiation. This finding is consistent with previous literature suggesting that older HIV positive males are still more likely to present late to ART treatment compared to women in sub-Saharan Africa (1,8, 12,13). Furthermore, the health seeking behaviors of women and the expansion of HIV testing for pregnant women during antenatal care through prevention of mother to child treatment (PMTCT) programs in sub-Saharan Africa, may be some of the reasons why women tend to initiate ART earlier than men (2,14). PMTCT programs have been shown to contribute to earlier diagnosis and treatment uptake among asymptomatic reproductive aged women (14–16). The importance of early initiation to ART treatment in order to maximize the benefits of ART has been established (17,18). In particular, early uptake of ART is key to deterring the onset of opportunistic infections (OIs) and Acquired Imunne Deficiency Syndrome (AIDS), reducing HIV transmission and early mortality (1,18). This therefore signifies the need for intensified and targeted efforts aimed at increasing earlier diagnosis and treatment uptake for HIV positive males.

A distinct direction was not observed for the among all patients initiating ART across the study period. Changes in national HIV treatment guidelines, environmental, program and individual factors may have contributed to the observed undulating patterns. This finding is comparable with a meta-analysis of median CD4 cell count at ART initiation in sub-Saharan Africa that did not find any significant change in the trend of CD4 count at ART initiation between 2002-2013 (19). In spite of the fluctuations observed in this study, the overall median CD4 cell count (243.5 cells/μl) was higher than previously observed trends in most sub-Saharan African countries (2,6). Of all the sub-Saharan African countries, Rwanda was the first to record median CD4 cell count greater than 200 cells/μl at ART initiation (7). Additionally, the observed increase from 255 cells/μl in 2013 to 278 cells/μl in 2015 in this study may be attributable to the pilot test of the 'test and treat all' strategy implemented in the south-south of Nigeria. The subsequent decrease in median CD4 cell in 2016 to 233 cells/μl and increase to 244 cells/μl in 2017 may have been influenced by other contextual, program or individual factors not addressed in this study. Also, our study found that while median CD4 cell count started increasing among women in 2017, it continued to decrease among men from 206cells/μl in 2015 to 159 cells/μl in 2017. This may imply that there is still a widening health disparity across gender in Nigeria which threatens the effectiveness of HIV care

and treatment scale-up in the nation. Future studies are needed to shed light on the effects of possibly modifiable factors that determine these outcomes and suggest strategies for gender-based interventions that promote earlier ART initiation among men.

In multivariate models, our study found that patients aged 36-45 years and 46 years and above relative to those aged 15-25 years had about twice the odds of presenting with advanced HIV disease stage at ART initiation (Table 5). This is consistent with other studies in the sub-Saharan region (2,7,14). Even though sex was not significantly associated with presentation with advanced disease stage, other studies from sub-Saharan Africa have reported that older HIV positive males have been found more likely to present late to ART treatment with a lower median CD4 cell count and advanced disease stage and have a slower immune response compared to women (7,8,20–22). This suggests a persistent gap in the HIV care system to eliminate gender disparities in the timeliness of ART initiation across gender and age. Thus, more research is needed to elucidate drivers of the gap and identify opportunities to address these disparities.

The strength of this study includes a sex-specific analysis and the use of routinely collected patient data rather than data collected solely for the purpose of research only. Our study also reviews data over 5 years from 2013 to 2017, a period when the Nigerian national HIV guidelines where changed and our study location participated in the pilot test of the new guidelines. Our study has some limitations. First, our sample was limited to only patients enrolled into care at the target hospital, which may not represent the various types of HIV care settings across the country. Additionally, our study site collected data manually giving room for errors during data entry as well as data abstraction. Finally, about 6% of patients were excluded from the analysis due to missing data on parameters of interest for this study i.e. advanced disease stage thus, highlighting the importance of a thorough assessment of patients and an accurate documentation of laboratory and clinical findings.

CONCLUSIONS

In conclusion, the trends observed in our study points to a persistent and widening disparity in early diagnosis of HIV and treatment uptake between male and female HIV positive individuals in Nigeria. Consequently, additional research on the determinants of late ART initiation in the

‘treat all’ policy era with improved ART coverage is imperative. Age and gender specific interventions are needed to effectively identify, enroll and initiate ART treatment among HIV positive individuals in a timely manner. Without such efforts targeting mechanisms that mitigate early ART treatment initiation, the effectiveness of HIV treatment scale-up programs including its direct benefit to the individual and indirect benefits on population HIV incidence may be reduced over time.

Table 1: Patient characteristics

	N	Advanced HIV at ART Initiation		P-value
		Yes	No	
Sex				
Male	338 (34.28)	89 (38.70)	249 (32.94)	0.11
Female	648 (65.72)	141 (61.30)	507 (67.06)	
Age				
Median (IQR)	34 (29, 40)			
15-25	123 (12.47)	19 (8.26)	104 (13.74)	0.09
26-35	442 (44.83)	101 (43.91)	341 (45.11)	
36-45	289 (29.31)	73 (31.74)	216 (28.57)	
≥46	132 (13.39)	37 (16.09)	95 (12.57)	
Year of ART Initiation				
2013	88 (9.06)	15 (6.67)	73 (9.79)	0.02
2014	261 (26.88)	55 (24.44)	206 (27.61)	
2015	349 (35.94)	72 (32.00)	277 (37.13)	
2016	191 (19.67)	58 (25.78)	133 (17.83)	
2017	82 (8.44)	25 (11.11)	57 (7.64)	
Documented TB				
Yes	96 (9.85)	30 (13.45)	66 (8.78)	0.04
No	879 (90.15)	193 (86.55)	686 (91.22)	

Figure 1: Median CD4 at ART initiation by Year of ART start

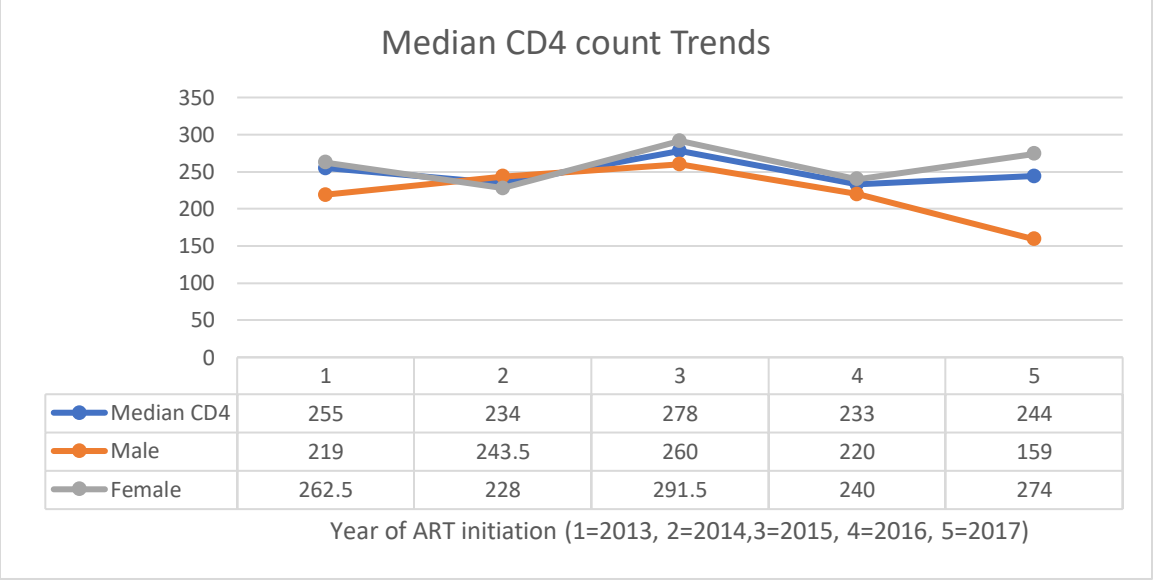

Figure 2: Advanced HIV Disease Stage by Year of ART Start

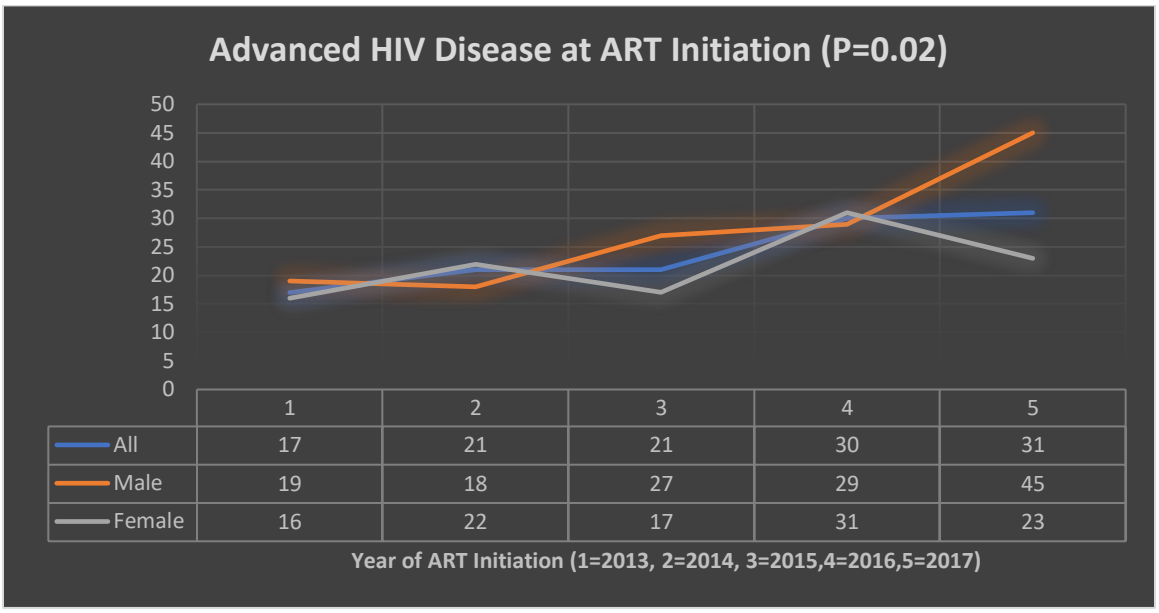

Table 2: Crude and Adjusted Odds Ratio of factors associated with Advanced HIV Disease Stage at ART initiation

Characteristic	N	% Advanced HIV Disease	Crude OR	95% CI	P- value	Adjusted OR	95% CI	P value
Sex								
Male	89	26.33	1.29	0.95-1.74	0.11	1.17	0.84-1.62	0.35
Female	141	21.76	Ref			Ref		
Age								
15-25	19	15.45	Ref			Ref		
26-35	101	22.85	1.62	0.95-2.77	0.08	1.59	0.91-2.77	0.11
36-45	73	25.26	**1.85**	**1.06-3.23**	**0.03**	**1.80**	**1.01-3.23**	**0.05**
46+	37	28.03	**2.13**	**1.15-3.96**	**0.02**	**2.10**	**1.10-3.99**	**0.02**
Year of ART Initiation								
2013	15	17.05	Ref			Ref		
2014	55	21.07	1.30	0.69-2.44	0.42	1.16	0.61-2.19	0.66
2015	72	20.63	1.26	0.69-2.34	0.45	1.09	0.58-2.04	0.78
2016	58	30.37	**2.12**	**1.12-4.01**	**0.02**	**2.06**	**1.08-3.91**	**0.03**
2017	25	30.49	**2.13**	**1.03-4.42**	**0.04**	2.01	0.96-4.20	0.06
Treat all era	622	68.89	Ref					
Pre -treat all era	349	31.11	0.76	0.55-1.04	0.09	-	-	-
Documented Tuberculosis								
Yes	30	31.25	**1.62**	**1.02-2.56**	**0.04**	**1.79**	**1.09-2.92**	**0.02**
No	193	21.96	Ref			Ref		

Bolded=P value ≤0.05

Adjusted for age, sex and presence of TB

References:

1. Kigozi IM, Dobkin LM, Martin JN, et al. Late-disease stage at presentation to an HIV clinic in the era of free antiretroviral therapy in Sub-Saharan Africa. *J. Acquir. Immune Defic. Syndr.* 2009;52(2).
2. Lahuerta M, Wu Y, Hoffman S, et al. Advanced HIV disease at entry into HIV Care and Initiation of Antiretroviral Therapy during 2006-2011: Findings from four sub-saharan African countries. *Clin. Infect. Dis.* 2014;58(3).
3. Laurent C, Ngom Gueye NF, Ndour CT, et al. Long-term benefits of highly active antiretroviral therapy in Senegalese HIV-1-infected adults. *J. Acquir. Immune Defic. Syndr.* 2005;38(1):14–17.
4. Ugbena R, Aberle-Grasse J, Diallo K, et al. Virological Response and HIV Drug Resistance 12 Months After Antiretroviral Therapy Initiation at 2 Clinics in Nigeria. *Clin. Infect. Dis.* [electronic article]. 2012;54(suppl 4):S375–S380. (https://academic.oup.com/cid/article-lookup/doi/10.1093/cid/cir1064). (Accessed January 13, 2018)
5. World Health Organization. WHO| HIV/AIDS-Data and Statistics. 2018;(http://www.who.int/hiv/data/en/). (Accessed October 23, 2018)
6. Nash D, Wu Y, Elul B, et al. Program-level and contextual-level determinants of low-median CD4 + cell count in cohorts of persons initiating ART in eight sub- Saharan African countries for the International Center for AIDS Care and Treatment Programs. *AIDS July* [electronic article]. 2011;31(2512):1523–1533. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3422866/pdf/nihms391503.pdf)
7. Mutimura E, Addison D, Anastos K, et al. Trends in and correlates of CD4+ cell count at antiretroviral therapy initiation after changes in national ART guidelines in Rwanda. *AIDS*. 2015;29(1).
8. Lahuerta M, Ue F, Hoffman S, et al. The problem of late ART initiation in Sub-Saharan Africa: a transient aspect of scale-up or a long-term phenomenon? *J. Health Care Poor Underserved*. 2013;24(1).
9. Stafford KA, Odafe SF, Lo J, et al. Evaluation of the clinical outcomes of the Test and Treat strategy to implement Treat All in Nigeria: Results from the Nigeria Multi-Center

ART Study. *PLoS One*. 2019;14(7):e0218555.

10. WHO. WHO | HIV/AIDS. *WHO* [electronic article]. 2017;(http://www.who.int/mediacentre/factsheets/fs360/en/). (Accessed January 3, 2018)
11. UNAIDS/Nigeria. Nigeria | UNAIDS- Overview. 2017;(http://www.unaids.org/en/regionscountries/countries/nigeria). (Accessed January 9, 2018)
12. Maskew M, Brennan AT, Westreich D, et al. Gender differences in mortality and CD4 count response among virally suppressed HIV-positive patients. *J. Womens. Health (Larchmt).* [electronic article]. 2013;22(2):113–20. (http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3579326&tool=pmcentrez&rendertype=abstract)
13. Clouse K, Pettifor AE, Maskew M, et al. Patient retention from HIV diagnosis through one year on antiretroviral therapy at a primary health care clinic in Johannesburg, South Africa. *J. Acquir. Immune Defic. Syndr.* [electronic article]. 2013;62:e39-46. (http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3548953&tool=pmcentrez&rendertype=abstract)
14. Lahuerta M, Lima J, Nuwagaba-Biribonwoha H, et al. Factors Associated with Late Antiretroviral Therapy Initiation among Adults in Mozambique. *PLoS One* [electronic article]. 2012;7(5):e37125. (http://dx.plos.org/10.1371/journal.pone.0037125)
15. Dalhatu I, Onotu D, Odafe S, et al. Outcomes of Nigeria's HIV/AIDS treatment program for patients initiated on antiretroviral treatment between 2004-2012. *PLoS One*. 2016;11(11):1–25.
16. Chan AK, Kanike E, Bedell R, et al. Same day HIV diagnosis and antiretroviral therapy initiation affects retention in Option B+ prevention of mother-to-child transmission services at antenatal care in Zomba District, Malawi. *J. Int. AIDS Soc.* 2016;19(1).
17. Young S, Wheeler AC, McCoy SI, et al. A Review of the Role of Food Insecurity in Adherence to Care and Treatment Among Adult and Pediatric Populations Living with HIV and AIDS. *AIDS Behav.* 2014;18:505–515.
18. Anejo-Okopi, Ugoagwu P, Abah IO, et al. HIV-1 INFECTION AMONG LATE DIAGNOSED PATIENTS ACCESSING ANTIRETROVIRAL THERAPY IN JOS, NIGERIA. *African J. Nat. Sci.* 2014;17:49–60.

19. Siedner MJ, Ng CK, Bassett I V., et al. Trends in CD4 count at presentation to care and treatment initiation in Sub-Saharan Africa, 2002-2013: A meta-analysis. *Clin. Infect. Dis.* 2015;60(7).
20. Rosen S, Maskew M, Fox MP, et al. Initiating Antiretroviral Therapy for HIV at a Patient???s First Clinic Visit: The RapIT Randomized Controlled Trial. *PLoS Med.* 2016;13(5).
21. Kigozi IM, Dobkin LM, Martin JN, et al. Late disease stage at presentation to an HIV clinic in the era of free antiretroviral therapy in sub-Saharan Africa. *October*. 2010;52(2):1–21.
22. Kate Clouse, Audrey Pettifor, Mhairi Maskew, Jean Bassett, Annelies Van Rie, Cyinthia Gay, Frieda Behets, lan Sanne and MPF. Initiating ART when presenting with higher CD4 counts results in reduced loss to follow-up in a resource-limited setting. 2014;27(4):645–650.

JOURNAL ARTICLE 2

The Association between Baseline Clinical Characteristics and Long-term Antiretroviral Treatment Retention among HIV patients in Nigeria.

Journal: BMC Infectious Diseases

Abstract:

Background: Long-term ART treatment retention among HIV patients is crucial in increasing immune response and ensuring patient attains viral suppression.

Methods: Data was abstracted from clinic records of 1050 HIV positive adults aged ≥15 who initiated ART between 2013 and 2017 at a comprehensive clinic in Nigeria. All data was analyzed using STATA version 15.

Results: The study population was 66.95% females and the median age was 34 years (inter quartile range [IQR], 29-40). Most participants started ART in 2014 (26.70%) and 2015 (35.24%). ART treatment retention was 71.39%, 79.50%, 74.01% and 62.67% at 6, 12, 24 and 36 months respectively. CD4 cell count <100 was inversely predictive of retention (AOR 0.55; 95% CI, 0.37-0.82) while female gender (AOR, 2.00; 95% CI, 1.02 – 3.89), older age (AOR, 1.88; 95% CI, 1.01-3.51), TB at start (AOR, 2.21; 95% CI, 1.02-4.75). and CD4 cell count 100-199 (AOR, 2.54; 95% CI, 1.04-6.20) were significantly associated with retention.

Conclusion: Long-term HIV treatment retention in Nigeria like most other sub-Saharan nations continue to show a decrease in retention rates over duration in treatment. While it is important to address patient-related and structural barriers, multi-pronged care approaches are advocated to attain improved quality of life and sustainable viral suppression. Further research examining multiple factors that affect retention is recommended.

Keywords: *Gender, CD4 cell count, TB, HIV treatment, Long-term retention, Resource- limited setting*

Background

Antiretroviral therapy (ART) treatment retention is at the core for attaining improved patient health outcome among Human Immunodeficiency Virus (HIV) infected individuals (1,2). It is the sustained retention in treatment of HIV patients that ensures the benefits of ART are achieved by both individuals and public health (3). ART treatment retention provides an avenue for HIV patients to continue to receive ART medications as well as clinical management of any opportunistic infections (OIs) that may occur (3). Since ART treatment retention is defined as the a patient's continued participation in HIV medical care including adherence to medication and clinic visits (3), attaining long-term care of HIV patients is imperative to mitigate the burden of HIV.

Since 2006, Nigeria has continued to expand ART provision and care for people infected with HIV through partnerships with public and private stakeholders and the decentralization of treatment programs to tackle patient concerns regarding access to ART (1,2,4). With increased access to ART, treatment enrollment increased from 90,008 in 2006 to about 1,016,346 in 2018 showing a remarkable increase in ART treatment uptake in Nigeria (1,5,6). Notwithstanding the increased provision of ART treatment and related care to provide a panacea to individuals infected with HIV, there remain unresolved and daunting challenges in ensuring long-term retention of HIV infected individuals in treatment and care (7–9). This is especially so for HIV patients in low and medium-income settings where people face more barriers like cost of transport to clinic and inadequate drug availability while trying to access ART (8–11). These barriers may contribute to lower retention rates and increased negative health consequences such as drug resistance, sub-optimal viral suppression and early mortality observed in these regions. Clinical baseline characteristics of patients have also been shown to impact retention rates over time. Data from an assessment of patient retention in ART care in the sub-Saharan Africa, showed rates of 85.6% at 12 months, 79.3% at 24 months, 76% at 36 months and 73.1% at 48 months (10). These rates would mean that of 100 patients starting care, only about 30 patients would be retained at 48 months. Furthermore, a current systematic review of HIV cohorts showed that every third patient initiating ART was

classified as lost to follow-up within 3 years of care (12,13). Consequently, these ART treatment retention rates imply a public health concern for the sub-Saharan Africa region.

The high burden of HIV in Nigeria and her disproportionate prevalence rates continue to place her at the forefront of HIV research. Nigeria, a sub-Saharan country and the most populous country in West Africa has one of the highest numbers of people living with HIV (14). Data from Nigeria also show a decreasing ART retention rate over time (1,3). A study of HIV treatment programs across Nigeria reported retention rates ranged from 81% - 62% over a 4- year follow up period (2). These rates call into question the effectiveness of the programs offered to increase retention among HIV patients while raising the need to understand the possible interaction of multiple factors that impact ART treatment retention. Identifying correlates to retention in our study may assist in better HIV program intervention designs and resource allocation aimed at increasing ART treatment retention. Therefore, we aim to examine the long-term retention of HIV patients assessing ART at a comprehensive hospital in South-South Nigeria.

Methods

We conducted a retrospective cohort analysis of HIV infected individuals receiving ART treatment at a HIV clinic in a comprehensive hospital in south-south Nigeria from January 2013 to December 2017.

Data Source

Patient information routinely collected at HIV treatment enrollment and during subsequent clinic visit was documented by clinic staff on standard forms used nationally. Trained data clerks manually abstracted 1,050 adult (aged ≥15 years) medical records from the hospital HIV clinic records and entered then into an electronic database. Data quality assessments were carried out every month to assess for accuracy and completeness until data collection was completed. Data was de-identified for analysis.

Definitions and Outcomes

ART treatment retention was defined as retention of patients receiving ART with continuous visits, i.e., no gap >90 days from next clinic appointment (12) in the first 6 months of care (defined as retained for 6 months) and in the following 6 months of care (defined as retained for 12 months).

Data Analysis

We examined characteristics of all study eligible patients initiating ART at the clinic. We then assessed the proportion of patients with retained in ART care at 6, 12, 24 and 36months. Bivariate analysis of each of the covariates and retention was assessed and reported. Multiple multivariable models with each treatment retention category were built and the covariates were added to determine any significant correlates to retention. We adjusted for age and gender. Odds ratios, adjusted odds ratios, 95% confidence interval and a p value were calculated. Significance was determined from a p value of < 0.05. Missing data were assumed as missing at random and were not included in the analysis. All statistical analysis was performed using Stata 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

Ethical Consideration

IRB approval was obtained from the research approval committee of the study clinic, and The University of Texas Health Science Center at Houston.

Results

A total of 1050 patients were eligible for this study. Males accounted for 33.05% while females were 66.95% of the study population (Table 1). The median age was 34 years (inter quartile range [IQR], 29-40). Most of the participants initiated ART in 2014 (26.70%) and 2015 (35.24%). Table 1 also shows retention was 71.39% at 6 months, 79.50% at 12 months, 74.01% at 24 months and 62.67% at 36 months. There was no significant difference in retention at 6, 12, 24 and 36 months across gender or year of treatment entry. Table 1 shows the median CD4 cell count at baseline was 243.5 cells/μl. While females presented with higher median CD4 cell counts at baseline (246 cells/μl), males presented with a lower median of 229.5 cells/μl at baseline. Females had a slightly higher proportion of documented tuberculosis compared to males (10% versus 9%) at baseline. Females were also more likely to start ART treatment on the same day they were enrolled into care compared to the males (71.99 versus 67.66%).

In bivariate analyses shown in Table 2, CD4 cell count <100 compared to CD4 cell count ≥350 was a significant predictor of retention at 6 and 24 months (crude odds ratio [COR], 0.53; 95% CI, 0.36-0.78 and COR, 0.44; 95% CI, 0.25-0.79 respectively) such that those who have <100 have lower odds of been retained in treatment at 6 and 24 months, same day ART start compared to

those who did not start ART on same day of treatment enrollment was predictive of retention at 6 months as well, a positive TB status at baseline compared to a negative TB status was also predictive of retention at 12 months (COR, 2.22; 95% CI, 1.04-4.74). The association between same day ART start and retention at 12 months was not significant in multivariate analyses while all other significant bivariate associations remained significant in multivariate analyses (a) CD4 cell count <100 compared to CD4 cell count ≥350 at 6 and 24 months (adjusted odds ratio [AOR] 0.55; 95% CI, 0.37-0.82; AOR, 0.46; 95% CI, 0.25-0.84) (b) a positive TB status at baseline compared to a negative TB status (AOR, 2.21; 95% CI, 1.02-4.75). Also, CD4 cell count of 100-199 compared to CD4 cell count ≥350 (AOR, 2.54; 95% CI, 1.04-6.20) and female gender compared to male (AOR, 2.00; 95% CI, 1.02 – 3.89) was significantly associated with retention at 36 months and age group 36-45 compared to age 46+ (AOR, 1.88; 95% CI, 1.01-3.51) was predictive of 12 months retention as shown in Table 3.

Discussion

This study examined retention in ART treatment over a 3-year period among HIV patients receiving treatment at a comprehensive hospital in Nigeria. The findings in this study are similar to retention rates reported in previous studies in Nigeria and other sub-Saharan countries (2,9,10). A systematic review of patient retention in sub-Saharan Africa between 2002-2009 showed a 64.6% retention at 36months after adjusting for variable follow-up time in a sensitivity analysis (8). Previous studies reviewing data across Nigerian ART service programs also found similar results of decreasing retention rates over time (1,2). This continued decrease in retention rates over time has been attributed to reasons such as loss to follow up, death, treatment transfers, religious and economic factors as well as intentional discontinuation of treatment due to improved health (1,16). Specifically, this study observed that patients who presented with advanced HIV disease stage (CD4 cell count <100) were less likely to be retained in treatment at 6 and 24 months follow up. This finding collaborates reports from previous studies in Nigeria that suggest lower retention among patients presenting with CD4 cell counts <100 at ART initiation (2,17,18). Research has also suggested patients with advanced HIV disease stage have lower odds of immune recovery and may contribute a high proportion of early mortality thus lower observed retention rates (19,20). The early mortality rates may also explain why we did not observe any significant association between CD4 cell count <100 and retention at 36 months. On the other hand, our study observed

a significant association between documented positive TB status at baseline with retention at 12 months. This may be due to the National Tuberculosis Control Program (NTP) implemented in Nigeria since 2007 with extra program retention strategies provided to TB patients to ensure treatment adherence and disease containment (21). In a study where patients were traced to their homes, patients and/or family members were reported to express excitement at the home visits and made decisions to come in to clinic at the next appointment (22). Also, researchers found patient engagement through extra in person follow-ups and via mobile device, text messages, neighborhood peer counselors, home visits, phone calls and contact tracking were effective in maintaining treatment retention (23–25). This implies that targeted and consistent patient follow-up may boost treatment retention.

Like previous studies, our study found females had higher odds of been retained in long-term treatment (2,18). In addition, our study found older age (36-45 years) was predictive of treatment retention at 12 months. While studies have shown gender-differences in health-seeking behaviors, PMTCT programs in sub-Saharan Africa which target women have been shown to increase retention in care among women (26,27). Yet, there are still little or no programs directly targeted at increasing ART treatment uptake and retention among males. Culturally- sensitive programs are needed to minimize the long-standing disparity in treatment uptake and retention across gender in Nigeria. Likewise, age-appropriate programs are necessary to ensure adequate service uptake and long-term retention across all age groups.

The strength of this study includes the review of routinely collected data over a period of time. However, our study was limited due to difficulties rising from incomplete data. Some initial variables of interest that may be associated with the outcome variable could not be examined due to incomplete data. We recommend further studies that review multiple factors associated with retention and advocate for advanced health care data management systems in Nigeria to improve study results that drive HIV policies and programs.

Conclusions

Long-term ART retention among HIV patients is vital to restoring health and improving quality of life by achieving viral suppression. Achieving viral suppression means patient viral load is

undetectable hence untransmittable. This study demonstrates that long-term ART retention is still a challenge for the Nigerian HIV care program. While differentiated and multi-pronged care approaches are advocated, structural and patient-related barriers should be addressed to ensure that ART retention strategies are effective and more importantly sustainable.

Table 1: Patient characteristics at ART Treatment Start

Variable	N (%)	Retention at 6 months	Retention at 12 months	Retention at 24 months	Retention at 36 months
	1050 (100%)	721 (71.39)	539 (79.50)	336 (74.01)	141 (62.67)
Sex					
Male	347 (33.05)	237 (71.17)	174 (76.99)	106 (73.61)	36 (55.38)
Female	703 (66.95)	484 (71.49)	365 (80.75)	230 (74.19)	105 (65.62)
Age, y					
Median (IQR)	34 (29, 40)				
15-25	136 (12.95)	91 (71.65)	65 (76.47)	44 (80.00)	20 (62.50)
26-35	477 (45.43)	313 (68.19)	232 (78.91)	142 (71.00)	59 (61.46)
36-45	301 (28.67)	220 (75.34)	175 (83.33)	111 (77.08)	46 (63.89)
≥46	136 (12.95)	97 (73.48)	67 (75.28)	39 (70.91)	16 (64.00)
Year of ART Treatment start					
2013	93 (9.03)	71 (76.34)	55 (77.46)	38 (70.37)	26 (70.27)
2014	275 (26.70)	202 (73.72)	168 (83.58)	141 (84.43)	114 (82.01)
2015	363 (35.24)	255 (71.43)	208 (82.21)	156 (75.36)	-
2016	198 (19.22)	139 (70.92)	102 (73.38)	-	-
2017	101 (9.80)	52 (59.77)	-	-	-
CD4 count cell/µl					
Median (IOR)	243.5 (107-405)				
<100	230 (23.33)	141 (63.23)	98 (74.81)	47 (57.32)	24 (66.67)
100-199	173 (17.55)	119 (71.26)	91 (79.13)	59 (77.63)	31 (70.45)
200-349	269 (27.28)	207 (78.71)	164 (82.00)	121 (82.88)	51 (60.71)
≥350	314 (31.85)	230 (76.41)	175 (81.40)	106 (75.18)	33 (55.93)
Documented Tuberculosis					
Yes	98 (9.50)	74 (77.89)	65 (12.08)	52 (15.48)	17 (12.06)
No	934 (90.50)	643 (71.05)	473 (87.92)	284 (84.52)	124 (87.94)
Same Day ART Start					
Yes	719 (70.56)	495 (68.85)	368 (68.40)	222 (66.07)	97 (68.79)
No	300 (29.44)	224 (31.15)	170 (31.60)	114 (33.93)	44 (31.21)

Table 2: Bivariate association between variables of interest and treatment retention at 6, 12, 24 and 36 months

VARIABLES	(1) **Crude OR (CI)**	(2) **Crude OR (CI)**	(3) **Crude OR (CI)**	(4) **Crude OR (CI)**
Sex				
Male	Ref	Ref	Ref	Ref
Female	1.02 (0.76-1.38)	1.25 (0.85 - 1.85)	1.03(0.65-1.62)	1.54 (0.85 - 2.77)
Age				
15-25	0.91(0.53-1.57)	1.07 (0.53-2.14)	1.64 (0.68-3.96)	0.94(0.32-2.78)
26-35	0.77 (0.50-1.19)	1.23 (0.70 - 2.15)	1.00 (0.53-1.94)	0.90 (0.36-2.24)
36-45	1.10 (0.69-1.76)	1.64 (0.90- 3.00)	1.38 (0.69-2.78)	1.00 (0.39-2.57)
46+	Ref	Ref	Ref	Ref
CD4 at ART Start				
<100	**0.53 (0.36-0.78)**	0.68 (0.40-1.15)	**0.44 (0.25-0.79)**	1.58 (0.83-5.85)
100-199	0.77 (0.50-1.17)	0.87 (0.49 - 1.53)	1.15 (0.59-2.22)	1.88 (1.14-8.11)
200-349	1.14 (0.77-1.70)	0.81 (0.63 - 1.71)	1.60 (0.90-2.84)	1.22 (1.03-4.91)
≥350	Ref	Ref	Ref	Ref
Documented TB				
Yes	1.44 (0.87-2.38)	**2.22 (1.04-4.74)**	1.60 (0.82-3.12)	0.69 (0.32-1.47)
No	Ref	Ref	Ref	Ref
Same day ART Start				
Yes	**0.72 (0.53-0.98)**	0.91 (0.60-1.36)	0.73 (0.46-1.17)	0.88 (0.49-1.59)
No	Ref	Ref	Ref	Ref

Retention at 6 months (1), Retention at 12 months (2), Retention at 24 months (3) and Retention at 36 months (4). Bolded values show P value ≤0.05

Table 3: Multivariate association between variables of interest and treatment retention at 6, 12, 24 and 36 months

VARIABLES	(1) Adjusted OR (CI)	(2) Adjusted OR (CI)	(3) Adjusted OR (CI)	(4) Adjusted OR (CI)
Sex				
Male	Ref	Ref	Ref	Ref
Female	1.16 (0.84-1.60)	1.32 (0.87-2.01)	1.12 (0.68-1.85)	**2.00 (1.02 – 3.89)**
Age				
15-25	0.87(0.47-1.60)	1.00 (0.47-2.10)	2.11 (0.78-5.69)	0.63 (0.20-2.04)
26-35	0.75 (0.47-1.21)	1.18 (0.66-2.11)	1.02 (0.50-2.06)	0.62 (0.23-1.67)
36-45	1.04 (0.63-1.71)	**1.88 (1.01-3.51)**	1.45 (0.70-3.00)	0.80 (0.30-2.15)
46+	Ref	Ref	Ref	Ref
CD4 at ART Start				
<100	**0.55 (0.37-0.82)**	0.62 (0.36-1.06)	**0.46 (0.25-0.84)**	1.71 (0.70-4.17)
100-199	0.75 (0.49-1.16)	0.72 (0.40-1.30)	1.15 (0.57-2.29)	**2.54 (1.04-6.20)**
200-349	1.15 (0.77-1.72)	0.99 (0.59-1.64)	1.70 (0.95-3.07)	1.39 (0.69-2.80)
≥350	Ref	Ref	Ref	Ref
Documented TB				
Yes	1.48 (0.59-2.59)	**2.21 (1.02-4.75)**	1.67 (0.82-3.41)	0.53 (0.23-1.21)
No	Ref	Ref	Ref	Ref
Same day ART Start				
Yes	0.87 (0.63-1.21)	0.99 (0.65-1.51)	0.79 (0.49-1.28)	0.96 (0.52-1.78)
No	Ref	Ref	Ref	Ref

Retention at 6 months (1), Retention at 12 months (2), Retention at 24 months (3) and Retention at 36 months (4).
Bolded values show P value ≤0.05
Adjusted for covariates

References:

1. Babatunde O, Ojo OJ, Atoyebi OA, et al. Seven year review of retention in HIV care and treatment in federal medical centre Ido-Ekiti. *Pan Afr. Med. J.* 2015;22.
2. Dalhatu I, Onotu D, Odafe S, et al. Outcomes of Nigeria's HIV/AIDS treatment program for patients initiated on antiretroviral treatment between 2004-2012. *PLoS One*. 2016;11(11):1–25.
3. Holtzman CW, Brady KA, Yehia BR, et al. Retention in Care and Medication Adherence: Current Challenges to Antiretroviral Therapy Success. 2016;75(5):445–454.
4. Odafe S, Torpey K, Khamofu H, et al. The Pattern of Attrition from an Antiretroviral Treatment Program in Nigeria. *PLoS One* [electronic article]. 2012;7(12):e51254. (http://dx.plos.org/10.1371/journal.pone.0051254). (Accessed January 13, 2018)
5. Odafe S, Idoko O, Badru T, et al. Patients' demographic and clinical characteristics and level of care associated with lost to follow-up and mortality in adult patients on first-line ART in Nigerian hospitals. *J. Int. AIDS Soc.* [electronic article]. 2012;15(2). (http://doi.wiley.com/10.7448/IAS.15.2.17424). (Accessed January 13, 2018)
6. UNAIDS. Country factsheets Pakistan | 2016 HIV and AIDS Estimates Adults and children living with Country factsheets Pakistan | 2016 HIV testing and treatment cascade People living with HIV Coverage of adults and children. 2016;1–6. (http://www.unaids.org/en/regionscountries/countries/pakistan)
7. Ware NC, Wyatt MA, Geng EH, et al. Toward an Understanding of Disengagement from HIV Treatment and Care in Sub-Saharan Africa: A Qualitative Study. *PLoS Med.* 2013;10.
8. Fox MP, Rosen S. Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007-2009: Systematic review. *Trop. Med. Int. Heal.* 2010;15:1–15.
9. Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: A systematic review. *PLoS Med.* 2007;4(10):1691–1701.
10. Tassie J-M, Baijal P, Vitoria MA, et al. Trends in retention on antiretroviral therapy in national programs in low-income and middle-income countries. *J. Acquir. Immune Defic. Syndr.* 2010;54:437–441.
11. Cornell M, Grimsrud A, Fairall L, et al. Temporal changes in programme outcomes among adult patients initiating antiretroviral therapy across South Africa, 2002-2007. *AIDS*. 2010;24(14):2263–2270.
12. Haas AD, Zaniewski E, Anderegg N, et al. Retention and mortality on antiretroviral therapy in sub-Saharan Africa: Collaborative analyses of HIV treatment programmes: Collaborative. *J. Int. AIDS Soc.* 2018;
13. Fox MP, Rosen S. Retention of Adult Patients on Antiretroviral Therapy in Low- and Middle-Income Countries: Systematic Review and Meta-analysis 2008-2013. *J. Acquir. Immune Defic. Syndr.* 2015;
14. World Health Organization. WHO| HIV/AIDS-Data and Statistics. 2018;(http://www.who.int/hiv/data/en/). (Accessed October 23, 2018)
15. Ahonkhai AA, Noubary F, Munro A, et al. Not all are lost: Interrupted laboratory monitoring, early death, and loss to follow-up (LTFU) in a large south african treatment program. *PLoS One*. 2012;7(3).
16. Rasschaert F, Koole O, Zachariah R, et al. Short and long term retention in antiretroviral

care in health facilities in rural Malawi and Zimbabwe. *BMC Health Serv. Res.* 2012;12:444.
17. Eguzo K, Lawal A, Umezurike C, et al. Predictors of loss to follow-up among HIV-infected patients in a rural South-Eastern Nigeria Hospital: A 5-year retrospective cohort study. *Ann. Med. Health Sci. Res.* [electronic article]. 2015;5(6):373. (http://www.amhsr.org/text.asp?2015/5/6/373/177988)
18. Ugoji C, Okere N, Dakum P, et al. Correlates of Patient Retention in HIV Care and Treatment Programs in Nigeria. *Curr. HIV Res.* [electronic article]. 2015;13(4):300–307. (http://www.eurekaselect.com/openurl/content.php?genre=article&issn=1570-162X&volume=13&issue=4&spage=300). (Accessed January 13, 2018)
19. Kigozi IM, Dobkin LM, Martin JN, et al. Late-disease stage at presentation to an HIV clinic in the era of free antiretroviral therapy in Sub-Saharan Africa. *J. Acquir. Immune Defic. Syndr.* 2009;52(2).
20. Lahuerta M, Ue F, Hoffman S, et al. The problem of late ART initiation in Sub-Saharan Africa: a transient aspect of scale-up or a long-term phenomenon? *J. Health Care Poor Underserved*. 2013;24(1).
21. Ogbuabor DC, Onwujekwe OE. Governance of tuberculosis control programme in Nigeria. *Infect. Dis. Poverty*. 2019;8(1):1–11.
22. Onoka CA, Uzochukwu BS, Onwujekwe OE, et al. Retention and loss to follow-up in antiretroviral treatment programmes in southeast Nigeria. *Pathog. Glob. Health*. 2012;106(1):46–54.
23. Geng EH, Nash D, Kambugu A, et al. Retention in Care among HIV-infected patients in Resource-Limited Settings: Emerging Insights and New Directions. 2011;7(4):234–244.
24. Lawn S, Robin W, Kaplan R, et al. Promoting Retention in Care : *Clin. Infect. Dis.* 2007;45:522413.
25. Horstmann E, Brown J, Islam F, et al. Retaining HIV-Infected Patients in Care: Where Are We? Where Do We Go from Here? *Clin. Infect. Dis.* 2010;50:100201102709029–000.
26. Chan AK, Kanike E, Bedell R, et al. Same day HIV diagnosis and antiretroviral therapy initiation affects retention in Option B+ prevention of mother-to-child transmission services at antenatal care in Zomba District, Malawi. *J. Int. AIDS Soc.* 2016;19(1).
27. Tweya H, Gugsa S, Hosseinipour M, et al. Understanding factors, outcomes and reasons for loss to follow-up among women in Option B+ PMTCT programme in Lilongwe, Malawi. *Trop. Med. Int. Heal.* 2014;19(11).

JOURNAL ARTICLE 3

Food Security Levels and Treatment Support Programs are Associated with ART Adherence among HIV patients in a semi-urban Uganda setting.

Journal: BMC AIDS RESEARCH AND THERAPY

Abstract:

Background: Antiretroviral therapy (ART) adherence is vital in minimizing virologic failure, progression to AIDS and mortality among people living with HIV. ART adherence decreases the likelihood of HIV transmission. However, food insecuirty increases susceptibility to HIV infection and worsens poor clinical outcomes among HIV patients.

Methods: A one-time structured cross-sectional survey conducted between November 2017 and February 2018 among HIV patients aged ≥18 years in Eastern Uganda. Food security level was measured using the Household Food Insecurity Access Scale (HFIAS) and was categorized into two groups- food secure and food insecure. Good adherence level is set at >90% from self- reported ART adherence for a 4 week recall from the time of data collection. All data was analyzed using STATA version 15.

Results: Of the 545 participants, over two-thirds of the participants were females (77%) and median age was 35 years (inter quartile range [IQR], 29-43). Overall food security level in Uganda was 65.5%. HIV positive males reported higher food security levels compared to females (77.60% vs 61.90). Food security (AOR, 1.76; 95% CI, 1.03-3.01), income (AOR 2.69; 95% CI, 1.14-6.34) and nutrition counseling (AOR, 1.99; 95% CI, 1.12-3.54) were significantly associated with good adherence.

Conclusion: Male-led households were found to be more food secure compared to female-led households. Promoting food security and treatment support programs may be effective in advancing HIV care in the sub-Saharan Africa. Additional research aimed at understanding the interactions between treatment support programs, food security levels and ART adherence are needed.

Keywords: *Gender, Food security, Treatment support, Food support, ART adherence, Resource-limited setting*

Introduction

Antiretroviral therapy (ART) is crucial for the optimal health outcome of individuals infected with Human Immuno-deficiency Virus (HIV) (1–3). Adequate adherence to ART is important in minimizing virologic failure, progression to AIDS and mortality among people living with HIV (1,2,4). Adequate ART adherence means sticking to a firm HIV regimen by taking medications daily and as prescribed (5,6). Adherence to ART also decreases the likelihood of HIV transmission, emphasizing the importance of adherence for secondary prevention (2). Despite the established importance of ART, a meta-analysis found that the proportion of patients attaining optimal ART adherence was 77% in sub-Saharan Africa (2,7). Therefore, there is a need to continue to examine the determinants of ART adherence in this region particularly as research suggests ART adherence levels of less than or equal to 80% of medications taken on time may have a treatment failue of 80% (1).

Data from studies in low-income settings suggest a growing knowledge of the association between food insecurity and poor ART adherence among HIV patients (3,8–10). Food insecurity has been defined as 'the state when people do not have physcial, social and economic access to sufficient safe and nutritious foods that meet their dietary needs and food preferences for an active and healthy life' (11). Studies have also identified a vicious cycle between food insecurity and HIV (2,3,9,12). A meta-analysis reviewed the drivers of food insecurity and found poverty, prevalence of HIV/AIDS, lack of educational and employment status were key determinants of household food insecurity (13). Moreover, data show that food consumption often dropped by about 40% in households affected by HIV/AIDS (14,15). This was either due to reduced prodcutivity and income or increased health care needs (14). Food insecuirty not only increases susceptibility to HIV infection but also worsens poor clinical outcomes among HIV patients (9). Weiser et al found that HIV patients who reported limited access to food were more likely not to be ART adherent; thereby resulting in health decline and greater difficulty in accessing food (16). Qualitative data from resource- poor settings also identified that food insecurity is a key reason for ART non-adherence (16–19) due to factors such as decreased income, increased hunger and competing subsistence needs and they could consequently led to poor adherence (3,20).

With current recommendations from policymakers for a more comprehensive approach to HIV care, intervention programs are increasingly adding several components to HIV care such as food assistance, livelihood support, adherence and nutritional counseling as well as support groups among others to drive ART adherence and treatment retention. Early data suggests counseling services and food assistance may increase food security levels, clinic visits, ART adherence, retention in care and survival of HIV patients (21–24). However, the effect of such support services on ART adherence is still not very clear in this study setting. While some studies show food assistance alone was significant in increasing ART adherence, others suggest food assistance with other support programs were more effective (2). As more resources are directed towards ART treatment support interventions, it is imperative to examine if these support services are effective in improving ART adherence in resource-constraint settings.

Uganda, a resource-constraint nation in sub-Saharan Africa has a high prevalence of both HIV and food insecurity (16,25). Current data show a national HIV prevalence of 5.9% with about 1.2 million people living with HIV in Uganda (26). Annually in Uganda, 12% of the people aged 15 to 49 years old die of AIDS (15,20). This decrease in the productive age group has contributed to increased food insecurity among HIV affected households due to reduced income and competing needs (15). According to a Ugandan study on HIV infected individuals, 22% of the households reported that sometimes or often all household members had no food to eat for an entire day (15,16). Around 62% of the study participants also reported that sometimes or often all household members had to skip meals and 95% reported that household members sometimes or often had to eat less preferred foods (15,16). Another study in Uganda found that consuming only one meal per day and being dependent on caregivers for food were risk factors for poor ART adherence (16,27). Likewise, other studies found that HIV patients who are food insecure are less likely to adhere to treatment and may experience treatment interruptions leading to treatment drop out (15,16,20,25). Besides, existing gender-based food norms in Uganda also affects the occurrence of household food insecurity among male- and female- led households (19,28).

Factors contributing to the association between food insecurity and ART adherence in Uganda may be aggravated or lessened by patient socio-demographics as well as socio-cultural norms. Also, the different indigenous ethnic groups in Uganda are defined by their traditional food

preferences to a certain extent (29). Educational level, family income and assets, number of dependents and martial status have also been found to contribute to household food insecurity (29). Study participants who were single or widowed and/or had more than four children were more likely to be food insecure and non-adherent to ART (16,30). While socio-cultural norms will not be explored in this study, it is important to mention that gender-based food taboos, cultural norms and myths in Uganda may influence household food insecurity levels (28,29). A qualitative study with 133 participants in Uganda found that all women, regardless of their physiological status (non-pregnant or pregnant or lactating), were restricted from eating various animal-based foods and some plant-based foods as well (28). In most cultures with food taboos, women and children are generally the most affected (29).

Since ART medication requires lifelong adherence, reviewing household food security levels is fundamental to the four core pillars of a holistic response in HIV prevention, care, treatment and mitigation. Given that food insecurity is endemic in sub-Saharan Africa, it is important to determine the degree of the association between food security levels and ART adherence in areas such as Uganda where other socio-demograhic and cultural factors may contribute to the effects of food security on ART adherence (3,20) and identify effective interventions that could improve patient health outcomes. Given the scope of this study, we plan to review socio-demographic characteristics and food security levels of patients receiving ART care in Uganda and hypothesize that HIV patients who are food secure have higher odds of better ART adherence.

Methods

Data Source:

We conducted a cross-sectional study involving HIV patients receiving ART at two level 3 health care centers in semi-urban communities in Eastern Uganda. Clinics in the region participate in various funded food assistance program and provide care to over 1000 HIV patients annually. Data were collected from any consenting male and female HIV patients aged 18 years old and above who attended clinic on a given data collection day using a one-time structured survey between November 2017 and February 2018. Data obtained included patient socio-demographic characteristics, HIV- related health services and care practices, ART treatment adherence,

nutritional exposures and food security assessments. At the end of the study period, 545 questionnaires were completed with a 90% consent rate.

Definitions and Outcomes

Good adherence level is set at >90% from self- reported ART adherence for a 4 week recall from the time of data collection (5,9). To measure the primary dependent variable (self-reported adherence), a validated Visual Analogue Scale assessed adherence over the past month (31). This tool consists of questions measuring adherence over a period of time (past 30 days) and recall questions to reduce situations of potential bias in missed- ART doses.

Food security level is categorized into two groups- food secure and food insecure. To measure the primary independent variable (household food security), the Household Food Insecurity Access Scale (HFIAS) was utilized. HFIAS has nine yes/no questions (e.g. Did you worry that your household would not have enough food? Were you or any household member not able to eat the kinds of foods you preferred because of a lack of resources?) (9,32). The HFIAS score is computed to categorize patients into food insecure and food secure groups using a distribution- based category (33,34). This tool has been adapted to fit rural and urban study settings and it has been broadly used in different cultural settings (32).

Data Analysis

We examined socio-demographic characteristics of all consenting and eligible HIV infected individuals (male and female) aged 18 years and above participating in the study. We then assessed the level of food security among study participants using the nine item- Household Food Insecurity Access Scale (HFIAS). The scale has a maximum score of 27. Study participants with higher scores are considered food insecure. Chi square tests were conducted to assess the association between covariates and food security levels. Bivariate analysis of ART adherence and the main independent variable as well as each of the covariate was assessed and reported. All variables were added to a multivariable model to determine any significant correlates to ART adherence while adjusting for age, gender and income. Odds ratios, adjusted odds ratios, 95% confidence interval and a p value was calculated. Significance was set from a p value of < 0.05. Missing data were

assumed as missing at random and were not included in the analysis. All statistical analysis was performed using Stata 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

Ethical Consideration:

Initial data collection IRB approval for this study was obtained from the research approval committee of the health center administration in Jinja district in Uganda. Another IRB was obtained from The University of Texas Health Science Center at Houston for the use of de-identified secondary data.

Results

Characteristics of study participants

The socio-demographic characteristics of 545 adults aged 18 and above who participated in this study are presented in Table 1. Over two-thirds of the participants were females (77%). The median age was 35 years (inter quartile range [IQR], 29-43); about half of the participants had a primary school education (47%) and four or more children (46%). Most (78%) of the participants earned less than 500,000 Ugandan shillings per month and 54% were either married or cohabiting with a partner.

Proportion of participants that received support services after HIV Diagnosis

The proportion of participants that received different kinds of support services from the treatment clinics after HIV diagnosis are reported in Table 2. Only few study participants reported receiving adherence support/counseling (8%), adherence support group (2%) and food support or package (3%). However, about two-thirds of the participants reported that they received nutrition counseling (76%) after HIV diagnosis.

Food security assessment of participants

The nine-item Household Food Insecurity Assessment Scale (HFIAS) was used to assess the food security level of the study participants. When asked to recall assessment questions for the past month, about one-third of the study participants reported they worried their household would not

have enough food, were not able to eat the kinds of foods they preferred because of lack of resources, had to eat a limited variety of foods due to lack of resources, ate some foods they did not really want to eat because of lack of resources to obtain other food types, ate a smaller meal than needed because there was not enough food and ate fewer meals in a day because there was not enough food. For the questions 'was there ever no food to eat of any kind in your household because of lack of resources to get food' and 'did you or any household member go to sleep at night hungry because there was not enough food', about 20% of participants gave a positive response. About 16% said they or some household member went the whole day and night without eating on some days in the four weeks recall period. Overall, 65.5% were classified as food secure in this population.

Factors associated with Food Security Level

Chi-square test was used to determine the association between socio-demographic characteristics and food security levels (Table 1). Gender, education and income were significantly associated with food security levels while age, number of children and head of household were not significantly associated with food security level.

Factors associated with ART Adherence

In bivariate and multivariable analyses, income and food security levels were significantly associated with ART adherence (Table 3). Participants who earned ≥500, 000 Ugandan shillings per month compared to those who earned <500,000 showed higher odds of adhering to their ART (crude odds ratio [COR], 2.76; 95% CI, 1.23-6.19; adjusted odds ratio [AOR], 2.69; 95% CI, 1.14-6.34). Participants who were food secure also showed higher odds of ART adherence compared with the food insecure group (COR, 1.77; 95% CI, 1.06-2.96; AOR, 1.76; 95% CI, 1.03-3.01). In the multivariable model alone, higher odds of ART adherence was observed among study participants who received nutrition counseling after HIV diagnosis compared to those who did not report receiving nutrition counseling (AOR, 1.99; 95% CI, 1.12-3.54).

Discussion

Our study observed a high proportion of the participants were food secure (65.5%). The proportion of food secure participants observed in this study is higher than those reported in a previous study

in Uganda (21.5%) among HIV positive individuals, yet lower than the current FAO projection of food secure Ugandans (89%). This variation may be due to the reported disproportionate spread of food security levels across the northern and southern parts of the country. The northern part of Uganda is reported to experience low rainfall and drought, which results in lower agricultural produce leading to higher levels of food insecurity. Since, our study was conducted in the eastern part of Uganda, the study participants may not have experienced harsh environmental changes that affect access to food.

Gender, level of education and monthly income were significantly associated with the food security levels of the participants. This finding is consistent with previous literature that found that educational levels and monthly income as well as gender of the head of the family were associated with food security levels (34,35). Gender disparities in food security levels have been reported across various sub-Saharan settings (16,29,35,36). Male led-households were more likely to be food secure compared to female led-households. This may be because women, especially those who are single or widowed were poorer yet solely responsible for feeding family members (16,35). Also, participants with higher levels of education and income were more likely to be food secure compared to those with lower educational levels and income. Data shows even HIV infected individuals with higher educational status are more likely to get better paying jobs thus higher income and earnings. People who report higher earnings are more likely to satisfy their dietary needs and maintain adequate food security levels (34). On the other hand, HIV infected individuals may experience loss of earnings and face economic challenges due to more frequent sick days. Thus, if there are no support measures in place, HIV can very quickly turn food security levels negative through limited ability to work and ultimately worse health outcomes.

Our study also observed a high proportion of the participants reported optimal ART adherence greater than the proportion of patients attaining optimal ART adherence in sub-Saharan Africa (87.34% vs 77%). This may be explained by the self-reported measure of ART adherence we used. Even though VAS is a validated tool, study participants may have reported ART adherence in a manner they perceived as more favorable. However, in a qualitative study conducted in Uganda, results showed high motivation for ART adherence even when other obstacles existed (16) suggesting the potential for increase in ART adherence within suitable conditions.

In multivariate analysis, our study showed a significant association between food security levels and ART adherence. This association remained significant after adjusting for income, education and gender. This finding is consistent with previous literature establishing a link between food security and good ART adherence (2,9,30). Previous studies found better food security levels minimized ART treatment interruptions and improved ART adherence (21,22). In a prospective cohort study conducted in Haiti, HIV patients who were provided food assistance showed improved body mass index, improved food security level and improved ART adherence (22). Furthermore, findings in this study showed nutrition counseling was also significantly associated with good ART adherence after adjusting for covariates. This is also consistent with a literature review that found nutrition counseling had an enabling effect on ART adherence and improved adherence and/or treatment completion (37). Besides, policymakers recommend the use of nutrition assessment, counseling and support (NACS) intervention approach in strengthening the care continuum of HIV infected individuals (8,37,38). Even though food support, adherence support group and adherence counseling were not significantly associated with ART adherence in this study, a combination of various support programs have been shown to improve ART adherence and retention across various sub-Saharan countries. While the low uptake of these services may explain the non-significance observed in this study, it may also suggest a gap in the access to recommended comprehensive care package offered to HIV patients. Thus, the need for further research to evaluate the feasibility of service uptake in various service settings with the goal to improve food security and treatment adherence. Furthermore, since ART is a life-long treatment, minimizing the adverse and likely bidirectional association between food insecurity and ART adherence is imperative in achieving the optimal benefits of ART among HIV patients and the populace.

There were several limitations to our study due to the cross-sectional study design. The study was conducted at semi-urban treatment clinics and participants were recruited among patients who attended clinic on data collection days and consented to participate in the study. This may limit the generalizability of the study findings to other populations. Social desirability bias and recall bias are potential limitations that may have also occurred in this study. Yet, the finding that food security was significantly associated with ART adherence in crude and adjusted analysis suggests

a strong relationship as observed in previous studies as well. Further research with varying study designs are required to determine the scope of the relationship between treatment support programs and ART adherence.

Conclusion

This study demonstrates that various factors drive food security levels among HIV-infected individuals in semi-urban Uganda. Findings also suggest a difference in male and female-led household food security levels. Our study points to a relationship between food security levels, nutrition counseling and ART adherence. Additional research to fully understand the interactions between food security levels and food support programs; adherence support programs and ART adherence are needed. Also, program evaluations that review the long- term efficacy of support programs for ART treatment adherence are essential to developing strategies to minimize the adverse effects of poor food security levels on the overall health outcomes of HIV patients.

Table 1: Socio-demographic characteristics of study participants by Food Security and ART Adherence

Characteristic	N (%)	Food Secure	Good ART Adherence
Gender			
Male	125 (22.94)	97 (77.60)*	112 (23.53)
Female	420 (77.06)	260 (61.90)	364 (76.47)
Age			
Median (IOR)	35 (29-43)		
18-29	138 (25.32)	98 (71.01)	118 (24.79)
30-39	220 (40.37)	141 (64.09)	195 (40.97)
40-49	128 (23.49)	81 (63.28)	112 (23.53)
50+	59 (10.83)	37 (62.71)	51 (10.71)
Education			
No School	103 (18.90)	60 (58.25)	86 (18.07)
Primary	257 (47.16)	156 (60.70)	228 (47.90)
Secondary and Higher	185 (33.94)	141 (76.22)*	162 (34.03)
Number of children			
0-3	295 (54.13)	200 (67.80)	254 (53.36)
4+	250 (45.87)	157 (62.80)	222 (46.64)
Income (Uganda shillings)			
<500,000	425 (77.98)	259 (60.94)	425 (77.98)*
≥500, 000	120 (22.02)	98 (81.67)*	120 (22.02)
Head of Household			
One	252 (46.24)	160 (63.49)	217 (45.59)
Two	293 (53.76)	197 (67.24)	259 (54.41)

*=$p<0.05$

Table 2: Support Services offered after HIV Diagnosis

Support Services	N (%)	Good ART Adherence
Adherence support/ counseling		
Yes	43 (7.89)	39 (8.19)
No	502 (92.11)	437 (91.81)
Nutrition counseling		
Yes	412 (75.60)	366 (76.89)*
No	133 (24.40)	110 (23.11)
Adherence support group		
Yes	11 (2.02)	10 (2.10)
No	533 (97.98)	466 (97.90)
Food support/package		
Yes	15 (2.75)	13 (2.73)
No	530 (97.25)	463 (97.27)

Table 3: Factors associated with ART adherence

Variables	**Good ART Adherence (>90)**	
	Crude OR (95% CI)	**Adjusted OR (95% CI)
Gender		
Male	1.33 (0.70-2.51)	1.09 (0.55-2.16)
Female	Ref	Ref
Age		
18-29	Ref	Ref
30-39	1.32 (0.70-2.48)	1.21 (0.62-2.39)
40-49	1.19 (0.59-2.40)	1.07 (0.47-2.42)
50+	1.08 (0.45-2.61)	0.99 (0.37-2.65)
Education		
No school	Ref	Ref
Primary	1.55 (0.81-2.97)	1.60 (0.82-3.15)
Secondary and Higher	1.39 (0.71-2.75)	1.23 (0.58-2.59)
Number of Children		
0-3	Ref	Ref
4+	1.28 (0.78-2.14)	1.31 (0.73-2.37)
Income		
<500,000	Ref	Ref
≥500, 000	**2.76 (1.23-6.19)**	**2.69 (1.14-6.34)**
Head of Household		
One	Ref	Ref
Two	1.23 (0.74-2.04)	1.02 (0.60-1.74)
Food security		
Food secure	**1.77 (1.06-2.96)**	**1.76 (1.03-3.01)**
Food insecure	Ref	Ref
Adherence support/ counseling		
Yes	1.45 (0.50-4.19)	1.68 (0.56-5.07)

No	Ref	Ref
Nutrition counseling		
Yes	1.66 (0.97-2.87)	**1.99 (1.12-3.54)**
No	Ref	Ref
Adherence support group		
Yes	1.46 (0.18-11.58)	1.42 (0.16-12.43)
No	Ref	Ref
Food support/package		
Yes	0.94 (0.21-4.26)	0.76 (0.15-3.72)
No	Ref	Ref

Bolded if P value= ≤0.05

**Adjusted for confounders

References

1. Eyassu MA, Mothiba TM, Mbambo-Kekana NP. Adherence to antiretroviral therapy among HIV and AIDS patients at the Kwa-Thema clinic in Gauteng Province, South Africa. *African J. Prim. Heal. Care Fam. Med.* [electronic article]. 2016;8(2):7. (https://phcfm.org/index.php/phcfm/article/view/924%0Ahttps://phcfm.org/index.php/phcfm/article/view/924/0)
2. Singer AW, Weiser SD, McCoy SI. Does Food Insecurity Undermine Adherence to Antiretroviral Therapy? A Systematic Review. *AIDS Behav.* [electronic article]. 2015;19(8):1510–1526. (http://dx.doi.org/10.1007/s10461-014-0873-1)
3. Musumari PM, Wouters E, Kayembe PK, et al. Food Insecurity Is Associated with Increased Risk of Non-Adherence to Antiretroviral Therapy among HIV-Infected Adults in the Democratic Republic of Congo: A Cross-Sectional Study. *PLoS One* [electronic article]. 2014;9:1–15. (http://dx.doi.org/10.1371/journal.pone.0085327)
4. Oku AO, Owoaje ET, Ige OK, et al. Prevalence and determinants of adherence to HAART amongst PLHIV in a tertiary health facility in south-south Nigeria. *BMC Infect. Dis.* [electronic article]. 2013;13(1):401. (http://www.biomedcentral.com/1471-2334/13/401). (Accessed July 24, 2015)
5. AIDSinfo.nih.gov. AIDSinfo Glossary of HIV/AIDS-Related Terms. *@AIDSinfo.nih.gov*. 2018;9:1–204.
6. U.S. Department of Health and Human Services. HIV Treatment HIV Medication Adherence. 2018;9:17–19.
7. Mills EJ, Nachega JB, Buchan I, et al. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: A meta-analysis. *J. Am. Med. Assoc.* 2006;296(6):679–690.
8. Claros JM, de Pee S, Bloem MW. Adherence to HIV and TB Care and Treatment, the Role of Food Security and Nutrition. *AIDS Behav.* 2014;18:459–464.
9. Young S, Wheeler AC, McCoy SI, et al. A Review of the Role of Food Insecurity in Adherence to Care and Treatment Among Adult and Pediatric Populations Living with HIV and AIDS. *AIDS Behav.* 2014;18:505–515.
10. Anema A, Vogenthaler N, Frongillo E, et al. Food Insecurity and HIV/AIDS: Current Knowledge, Gaps, and Research Priorities. *Curr HIV/AIDS Rep Curr HIV/AIDS Rep*

Author Manuscr. . Author manuscript; available PMC 2018 April 26. . 2009 Novemb. ; 6(4) 224–231. 2015;12(2):130–140.

11. Food and Agriculture Organization of the United Nations. The State of Food Insecurity in the World Addressing food insecurity in protracted crises 2010 Key messages. 2010.
12. Heestermans T, Browne JL, Aitken SC, et al. Determinants of adherence to antiretroviral therapy among HIV-positive adults in sub-Saharan Africa: a systematic review. *BMJ Glob. Heal.* [electronic article]. 2016;1(4):e000125. (http://gh.bmj.com/lookup/doi/10.1136/bmjgh-2016-000125)
13. Misselhorn AA. What drives food insecurity in southern Africa? a meta-analysis of household economy studies. *Glob. Environ. Chang.* 2005;
14. Topouzis D. The Implications of HIV/AIDS for Household Food Security in Africa. *United Nations Econ. Comm. Africa Food Secur. Sustain. Dev. Div.* 1999;(October).
15. Bukusuba J, Kikafunda JK, Whitehead RG. Food security status in households of people living with HIV/AIDS (PLWHA) in a Ugandan urban setting. *Br. J. Nutr*. 2007;98(1):211–217.
16. Weiser SD, Tuller DM, Frongillo EA, et al. Food insecurity as a barrier to sustained antiretroviral therapy adherence in Uganda. *PLoS One*. 2010;5(4).
17. Goudge J, Ngoma B. Exploring antiretroviral treatment adherence in an urban setting in South Africa. *J. Public Health Policy*. 2011;
18. Musheke M, Bond V, Merten S. Individual and contextual factors influencing patient attrition from antiretroviral therapy care in an urban community of Lusaka, Zambia. *J. Int. AIDS Soc.* 2012;15 Suppl 1:1–9.
19. Nagata JM, Magerenge RO, Young SL, et al. Social determinants, lived experiences, and consequences of household food insecurity among persons living with HIV/AIDS on the shore of Lake Victoria, Kenya. *AIDS Care - Psychol. Socio-Medical Asp. AIDS/HIV*. 2012;24(6):728–736.
20. Weiser SD, Tsai AC, Gupta R, et al. Food insecurity is associated with morbidity and patterns of healthcare utilization among HIV-infected individuals in a resource-poor setting. *Aids*. 2012;26(1):67–75.
21. Lamb MR, El-Sadr WM, Geng E, et al. Association of adherence support and outreach services with total attrition, loss to follow-up, and death among art patients in Sub-

Saharan Africa. *PLoS One*. 2012;7(6).

22. Ivers LC, Chang Y, Gregory Jerome J, et al. Food assistance is associated with improved body mass index, food security and attendance at clinic in an HIV program in central Haiti: A prospective observational cohort study. *AIDS Res. Ther.* 2010;7:1–8.
23. Cantrell RA, Sinkala M, Megazinni K, et al. A pilot study of food supplementation to improve adherence to antiretroviral therapy among food-insecure adults in Lusaka, Zambia. *J. Acquir. Immune Defic. Syndr.* 2008;49(2):190–195.
24. Serrano C, Laporte R, Ide M, et al. Family nutritional support improves survival, immune restoration and adherence in HIV patients receiving ART in developing country. *Asia Pac. J. Clin. Nutr.* 2010;19(1):68–75.
25. Palermo T, Rawat R, Weiser SD, et al. Food Access and Diet Quality Are Associated with Quality of Life Outcomes among HIV-Infected Individuals in Uganda. *PLoS One*. 2013;
26. Ministry of Health Uganda, ICAP. Uganda Population-Based Hiv Impact Assessment. 2016;(August 2017):62–65. (http://www.afro.who.int/sites/default/files/2017-08/UPHIA Uganda factsheet.pdf)
27. Olupot-Olupot P, Katawera A, Cooper C, et al. Adherence to antiretroviral therapy among a conflict-affected population in Northeastern Uganda: A qualitative study. *AIDS*. 2008;
28. Muggaga C, Ongeng D, Mugonola B, et al. Influence of Sociocultural Practices on Food and Nutrition Security in Karamoja Subregion of Uganda. *Ecol. Food Nutr.* [electronic article]. 2017;56(5):424–447. (https://doi.org/10.1080/03670244.2017.1366318)
29. Olum S, Okello-Uma I, A. Tumuhimbise G, et al. The Relationship between Cultural Norms and Food Security in the Karamoja Sub-Region of Uganda. *J. Food Nutr. Res.* [electronic article]. 2017;5(6):427–435. (http://pubs.sciepub.com/jfnr/5/6/10/index.html)
30. Weiser SD, Palar K, Frongillo EA, et al. Longitudinal assessment of associations between food insecurity, antiretroviral adherence and HIV treatment outcomes in rural Uganda. *AIDS* [electronic article]. 2014;28(1):115–20. (http://www.ncbi.nlm.nih.gov/pubmed/23939234)
31. Steel G., Nwokike J. JM. Development of a Multi-method Tool to Measure ART Adherence in Resource-Constrained Settings: The South Africa Experience. 2007;(http://www1.msh.org/projects/rpmplus/Documents/upload/07-157-ART-Adherence-Measurement-Tool_Technical-Report_RPM-Plus-MSH_08_07.pdf)

32. Coates J, Swindale a, Bilinsky P. Household Food Insecurity Access Scale (HFIAS) for measurement of food access: indicator guide. *Washington, DC Food Nutr. Tech. …*. 2007;(August):Version 3.
33. Wang EA, McGinnis KA, Fiellin DA, et al. Food insecurity is associated with poor virologic response among HIV-infected patients receiving antiretroviral medications. *J. Gen. Intern. Med.* 2011;
34. Tiyou A, Belachew T, Alemseged F, et al. Food insecurity and associated factors among HIV-infected individuals receiving highly active antiretroviral therapy in Jimma zone Southwest Ethiopia. *Nutr. J.* 2012;
35. Zakari S, Ying L, Song B. Factors Influencing Household Food Security in West Africa: The Case of Southern Niger. *Sustainability*. 2014;
36. Weiser S, Leiter K, Bangsberg D, et al. Food Insufficieny Is Associated with High-Risk Sexual Behavior among Women In Botswana And Swaziland. *PLoS One*. 2007;4(10):1589–1598.
37. de Pee S, Grede N, Mehra D, et al. The Enabling Effect of Food Assistance in Improving Adherence and/or Treatment Completion for Antiretroviral Therapy and Tuberculosis Treatment: A Literature Review. *AIDS Behav.* 2014;18:531–541.
38. Aberman NL, Rawat R, Drimie S, et al. Food Security and Nutrition Interventions in Response to the Aids Epidemic: Assessing Global Action and Evidence. *AIDS Behav.* 2014;18:554–565.