

Prevalence and factors associated with Advanced Disease among People Living with HIV in Masaka Region, Uganda

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Research Article

Keywords:

Posted Date: September 29th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10791020/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background: A large percentage (22%) of people living with HIV (PLHIV) present for care with advanced HIV disease (AHD), threatening the achievement of the 95-95-95 goals to end AIDS by 2030. For anyone over the age of five, AHD is defined as CD4 count <200 cells/mm³ or with a current WHO stage 3 or 4 events. This study aimed to examine the prevalence and factors related to AHD among newly diagnosed PLHIV in Masaka Region, Uganda.

Methods: We analyzed routinely collected electronic medical record data for newly diagnosed PLHIV who enrolled in HIV care across health facilities in 12 districts of the Masaka Region between October 2021 and September 2022. We assessed the proportion of participants with AHD and examined its association with sociodemographic and health-service characteristics, including age, sex, marital status, facility location, and point of entry into HIV care. Modified Poisson regression was used to estimate adjusted prevalence ratios (aPRs) and corresponding 95% confidence intervals (CIs) for factors associated with AHD.

Results: Of 3,452 newly diagnosed PLHIV on ART included in this study, 2,254 (65.3%) were females. The prevalence of AHD was 15% (518). The results from multivariable modified Poisson regression revealed that participants aged 18-35 years had lower risk of AHD compared to those aged 5-17 years (aPR=0.45; 95% CI: 0.27, 0.78). Married individuals were at lower risk of AHD compared to unmarried participants (aPR=0.67; 95% CI: 0.57, 0.79). Male participants (269/1,198, 22.5%) had higher risk of AHD compared to females (249/2,254, 11.1%; aPR=1.85; 95% CI: 1.57, 2.19). Participants receiving ART services from urban facilities had higher risk of AHD compared to participants receiving ART from rural sites (aPR=1.61; 95% CI: 1.35, 1.93). Participants who were enrolled into care through HIV testing service outreaches (aPR=0.72; 95% CI: 0.58, 0.90) had lower risk of AHD while participants from other care points (aPR=1.28; 95% CI: 1.06, 1.53) had higher risk of AHD compared to the general outpatient point.

Conclusions: The proportion of AHD in this cohort (15%) was lower than the national proportion of 22%. However, this work can be used to design interventions to address higher AHD prevalence among males, in urban facilities, and at care points other than HIV testing outreach sites and the general outpatient point.

Introduction

Human immunodeficiency virus (HIV) is a major public health concern globally [1]. By 2022, there were over 70 million cases and 32 million deaths [2]. Sub-Saharan Africa (SSA) carries over 75% of the global HIV burden [3]. Despite the scale-up of test and treat policy coupled with increased access to antiretroviral therapy (ART), a significant proportion of people living with HIV (PLHIV) develop advanced disease[4]. Advanced HIV disease (AHD), defined as having a CD4 of < 200 cells/μL, or the world Health Organization (WHO) HIV clinical stage 3 or 4 [5] for adults, adolescents, and older children (≥ 5years) [6].

In SSA, advanced HIV disease prevalence ranges between 32%-71%, with a 60% prevalence among PLHIV re-engaged in care following discontinuation [7]. Factors associated with AHD include age, sex, perception of barriers to health care and education level [8]. The high burden of AHD has greatly contributed to mortality among PLHIV. For instance, in 2020, the Joint United Nations Program on HIV/AIDS (UNAIDS) reported that 690,000 PLHIV died from AIDS related illnesses, higher than the UNAIDS target of < 500,000 [9]. In Africa, the Eastern and Southern regions contribute to over 45% of AIDS related deaths, with Uganda contributing 4% to the global mortality [9].

AHD remains an important challenge even in the era of widespread ART availability and universal treatment. People may present with AHD because of late HIV diagnosis and delayed linkage to care, while those previously initiated on ART may develop or return with AHD following treatment interruption, poor engagement with HIV services, treatment failure, or challenges with lifelong ART adherence [10]. WHO estimates indicate that approximately 15%–30% or more of people initiating or reinitiating ART in Africa continue to have AHD [10], [11]. This population is particularly vulnerable to severe opportunistic infections and death, with tuberculosis, cryptococcal meningitis, and severe bacterial infections accounting for a substantial proportion of AHD-related mortality [11]. Consequently, WHO continues to recommend early identification of AHD and a differentiated package of care that includes screening, diagnosis and prophylaxis for major opportunistic infections, rapid ART initiation or optimization, and enhanced adherence support [11].

Recent evidence also demonstrates substantial heterogeneity in the burden of AHD within Uganda. A 2024 study among ART-naïve adults enrolling in care at selected public health facilities in Kampala reported an AHD prevalence of 35.1%, with higher prevalence among men and adults aged 35–50 years [12]. In contrast, a 2025 retrospective cohort study involving 1,233 newly diagnosed PLHIV across 23 public health facilities in rural eastern Uganda reported an AHD prevalence of only 1.9% at diagnosis, with men having substantially higher odds of AHD than women [13]. These marked differences across settings underscore the importance of generating region-specific estimates and identifying populations at greatest risk of presenting with AHD.

In 2020, anecdotal data indicated that 20% of PLHIV enrolling in HIV care in Uganda had AHD. However, evidence on the burden and factors associated with AHD remains geographically limited in Uganda, with recent published studies concentrated in Kampala and rural eastern Uganda [12], [13]. Evidence from the greater Masaka region remains limited, despite the need for context-specific epidemiological data to identify populations at increased risk and inform strategies for earlier diagnosis and appropriate AHD care. This study set out to measure the prevalence and factors associated with AHD among newly diagnosed PLHIV in Masaka region Uganda.

Methods

Study design, setting:

The study was a cross-sectional study conducted by Rakai Health Sciences Program (RHSP). The RHSP, established in 1987, is a non-government non-profit organization located in Kyotera District, South central Uganda. Between 2017–2023, with funding from the President’s Emergency Plan for AIDS Relief (PEPFAR) through the Centers for Disease Control (CDC) Uganda, RHSP, served as the CDC implementing partner supporting comprehensive HIV prevention, care and treatment services in Masaka region. Masaka region comprised of the 12 districts Bukomansimbi, Butambala, Gomba, Kalangala, Kalungu, Kyotera, Lwengo, Lyantonde, Masaka, Mpigi, Rakai, Sembabule and the city of Masaka. In addition to supporting HIV services, RHSP was also funded to evaluate the impact of Combination HIV Prevention Interventions (the Combination HIV Prevention Impact Evaluation Protocol (CHPIE) and evaluate the HIV program in Masaka region (Masaka program evaluation protocol). The CHPIE protocol was implemented through the Rakai Community Cohort Surveillance (RCCS), and the Masaka program evaluation protocol through the program data in the health facilities and catchment communities in the Masaka region.

The program provided a wide range of HIV prevention, care and treatment services using a health systems strengthening approach. HIV prevention strategies included HIV testing services, promoting case finding among men, women and children with a special focus on key populations, elimination of mother-to-child transmission, pre-exposure prophylaxis, voluntary medical male circumcision and the ‘Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe (DREAMS) program for adolescent and young women, HIV care and treatment services included; TB prevention, diagnosis and treatment; management of advanced HIV disease, integration of non-communicable disease screening (e.g. cervical cancer screening) ; laboratory testing and provision of antiretroviral therapy. The program also supported and strategic information to support enhanced surveillance to understand HIV transmission dynamics, assess access to services, quality and coverage of HIV services. The expected program outcomes included improved access, quality and coverage of HIV services ensuring 95% of people living with HIV know their status; 95% of people diagnosed receive antiretroviral therapy; and 95% of those on treatment are virally suppressed.

Preliminary findings from this study were previously presented as a conference abstract at the 2024 Conference on Retroviruses and Opportunistic Infections (CROI) in Denver, Colorado, USA [14].

Study participants:

Data for this study was drawn from medical records of participants seeking HIV prevention, care and treatment services under the Masaka region PEPFAR program. Data on AHD was collected using routine Ministry of Health HIV care forms.

We set out to determine the magnitude and correlates of advanced HIV disease to inform HIV programming. We extracted data from 192 PEPFAR -Supported health facilities within Masaka region. We focused on HIV positive clients aged at least five years and above, newly enrolling in care during the Country Operational Plan 2021(COP21), (October 2021-Sep 2022)

Sample size

We calculated the required sample size using the **Kish Leslie formula**:

$$N = \frac{Z_{\alpha/2}^2 \cdot P(1 - P)}{d^2}$$

Assuming a 95% confidence level ($Z = 1.96$), an estimated prevalence of 20% ($P = 0.20$), and a margin of error of 4% ($d = 0.04$), the minimum sample size was determined to be 492 participants. To account for potential non-response, we applied a 10% adjustment, yielding a final target of 547 participants. However, in practice, we included all available records in the study, thereby maximizing data utilization and representativeness.

Variables

The main outcome was Advanced HIV Disease (AHD) and WHO defines AHD among persons as over the age of five years, as a CD4 count < 200 cells/mm³ or with a WHO stage 3 or 4 event. Children younger than five years of age with HIV regardless of CD4 cell count are considered as having advanced HIV disease due to high viremia and rapid disease progression with high mortality. However, children younger than 5 years who have been on ART for more than one year, are virally suppressed and clinically stable, are not considered to have AHD.

The dependent variable was binary; with patients classified as having WHO stage 3 or 4 or found to have a CD4 cell count < 200 cells/ μ l at enrolment in care being considered as having AHD. The independent variables included sex, age, marital status, location of facilities, and points of entry into care.

Data Analysis.

We did descriptive statistics by summarizing data and tabulation of frequencies and proportions using Stata Version 15.0. Chi-square test was conducted to establish relationship between each categorical variable and the main outcome. We conducted bivariate analysis between each independent factor against Advanced HIV disease status to assess relationships. Independent variables that were associated with Advanced HIV disease and having a p-value < 0.2 were included in the multivariable model. We further conducted Multivariate analysis to estimate prevalence ratios (PR) and 95% confidence intervals for the association between correlates and Advanced HIV disease.

Results

Of 3,452 newly diagnosed PLHIV on ART included in this study, 2,254 (65.3%) were females and with 2269(65.7%) being married. The proportion of AHD was highest among young people aged 5–17 years representing 25.6%, higher than older persons aged 45 years and above (22.6%), $p < 0.001$. Males had

the highest burden of AHD (65.3%) versus 34.7%, $p < 0.01$ for females. We observed a high proportion of AHD among unmarried clients (19.5%) compared to the married (12.6%). This is presented in Table 1.

Table 1
Socio-demographic characteristics of participants

Socio-demographic characteristics	All (n = 3,442)	No(n = 2,929)	Yes(n = 513)	P-value*
	n()	n(%)	n(%)	
Age (Years)				
13–17	29(0.8)	24(82.8)	5(17.2)	< 0.001
18–35	2,146(62.3)	1,906(88.8)	240(11.2)	
36–45	842(24.5)	670(79.6)	172(20.4)	
> 45	425(12.5)	329(77.4)	96(22.6)	
Sex				
Female	2248(65.3)	2002(89.1)	246(10.9)	< 0.001
Male	1194(34.7)	927(77.6)	267(22.4)	
Marital status				
Unmarried	1174(34.1)	948(80.5)	226(19.5)	< 0.001
Married	2268(65.9)	1981(87.4)	287(12.6)	
Location of health facilities				
Rural	1328(38.6)	1183(89.1)	145(10.9)	< 0.001
Urban	1658(48.2)	1352(81.5)	306(18.5)	
Fishing	456(13.2)	394(86.4)	62(13.6)	
Entry point of care				
Outpatient	1638(47.6)	1364(83.3)	274(16.7)	< 0.001
Outreach	975(28.3)	870(89.2)	105(10.8)	
Other care points	829(24.1)	695(83.8)	134(16.2)	

Table 2

Prevalence of Advanced HIV disease Overall, the prevalence of AHD was 15% (518/3452) when CD4 count < 200cells/ μ L criteria were used, and only 3.4% when only WHO staging criteria was used. (Table 2). The proportion of AHD for clients who had both CD4 less than 200 and WHO clinical stage 3/4 was low (1.6%).

Advanced HIV disease (WHO stage 3 or 4 and or CD4 level at ART initiation < 200c/u	Freq (%)
Yes	513(14.9)
No	2929(85.1)
Advanced HIV disease disaggregation	
Both CD4 < 200 & WHO stage is 3/4	53(1.6)
WHO stage is 3/4 but CD4 $\geq$ 200	115(3.3)
CD4 < 200 but WHO stage 1/2	345(10.0)
No advanced disease	2,929(85.1)

The bivariate analysis results revealed that, age, sex, marital status, location of the health facility, and entry point into care were all associated with Advanced HIV disease for example, participants aged 18–35 years were less likely to have AHD compared to those aged 5–17 years; (cPR = 0.44 [95% CI: 0.25, 0.75], $p = 0.003$). Married participants were less likely to have AHD compared to the unmarried (cPR = 0.65; [95% CI: 0.55, 0.76], $p < 0.0001$). Additionally, participants who were enrolled into care through community outreaches were less likely to have AHD compared to those enrolled through other care points (cPR = 0.65; [95% CI: (0.52, 0.80), $p < 0.001$). The prevalence of AHD was higher among males (cPR = 2.03; [95% CI: (1.74, 2.38)], $p < 0.001$, and among clients enrolled through urban facilities (cPR = 1.66; [95% CI: (1.38, 1.99), $p < 0.001$).

In a multivariable model, participants aged 18–35 years were more likely to have advanced HIV disease compared to those aged 5–17 years (aPR = 0.45, [95% CI: (0.27, 0.78], $p = 0.004$). Married participants (aPR = 0.67, [95% CI: (0.57, 0.79)], $p < 0.001$) and participants enrolled into care through HTS outreaches (aPR = 0.72, [95% CI: (0.58, 0.90)], $p = 0.003$) were less likely to have AHD. Male PLHIV had 85% higher risk of AHD than females (aPR = 1.85, [95% CI: (1.57, 2.19)], $p < 0.001$). Furthermore, PLHIV enrolled into care through urban health facilities were 61% more likely to have AHD compared to those in rural facilities. Finally, PLHIV identified from unspecified sources like bars and hotspots had 28% higher risk of AHD versus those identified from facilities (outpatient) (aPR = 1.28, [95% CI: (1.06, 1.53)], $p = 0.009$). This is presented in Table 3.

Table 3
shows unadjusted and adjusted results of advanced HIV disease

Variable	PR	95% CI	P-value*	aPR	95% CI	P-value*
Age (Years)						
5–17	Ref	95% CI				
18–35	0.44	0.44(0.25, 0.75)	0.003	0.45	0.45(0.27, 0.78)	0.004
36–45	0.8	0.80(0.46, 1.38)	0.419	0.73	0.73(0.42, 1.25)	0.25
> 45	0.88	0.88(0.50, 1.55)	0.659	0.75	0.75(.43, 1.30)	0.311
Sex						
Female	Ref					
Male	2.03	2.03(1.74, 2.38)	< 0.001	1.85	1.85(1.57, 2.19)	< 0.001
Marital status						
Unmarried						
Married	0.65	0.65(0.55, 0.76)	< 0.001	0.67	0.67(0.57, 0.79)	< 0.001
Location of health facilities						
Rural	Ref					
Urban	1.66	1.66(1.38, 1.99)	< 0.001	1.61	1.61(1.35, 1.93)	< 0.001
Fishing	1.22	1.22(0.92, 1.60)	0.165	1.31	1.31(0.99, 1.73)	0.057
Entry point of care						
Outpatient	Ref					
Outreach	0.65	0.65(0.52, 0.80)	< 0.001	0.72	0.72(0.58, 0.90)	0.003
Other care points	0.98	0.98(0.81, 1.18)	0.825	1.28	1.28(1.06, 1.53)	0.009

Discussion

Our study analyzed data for 3,452 newly diagnosed PLHIV, 65.3% of which were females. There was a relatively high prevalence of AHD (15%). Factors associated with high AHD were being male, receiving care from urban facilities, and enrolling on ART from other care points. Conversely, older age, being married and ART enrollment from outreach services were associated with low AHD.

The overall prevalence of AHD in our study was 15%. This prevalence was lower than other similar settings such as Ethiopia (20%-60%) [15], [16], Kenya (33%, reported between 2013–2015 [17], and Kenya, Tanzania, Mozambique and Rwanda at 29% [18]. The higher prevalence of AHD in these studies conducted earlier, relative to our study could be attributed to the likelihood that the current efforts, including HIV test and treat strategy, have enabled a significant proportion of PLHIV to start ART early, likely before severe immunological decline. The focused HIV care and treatment efforts, including adherence counseling, could have improved adherence to ART and hence lowered AHD. Conversely, AHD prevalence was higher than that reported in a study that analyzed secondary data for PLHIV in South Africa, Kenya, and Malawi, reported at 11% [19].

In our study, AHD was more prevalent among males, and findings are consistent with findings from [19], [20], [21], [22]. This could be attributed to lower healthcare seeking behaviors among males [23]. Participants receiving care in urban facilities had higher prevalence of AHD as compared to those in rural facilities and this is consistent with findings from [24], [25]. The prevalence of AHD was lower among those aged 18–35 years, compared to those aged 5–17 years, and these findings are consistent with findings from [19], [20], [21], [22], [26]. This could be explained by children's delayed diagnosis, weaker immunity, limited pediatric ART access, and a heavier burden of co-infections, highlighting a need for early infant diagnosis, improved pediatric ART coverage, and integrated care for co-infections to reduce advanced HIV disease among children. Other factors such as marital status and model of entry into care were associated with AHD in our study and have been reported to be associated with AHD in other studies [24], [25].

The major strength of our study is that it analyzed data from several health facilities across a wide geographical area of the greater Masaka region, making our findings generalizable across PLHIV in Central Uganda. The major limitation of this study is that some important variables (ART adherence, treatment interruptions, socioeconomic status, nutritional status, and psychosocial factors such as mental health and social support) that were not captured in the Electronic Medical Record were not adjusted for multivariable analysis.

Conclusions

Despite the full roll-out of the Test at Start policy, AHD was high in this cohort (15%) but lower than the national prevalence of 22%. These findings highlight the risk factors for AHD, and can be used in designing interventions to identify ART naïve PLHIV that are hard-to-reach for ART treatment

Declarations

Ethics approval and consent to participate

This study was conducted under the *Baseline, Midterm and End of Project Evaluation Protocol for CDC PEPFAR-supported Regional Implementing Mechanisms*, through which the Rakai Health Sciences Program (RHSP) evaluated HIV program implementation in the Masaka Region. The evaluation protocol was reviewed and approved by the Uganda Virus Research Institute Research Ethics Committee (UVRI REC; Ref. GC/127/654) and registered with the Uganda National Council for Science and Technology (UNCST; Ref. SS334ES), with additional ethical oversight from Western Institutional Review Board (Western IRB), USA. The present study involved secondary analysis of routinely collected, de-identified HIV program data and involved no direct interaction with participants. Under the approved evaluation protocol, individual informed consent was not required for this secondary analysis. Participant confidentiality was protected using computer-generated unique alphanumeric identifiers.

Consent for publication

Not applicable

Competing interests

[Mandatory]

Funding:

This project has been supported by the President's Emergency Plan for AIDS Relief (PEPFAR) through the Centers for Disease Control and Prevention under the terms of [NU2GGH002009]

Author Contribution

AD contributed to conception of this research idea including supporting all stages of this research. AK, ENK, JK, FN, GNK, RS, AS, GK contributed to study design, conceptualization, data analysis, and interpretation of findings. All authors reviewed and approved the final article.

Acknowledgements

[Mandatory]

We thank Rakai Health Sciences Program (RHSP) for implementation of HIV comprehensive services and data collection.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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