ORIGINAL PAPER

Late presentation: a stumbling block to HIV viral suppression in a low income country

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Abstract

Introduction: Tenofovir-based regimens have been recently introduced as first-line antiretroviral treatment (ART) to human immunodeficiency virus (HIV) patients in Tanzania. Limited information on HIV viral suppression and its' associated factors exists in Tanzania since the adoption of this intervention at a public health level. The aim of the present study was to determine HIV viral suppression rate and assess its' associated factors among patients attending Temeke Regional Referral Hospital care and treatment clinic after twelve months of using antiretroviral therapy.

Material and methods: Hospital-based cross-sectional study was performed to assess factors associated with HIV viral suppression. Viral load suppression was defined as HIV-RNA below 50 copies/ml, and late presentation was defined in a person who presented to care and treatment facility with WHO HIV clinical stage III or IV and/or baseline CD4+ T lymphocyte count of less than 350 cells/µl.

Results: Among the 188 participants who were interviewed, a total of 149 (79.3%) achieved viral suppression after one year of using ART. Late presentation to health facility (OR = 3.4; 95% CI: 1.6-7.4; $p < 0.01$) was independently associated with inability to achieve viral suppression at 12 months.

Conclusions: HIV testing services should be strengthened in order to achieve the UNAIDS 90-90-90 target through early detection of HIV disease.

HIV AIDS Rev 2022; 21, 2: 115-120
DOI: https://doi.org/10.5114/hivar.2022.115837

Key words: HIV, viral suppression, late presentation.

Introduction

Globally, human immunodeficiency virus (HIV) poses a serious public health threat with 37.9 million people being infected, accounting for a global prevalence of 0.8% in 2018. In the same year, 1.7 million of new HIV infections were reported, and an estimated 770,000 people died globally due to HIV-related illnesses, despite efforts undertaken by several stakeholders in tackling the disease. Despite the increase in universal antiretroviral treatment (ART) coverage, the number of individuals receiving ART globally is still low, with 62% of HIV-infected adults receiving ART globally [1].

Tanzania is among the most affected countries by HIV disease. Reports from the Joint United Nations Program on HIV and AIDS in 2016 estimated that 1.6 million people in Tanzania are living with HIV, while 72% of adults are on ART [2]. Although the incidence of HIV has been decreasing in the past 10 years, the number of people living with HIV is on the rise, despite scaling-up of ART services and HIV-related prevention programs [2].

Good viral suppression is one of the important factors to the success of fighting HIV pandemic, as it has been shown in several studies that patients with undetectable HIV viral load do not transmit the disease [3].

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Article history:
Received: 26.10.2020
Received in revised form: 02.10.2021
Accepted: 03.10.2021
Available online: 26.04.2022

Several factors have been associated with poor viral suppression, including complex treatment regimes, adverse effects, being away from home, social stigma, late presentation to health facilities, and lack of disclosure of HIV status [4, 5]. Adherence to clinic visits and medications after starting ART is another challenge in HIV care as well as treatment programs in low- and middle-income countries including Tanzania, where an estimated 16-19% of people living with HIV are not adhering to ART [4, 6, 7]. Change to single-tablet ART regimens has been adopted in Tanzania, and is expected to improve adherence to ART and improve viral suppression, as it has been reported in Asia [8]. However, studies assessing the level of HIV viral suppression and its' factors associated since initiation of a single-tablet regimen in our setup are insufficient. Therefore, this study was conducted to assess the magnitude of HIV viral suppression and determine its' associated factors since the introduction of a user-friendly single-tablet regimen.

Material and methods

Study design

A hospital-based cross-sectional study was conducted to assess the level of HIV suppression and determine its' associated factors among participants aged 18 years and above, who were attending HIV CTC and started ART between May and November 2016.

Table 1. Baseline social demographic, clinical and laboratory characteristics of study participants (*N* = 188)

Characteristics	Missing (%)	*n* (%)
Age groups (years)	0 (0.0)	
18-29		28 (14.9)
30-39		75 (39.9)
40-49		54 (28.7)
≥ 50		31 (16.5)
Sex	0 (0.0)	
Male		64 (34)
Female		124 (66)
Education level	32 (17.0)	
Primary and below		127 (81.4)
Above primary		29 (18.6)
Marital status	15 (8.0)	
Single		53 (30.6)
Married/co-habiting		73 (42.2)
Divorced/widowed		47 (27.2)
BMI (kg/m^2), median (IQR)	68 (36.2)	21.8 (18.9-25.0)
ART type	12 (6.4)	
Single-tablet regimen		175 (99.4)
Others		1 (0.6)
Initial presentation at CTC	3 (1.6)	
Early		65 (35.1)
Late		120 (64.9)

Study setting

This study was conducted at Temeke Regional Referral Hospital HIV CTC, a public Hospital located in Dar es Salaam, Tanzania, where patients are seen by clinicians and nurses during their visits.

Study protocol

A list of HIV patients who were still attending Temeke CTC 12 months after starting ART was extracted from an electronic HIV database. Patients were interviewed to gather information that is not routinely collected attended during their regular clinic visits. These included 30 days of ART adherence recall, occurrence of opportunistic infections, hospital admissions in the past year, and risky behaviors for the acquisition of new HIV strains, alcohol intake, illicit substance use, number of sexual partners, participation in different sexual practices, and status of disclosure of HIV status to family or others. A purpose-designed data collection sheet was used to collect participants' information, such as demographics, anthropometric, clinical, and laboratory variables, and type of ART from hospital patient files. Virological tests conducted between 9th and 15th month of using ART were taken as the viral load at 12 months due to clinic attendance intervals of participants.

Good adherence referred to self-reported compliance with more than 95% of the prescribed doses in previous 30 days, or attending more than 95% of clinic appointments.

Late presentation was defined as having HIV disease WHO clinical stage III or IV and/or baseline CD4+ T cell count less than 350 cells/μl at the time of ART initiation.

Data analysis

Completed data collection sheets were coded and entered into a computer using Epi-info software version 7. Data analysis was conducted using a statistical package for social sciences (SPSS) version 23. Categorical variables were summarized using proportions and compared with outcome variable (viral suppression) using χ^2 test.

Continuous variables were expressed as means, standard deviation (SD) or median interquartile range (IQR), and compared to categorical variables using Student's *t*-test. Multivariate logistic regression analysis was used to examine factors associated with HIV viral suppression. Where more than 2.5% of the data were missing for any independent variable, a separate category for the missing values was created.

Factors with $p \leq 0.2$ at univariate model were included in multivariate model. Any association with a *p*-value of less than 0.05 was regarded as statistically significant.

Ethics statement

This study was reviewed and received ethics approval by the Muhimbili University of Health and Allied Sciences institutional review board with an approval number: MU/PGS/SAEC/Vol. IX. Permission to conduct the study was obtained from Temeke Municipal council and Temeke Regional Referral Hospital administration.

Results

A total of 188 participants were interviewed in this study, out of which more than half were below 40 years of age, and 66% were females, while 81% had primary education or below, as shown in Table 1. Approximately, three-quarters of participants had achieved HIV viral suppression after using ART for 12 months. The median baseline CD4+ count was 201 cells/µl with interquartile range of 81-400 cells/µl. Nearly two-thirds of participants (64.9%) presented at either WHO HIV clinical stage III or IV, or baseline CD4+ count of less than 350 cells/µl (late presenters).

The proportion of patients with viral suppression was found to be the highest among people who started ART at WHO clinical HIV stage I (88.4%), and lowest in WHO clinical HIV stage IV (57.1%), p-value < 0.001, as shown in Table 2.

In addition, a higher proportion of females had viral suppression as compared to males (79.0% vs. 70.3%; $p = 0.21$). The gender disparity was much more noticeable among patients aged 40-50 years, where 93.3% of females were virally suppressed as compared to only 62.5% of males, as shown in Figure 1.

Early presenters to CTC had nearly four times higher likelihood of attaining HIV viral suppression rates at 12 months, as compared to late presenters independent of other variables (OR = 3.8; 95% CI: 1.6-9.2%, $p < 0.001$) (Table 3). Females presented early to CTC as compared to males (79.4% vs. 57.4%),

Table 2. Comparison of participants with and without HIV viral suppression (*N* = 188)

Characteristics	Missing (%)	Proportion/mean with suppressed HIV viral load (%) *n* = 143	Proportion/mean with unsuppressed HIV viral load (%) *n* = 45	*p*-value
Age, mean (years)	0 (0.0)	39.2	41.9	0.14
Age group (years)				
18-29	0 (0.0)	25 (89.3)	3 (10.7)	0.14
30-39		58 (77.3)	17 (22.7)	
40-49		36 (66.7)	18 (33.3)	
50+		24 (77.4)	7 (22.6)	
Gender				
Male	0 (0.0)	45 (70.3)	19 (29.7)	0.21
Female		98 (79.0)	26 (21.0)	
WHO HIV clinical stage				
I	3 (1.6)	38 (88.4)	5 (11.6)	0.01
II		36 (85.7)	6 (14.3)	
III		58 (67.4)	28 (32.6)	
IV		8 (57.1)	6 (42.9)	
Mean baseline CD4+ (cells/µl)				
< 200	118 (62.8)	21 (60.0)	14 (40.0)	0.10
200-350		13 (81.3)	3 (18.8)	
> 350		16 (84.2)	3 (15.8)	
ART type				
Single-tablet	5 (6.4)	129 (75.4)	42 (24.6)	
Other regimes		5 (100.0)	0 (0.0)	
BMI	68 (36.2)	22.9	21.9	0.45
Prior history of PTB				
PTB history		12 (66.7)	6 (33.3)	
No PTB history		131 (77.1)	39 (22.9)	

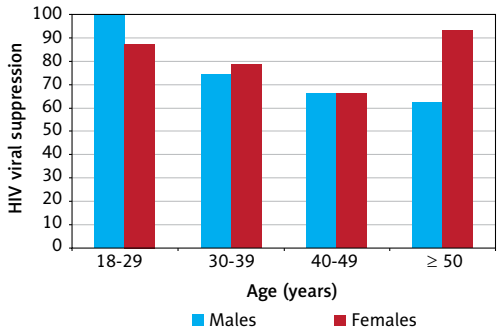

Figure 1. Proportion of HIV patients with viral suppression by age and sex

and older patients (> 60 years) were more likely to present at a late stage (88.9% vs. 63.6%) as compared to young patients, though the association was not statistically significant. In addition, there was no statistical difference in the level of drug adherence between the early and late presenters (80.8% vs. 83.2%, $p = 0.82$). Furthermore, patients who achieved HIV viral suppression after twelve months of ART using had a higher mean BMI as compared to those without viral suppression (22.9 kg/m^2 vs. 21.9 kg/m^2, $p = 0.45$). The level of suppression was also higher among patients who did not use alcohol, although the association was not statistically significant (OR = 2.0, $p = 0.15$). The proportion of viral suppression was

Table 3. Univariate and multivariate analysis of factors associated with HIV viral suppression (*N* = 188)

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Gender				
Male	Ref.	0.21	Ref.	0.65
Female	1.6 (0.8-3.2)		1.2 (0.6-2.5)	
Age group				
18-29	2.4 (0.6-10.5)	0.17	2.0 (0.4-9.3)	0.15
30-39	1.0 (0.4-2.7)		1.0 (0.4-2.9)	
40-49	0.6 (0.2-1.6)		0.5 (0.2-1.5)	
≥ 50	Ref.		Ref.	
Income, Tanzanian shillings				
< 250,000	Ref.	0.28		
≥ 250,000	0.5 (0.2-1.2)			
Missing	0.6 (0.2-1.5)			
Current alcohol use				
Yes	Ref.	0.14	Ref.	0.26
No	2.0 (0.8-4.9)		1.7 (0.7-4.5)	
Adherence to ART				
Good	1.5 (0.5-4.3)	0.61		
Poor	Ref.			
Initial presentation at CTC				
Early	3.8 (1.6-9.2)	0.00	3.8 (1.5-9.4)	0.00
Late	Ref.		Ref.	
Marital status				
Cohabiting/ married	1.1 (0.5-2.3)	0.85		
Single/ divorced/ widowed	Ref.			
Mean BMI (kg/m^2)	1.03 (1.0-1.1)	0.44		
ART type				
Single-tablet regimen	0.0 (0.0)	1.0		
Other	Ref.			
Occupation				
Employed	Ref.	0.60		
Not employed	1.6 (0.5-5.0)			
Level of education				
Primary and below	1.3 (0.5-3.4)	0.52		
Above primary	Ref.			

found to be higher among married patients as compared to single, divorced, and widowed individuals; however, there was no statistically significant association between HIV viral suppression and marital status. Late presentation was significantly associated with the inability to achieve HIV viral suppression after one year of ART use, independently of age, gender, BMI, adherence to medication, and alcohol intake (OR = 3.8; 95% CI: 1.5-9.4%, $p < 0.01$), as shown in Table 3.

Discussion

Approximately, three-quarters of HIV patients (75.9%) in this study achieved viral suppression after using ART for 12 months. The level of HIV viral suppression in our study is low compared to previous studies conducted in the Northwest, rural, and urban Tanzania, which reported HIV viral suppression ranging from 84% to 91% [9-11]. The differences observed may be attributed to different cut-off values used to define viral suppression. In our study, viral suppression was defined as having a viral load of less than 50 copies/ml, in line with the Tanzania HIV management guideline, while in the above-mentioned studies, viral load cut-offs of 400-1,000 HIV RNA copies/ml were used. Indeed, the level of suppression in our study increased to 89.9% if the cut-off was changed to 400 cells/μl.

In our study, a large proportion (64.9%) of patients presented late to health facility for ART initiation. This is higher than what was reported in other sites from sub-Saharan Africa, showing 15-43% of HIV patients as late presenters [12, 13]. This may be attributed to delayed HIV diagnosis or poor linkage to care and treatment facilities after HIV diagnosis [2]. Late presentation has been previously shown to affect morbidity and mortality of HIV patients in Uganda [14]. Further studies are needed to determine reasons behind late presentation in a routine clinical setup.

Among late presenters, the majority were males and aged more than 60 years, similar to what has been reported in other studies [12-14]; this may be caused by a fewer testing opportunities and reluctance of males in seeking health services [15]. Older HIV patients have been noted to have less HIV risk perception as compared to young patients, which may result in late presentation to HIV testing services [12, 13].

The use of alcohol was shown to be associated with poor viral suppression [16]. In our study patients who did not use alcohol had two times higher likelihood of attaining viral suppression, as compared to alcohol users ($p = 0.26$). This finding may be mediated by the negative cognitive and behavioral effects of alcohol consumption on HIV treatment therapy, related to poor adherence.

Higher BMI was also associated with a higher level of suppression in our study; this may be explained by the fact that in African setup, higher BMI is related to higher socio-economic status, hence better access to medical facilities [17].

The level of adherence in our study was higher when assessed in participants' medication-taking recall as compared to patients' CTC attendances (81.4% vs. 68.8%). This is similar to what has been reported in a study conducted in urban and rural Tanzania by Sangeda *et al.* [6, 18], and may be due to the fear of negative reaction when a patient reports non-adherence to ART medication.

This study was conducted in a routine CTC environment and therefore represents the situation of a clinical environment, which is scarcely reported in our setup. It was also conducted among patients who had used ART for 12 months, which is the recommended time by the WHO to assess patient-related factors in HIV care and treatment [19]. Limitations of the study were mainly related to its' cross-sectional nature, which resulted in the exclusion of patients who were not available during the time of data collection and those who had no viral load data.

Conclusions

This study finds a huge proportion of HIV patients presenting late to treatment facilities for ART initiation. Late presentation to care and treatment facility significantly affects the level of suppression attained after 12 months of ART use. HIV testing services should be strengthened to enable earlier initiation of ART to patients, and therefore attain the UNAIDS 90-90-90 targets.

Acknowledgment

The authors would like to thank all individuals who made this study possible.

Conflict of interest

The authors declare no conflict of interest.

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