ORIGINAL PAPER

Viral load suppression among patients receiving antiretroviral therapy in outpatient clinics in Democratic Republic of Congo

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Abstract

Introduction: Education and disease management have resulted in global decline of new HIV infections, from 2.8 million a year in 2000 to about 1.5 million in 2020 (46% reduction) as well as number of deaths, from 1.4 million in 2000 to 690,000 a year in 2020 (51% reduction). The purpose of this study was to examine factors associated with viral load (VL) suppression (< 1,000 copies/ml), including age, sex, and geographic and clinical characteristics of patients on antiretroviral therapy (ART) in outpatient clinics in Kinshasa and Haut-Katanga Provinces, Democratic Republic of Congo (DRC).

Material and methods: Using a retrospective cohort study design, we analyzed data of 5,338 people living with HIV (PLHIV) on ART from 116 HIV/AIDS clinics located in the Haut-Katanga and Kinshasa Provinces in DRC. χ^2 and multivariable logistic regression analyses were applied.

Results: Age and urban health zones were significantly associated with VL suppression. Eighty-six percent of adult patients (15 years or older) had achieved a VL suppression, compared to 73.5% of patients younger than 15 years. Average time on ART was less than three years, and majority of participants were 15 years of age or older, females, and mostly living in urban areas.

Conclusions: Our findings indicated that younger patients on ART and patients living in semi-rural areas (vs. urban) had a significantly lower probability of risk of VL suppression, underscoring the need for enhanced efforts targeting these populations.

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Key words: HIV, antiretroviral therapy, Democratic Republic of Congo, viral load suppression, Kinshasa.

Introduction

Medical breakthroughs in antiretroviral treatment (ART) had a tremendous impact on reducing the morbidity and mortality of human immunodeficiency virus (HIV) epidemic around the globe [1, 2]. Education and disease management have resulted in a global decline of new HIV infections, from 2.8 million a year in 2000 to about 1.5 million in 2020 (46% reduction) as well as number of deaths, from 1.4 million in 2000 to 690,000 a year in 2020 (51% reduction) [3]. Conse-

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quently, the prevalence of HIV had also increased, meaning that more people are living with a manageable HIV diagnosis. Despite the advances and effectiveness of new treatments and intervention efforts, HIV continues to present a significant public health challenge worldwide, specifically in sub-Saharan Africa, where approximately two-thirds of all new HIV cases were reported in 2020 [3]. Democratic Republic of Congo (DRC) had witnessed a dramatic decrease in all-age new infections, with an estimated 15,000 fewer new infections over ten years, from 2008 to 2018 [4]. Additionally, targeted efforts, such as the 'catch-up plan', aiming at guaranteed access to HIV treatment, allowed 2 million more people to know their HIV status, and in 2017 additional 34,000 people were reported to be on treatment since 2015 [5].

Ensuring that people living with HIV (PLHIV) have ART initiated early after a positive diagnosis provided desirable health outcomes [6]. Although various ART distribution models assist in the expansion of treatment access globally, the DRC follows WHO 2016 recommendations that ART treatment should be initiated in all HIV patients, regardless of their CD4+ counts or clinical stage [7]. WHO additionally recommends monitoring of viral load (VL) of patients on ART as a measure of treatment response and transmission risk, with an emphasis on VL suppression at a level of < 1,000 copies/milliliter (ml) [7]. High viral loads, > 1,000 copies/ml, are positively associated with increased disease progression and an increased risk of transmission to others [7]. Additionally, suppressing VL to less than 200 copies/ml, or in particularly lower to an undetectable level (generally less than 50 copies/ml) was proposed as an effective way to prevent transmission, as prevention treatment (TasP) [7], or U = U indicating undetectable viral load leading to un-transmissible HIV infection.

Double benefits of using ART as a treatment for HIV-1, the most widespread type globally, and also as a prevention method to avert the risk of HIV transmission, has been discussed as an ideal way to move forward in the fight to control HIV epidemic [8]. Thus, for this method to be used as a TasP approach, getting individuals to initiate and adhere to treatment is imperative. In sub-Saharan African countries, TasP efforts grapple with the need to increase HIV-testing, ART uptake, retention in care, and medication adherence, which are issues that require more research [9]. Specifically in DRC, barriers to prevention as treatment include lost to follow-up care and medication adherence [10]. Moreover, barriers to medication availability and adherence in African countries have also been linked to structural barriers, such as food insecurity, transportation, health system structure, political challenges, stigmas, family responsibilities, and lack of support services [11-13].

Among children and youths (14 years of age or younger), adherence is a challenging issue; however, disclosure of HIV-positive status to a child/adolescent was widely reported to be a significant factor in increasing ART adherence [14, 15]. Although, among parents and other caregivers, disclosing to a child/adolescent was associated with negative psychological and social factors that affect children and their families, such as emotional trauma, stigma, and discrimination [15, 16]. For example, a study in Kinshasa evaluated patterns of disclosure among caregivers of HIV-positive children (ages, 5-17), and found that caregivers believed that disclosing would make the child feel sad or impact their will to live [17]. However, caregivers agree that disclosure increases children's ability to take better care of themselves, which could include better ART management [17].

Issues surrounding disclosure are considered as a barrier to ART adherence, other factors include lack of food or nutritional support [18, 19], caregiver knowledge about ART, forgetting to take medications, treatment fatigue, lack of support from caregivers, and travel distance to healthcare facilities [20-23]. Lastly, lack of access to transportation and accessibility of the care facilities were also related to adherence [20-24]. However, a review of the literature found conflicting results about geographical location of residence, with different studies reporting a significant association between both rural and urban settings with poor adherence among children and youth. Hence, further investigation of factors that promote or hinder VL suppression is warranted in limited-resource settings, such as in sub-Saharan countries. The purpose of this study was to examine the factors associated with variation in viral load suppression levels (< 1,000 copies/ml), including patient age, sex, and geographic and clinical characteristics of patients on ART in outpatient clinics in Kinshasa and Haut-Katanga Provinces of the DRC.

Material and methods

Data

This study used data from 116 HIV/AIDS clinics in Kinshasa and Haut-Katanga, two of the 26 provinces in DRC. These clinics are government-owned facilities managed by the National HIV/AIDS Program (PNLS), with the support of the President's Emergency Plan for AIDS Relief (PEPFAR) through implementing partners that include local and international organizations that receive PEPFAR funds through U.S. government agencies to implement HIV activities. The clinics provide HIV counseling and testing as well as service delivery data using an electronic patient management system (EMS) called 'TIER.Net', developed by the University of Cape Town, and adopted by DRC National Aids Program. TIER.Net was in use in the clinics included in the study, all patients in this study who initiated ART were those whose initiation date was from January, 2014 to December, 2018. Initially, data file included a total of 22,974 patients. Of these, the last reported viral load was documented for 5,338 patients, which comprised the analyzable dataset.

Measures

Dependent variable: viral load

The viral load suppression status was computed based on patients' viral load values. If more than one value existed, viral load was assessed to be suppressed in < 1,000 copies/ml,

if one or more of viral load values were below this threshold. The variable was divided into not suppressed (1,000+ copies/ml) and suppressed (< 1,000 copies/ml). This threshold was selected following WHO's proposed viral load criterion of 1,000 copies/ml or more for treatment failure among patients on ART [25].

Independent variables

The independent variable 'age of patient' (at the time of viral load test), originally captured as a continuous variable, was divided into younger than 15 years, and 15 years or older, because the two groups present distinct challenges. Age of patient was computed based on two variables, including viral load test date and patient's date of birth. Sex of patient was a dichotomous variable, recorded as 'Male' and 'Female'. The contextual and clinical variables included province and rurality status of health zone. Province of a clinic's location, included Haut-Katanga and Kinshasa. The rurality /urbanicity variable had three attributes, such as rural, semi-rural, and urban based on health zones, in which clinics were located. Rural health zones included Kafubu, Kasenga, Kilwa, and Pweto; semi-rural zones were Kambove, Kipushi, and Nsele; and urban zones included Katuba, Kikula, Kimbanseke, Kingabwa, Kisanga, Kowe, Likasi, Masina 1, Mumbunda, Ngaba, and Tshiamilemba. Number of years on ART at the time of first reported viral load in data was computed based on the original variable included in dataset of 'months on ART', by dividing this original variable by 12. Transformation was made to obtain a change in odds ratios by increment of a year in independent variable, rather than increment of a month.

Table 1. Descriptive demographic and clinical characteristics of patients receiving antiretroviral therapy (N = 5,338)

Demographic and clinical characteristics	*n*	%
VL suppression status		
Not suppressed (> 1,000 copies/ml)	804	15.1
Suppressed (< 1,000 copies/ml)	4,534	84.9
Age (at the time of VL test)		
Younger than 15 years	446	8.4
15 years or older	4,892	91.6
Sex		
Male	1,590	29.8
Female	3,748	70.2
Province		
Haut-Katanga	3,487	65.3
Kinshasa	1,851	34.7
Rurality/urbanicity of the health zone		
Rural	326	6.1
Semi-rural	952	17.8
Urban	4,060	76.1
	n	Mean (SD)
Number of years on ART	5,338	2.8 (5.7)

VL – viral load, ART – antiretroviral treatment

Analytical methods

For contextual information about clinical characteristics and demographics of study participants, descriptive statistics, such as frequency distribution, percentages, and arithmetic means, were computed for all independent and dependent variables. Bivariate associations between categorical independent variables and dichotomous dependent variable were assessed using χ^2 test. Un-adjusted odds ratio was computed for assessing the association between dependent variable and continuous independent variable duration on ART. Multivariable logistic regression model was computed to estimate the association between dichotomous dependent variable viral load suppression status and each of independent variables, while controlling for other variables in the model. A $p \leq 0.05$ was used to assess statistical significance of differences for odds ratios. SPSS version 25 (SPSS Inc., Chicago, Illinois, USA) was applied for calculating descriptive statistics, bivariate associations, and multivariable logistic regression (details omitted for double-anonymized peer review). Institutional review board approved the study with a project protocol number of H l9260.

Results

Among the included HIV patients on ART, those with virologic failure (i.e., VL of 1,000 or more copies/ml) constituted 15.1% of the patients on ART in the participating PNLS clinics (Table 1). On average, these individuals had been on ART for 2 years and 8 months at the time of first VL documented in the database. At the time of VL test, 8.4% were younger than 15 years. A majority (70.2%) were females, and 65.3% were from the Haut-Katanga Province. Based on their health zone, rural patients constituted 6.1% of the patients, semi-rural represented 7.8%, and urban patients constituted 76.1%.

The results of the bivariate association of age and other independent variables with the dependent variable VL suppression (< 1,000 copies/ml) are presented in Table 2. The variable age (< 15 years vs. > 15 years) was statistically significantly associated with VL suppression at $p < 0.001$. A lower percent of younger patients ($p < 0.001$) had a VL below 1,000 copies/ml, with 73.5% among 15 years old or younger, and 86.0% of those 15 years or older had reached that threshold. Rurality/urbanicity was also significantly associated with VL suppression ($p < 0.001$), with a greatest proportion of patients with suppressed VL in urban health zones (86.4%) and lowest proportion of patients in semi-rural zones (79.3%). The association of the variables, province

Table 2. Bivariate analysis of factors associated with viral load suppression among patients receiving antiretroviral therapy

Demographic and clinical characteristics	% suppressed VL (< 1,000 copies/ml)	*p*-value[a]
Age (at the time of VL test)		
Younger than 15 years	73.5	< 0.001
15 years or older	86.0	
Sex		
Male	84.3	0.38
Female	85.2	
Province		
Haut-Katanga	85.3	0.33
Kinshasa	84.3	
Rurality/urbanicity of health zone		
Rural	83.7	< 0.001
Semi-rural	79.3	
Urban	86.4	
	OR	***p*-value**
Number of years on ART	1.1	< 0.001

ART – antiretroviral treatment, VL – viral load
[a]P-values based on χ^2 test for categorical variables.

Table 3. Adjusted odds ratio from logistic regression model of suppressed viral load among patients receiving antiretroviral therapy[a]

Demographic and clinical characteristics	AOR[b]	95% CI for AOR		*p*-value
		Lower	Upper	
Age (at the time of VL test)				
15 years or older	**2.12**	1.69	2.67	< 0.001
Younger than 15 years	–	–	–	–
Sex				
Male	0.99	0.84	1.17	0.92
Female	–	–	–	–
Province				
Haut-Katanga	**1.21**	1.03	1.42	0.02
Kinshasa	–	–	–	–
Rurality/urbanicity of health zone				
Rural	0.78	0.57	1.07	0.12
Semi-rural	**0.62**	0.52	0.75	< .001
Urban	–	–	–	–
Number of years on ART	**1.04**	1.01	1.07	0.01

ART – antiretroviral treatment
[a]Adjusted odds ratio computed using multivariable logistic regression.
[b]AORs in boldface indicate significant differences compared to reference category, indicated by '–'.

of health zone location (Haut-Katanga vs. Kinshasa), and sex of patients with variable VL suppression was not statistically significant. Duration on ART also had a statistically significant association ($p < 0.001$) with a VL < 1,000 copies/ml.

In Table 3, the adjusted odds of VL < 1,000 copies/ml were significantly higher among persons 15 years of age or older (AOR: 2.12; 95% CI: 1.69-2.67%) than those younger than 15 years. The adjusted odds of having VL < 1,000 copies/ml were significantly lower for patients in semi-rural areas compared to those in urban areas (AOR: 0.62; 95% CI: 0.52-0.75%). Patients with a longer duration on ART (in years) presented higher odds of VL < 1,000 copies/ml (AOR: 1.04; 95% CI: 1.01-1.07%). Patients in the Haut-Katanga Province had significantly higher odds of having a VL below 1,000 copies/ml than those in Kinshasa Province (AOR: 1.21; 95% CI: 1.03-1.42%). Table 3 also shows that after controlling for other variables, patients did not have any significant variation in odds of suppressed VL according to patient's sex.

Discussion

Using data from patients on ART at outpatient clinics in the Kinshasa and Haut-Katanga Provinces, our study examined patients' age and other factors for their association with suppression of VL below 1,000 copies/ml. The study findings provide valuable evidence for potential improvements in HIV treatment services for patients in PEPFAR-supported health facilities. Our study showed that 15.1% of PLHIV on ART had a VL of 1,000 or more copies/ml; the participants in our study had been on ART for an average of 2.8 years (2 years and 9 months) at the time of their first documented VL, and adults (15 years or older) were associated with significantly higher odds of VL lower than < 1,000 copies/ml.

Our findings indicated that youths (ages below 15 years) were significantly less likely to have their VLs below the threshold of 1,000 copies/ml or more, an indication for treatment failure among patients on ART, which could be a result of cultural, normative, and infrastructural barriers associated with access to care and compliance [7, 25]. In order to avoid social stigma associated with HIV status, adults can go to a different care facility rather than to that closest to their residence, but challenges for patients under the age of 15 may include their inability of moving away or self-transfer. Our study findings of differences in VL suppression among youths and adults may signify valuable evidence for focusing health policy efforts and programs on children and youths. Implementing a differentiated HIV service delivery model with a patient-centered approach, by using peer navigators and case managers, may improve health outcomes of adolescences. Also, removing barriers, such as user fees, ensuring patients' transportation, and providing translation in local languages, may enhance linkage and retention on HIV service delivery for younger patients, and eliminate age-related disparities [9-13].

In addition, among the variety of factors that might explain challenges relating to VL suppression among youths, difficultly in disclosure of HIV status to children and rules/norms surrounding such disclosure might be of central importance [16]. HIV status disclosure rules and norms for children and youths are significant in the success of HIV treatment and management, because disclosure increases children's ability to understand their health issues, take better care of themselves, and effectively manage ART [17]. The disclosure's rules and their enforcement are likely to be affected by social norms in the DRC context as well as the stigma surrounding HIV status and implications for maintaining confidentiality and privacy. A study in Kinshasa revealed that the providers felt to disclose HIV status to children and youths, because many anticipated benefits of such a disclosure by empowering youths to accept and discuss their HIV status with peers for better health outcomes. Those benefits included improvement in child's adherence to treatment, and children becoming advocates on raising HIV awareness among their peers, motivation among children to protect themselves, and awareness-raising on what caused children's suffering [26]. Since children and youths underage may have difficulty accessing clinics because of their dependence on an adult to assist with transportation, or effort to not miss school, the access to care may be a factor that HIV programs may need to implement into strategies to increase effectiveness of service delivery.

Our study also highlighted geographical differences associated with VL suppression, showing that patients in semi-rural zones had a lower likelihood of VL suppression compared to those in urban zones; although the differences between rural and urban zones were not significant. In contrast, other VL suppression studies have reported lower VL suppression among patients in rural areas compared to urban areas [27-30]. Factors associated with inadequate VL suppression or ART adherence in rural areas compared to urban regions included distance to clinic, poverty, and the need for transportation [30] as well as limited access to services and resources [28]. This situation may be a reflection of deeply rooted health disparity between rural and urban locations in resource-limited settings, such as DRC. Therefore, given the complexity of non-supportive environment and structural limitations of care system, rural patients may experience a more significant burden of the HIV epidemic.

Limitations

The findings of this study should be interpreted within the context of its' limitations. The data used was secondary data from government-owned HIV/AIDS clinics, which are managed by PNLS, with support from PEPFAR. The data included a limited number of demographic and clinical patients' characteristics, and consisted of patients, for which the last VL reported was available in a specific five-year range; however, the exact date of VL was not included in the data. Patients with no recorded VL within the clinics reporting the data were excluded. Our data revealed (not presented in Tables) that VL is tested only approximately once a year for most of patients, but for a small number of patients, our analysis could not measure sustained VL suppression over time due to being limited to the result of the last VL test only. In DRC, routine VL testing became available in 2015, before which, many patients who were on ART were without consistent periodic VL testing for many years. Ideally, the study should have used not only VL suppression at one specific point in time, but also sustained suppression over time. Measurement of sustained viral suppression was not possible because of the above-mentioned data limitations. For a large number of observations, VL below 1,000 copies/ml was reported as ≤ 999 copies/ml, therefore this variable was dichotomized with 1,000 copies/ml as our threshold for suppression.

Conclusions

Despite the advances in the medical field, which have radically changed the HIV epidemic globally, and the efforts to end HIV new infections, particularly in DRC, significant work remains in this country. Our examination of the variation in VL suppression among patients on ART in two provinces in DRC, demonstrated the need to continue these efforts. Our findings indicated that younger patients on ART and those living in semi-rural zones experienced a significantly lower likelihood of VL suppression compared to their older counterparts and those living in urban areas. More considerable efforts to ensure that this population remains virally suppressed can have a high impact on moving towards using treatment as prevention.

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The program implementing partners required that data be destroyed after publication. Original data are archived with the original data owners mentioned in the methods section.

Conflict of interest

The authors declare no conflict of interest.

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