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Factors associated with viral suppression among adults living with HIV on antiretroviral therapy in Nigeria: Analysis of a population-based survey, 2018

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Abstract

Objective: Viral load suppression (VLS) is critical in reducing morbidity and mortality associated with HIV as well as minimizing the likelihood of HIV transmission to uninfected individuals. The objective of this study was to identify factors associated with VLS among people living with HIV (PLWH) on antiretroviral (ARVs) therapy in a population-based survey to inform HIV program strategies in Nigeria.

Design and methods: Adult participants,15–64 years old, from the 2018 Nigeria HIV/AIDS Indicator and Impact Survey (NAIIS) who self-reported to be a PLWH or had detectable ARVs were analyzed to examine factors associated with VLS. NAIIS measured HIV prevalence, viral load, HIV incidence, HIV drug resistance, ARV, and hepatitis B among PLWH.

Results: Of 1,322 participants, 949 (71.8%) were women and 1,305 (98.7%) had detectable ARVs. The median age was 31 (interquartile range [IQR]: 39 – 48) years. Weighted prevalence

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of VLS was 80.6%. Compared to participants with detectable ARVs, those with undetected ARVs in their blood specimens had lower odds of VLS (adjusted odds ratio [aOR] = 0.24; 95% CI, 0.08–0.64). Those with hepatitis B infection (aOR = 0.29; 95% CI, 0.20–0.58) and non-nucleoside reverse transcriptase inhibitor-based regimen (aOR = 0.34; 95% CI, 0.12–1.01) were also associated with lower odds of VLS. However, older individuals, (45–54 vs. 15–24 years) had increased odds of VLS (aOR = 2.81; 95% CI, 1.14 – 6.90).

Conclusion: Young individuals and those with undetectable ARVs were less likely to be virally suppressed. Targeted interventions focusing on young individuals and improved adherence to medication are needed to achieve the 95-95-95 goals, critical to HIV epidemic control. The study also confirms the superiority of protease inhibitor-based regimen for ARV treatment.

Keywords

Viral suppression; people living with HIV; Antiretroviral; Survey

Introduction

In view of ending the HIV epidemic by 2030, the UNAIDS 95-95-95 targets recommend diagnosing 95% of people living with HIV (PLWH), linking 95% of those diagnosed to care and treatment, and achieving viral suppression in 95% of those linked in care and treatment [1]. Optimal viral load suppression (VLS) is critical in reducing morbidity and mortality associated with HIV and its associated opportunistic infections as well as minimizing the likelihood of HIV transmission to uninfected individuals [2–5]. Despite these benefits, challenges still exist and some patients receiving antiretroviral (ARV) therapy fail to achieve optimal viral suppression [6–8]. To achieve these UNAIDS targets, unbiased population-based data on the determinants of VLS are needed to inform targeted interventions.

Results from the 2018 Nigeria HIV/AIDS Indicator and Impact Survey (NAIIS) estimated the HIV prevalence among adults (15–49) years at 1.3%, about half of previous model based estimates [9]. NAIIS data showed that among adults aged 15–64 years, 96.4% self-reported being on ARV treatment or had detectable ARVs and 80.9% were virally suppressed. While impressive progress has been made following large-scale surge efforts in states with the highest prevalence of HIV and undiagnosed cases of HIV, more needs to be done to meet the UNAIDS targets and move Nigeria closer to epidemic control. The number of HIV-associated deaths and number of new infections decreased by 35% and 17%, respectively, from 2010 to 2019 [10] which is encouraging. Nevertheless, based on the strong relationship between VL and transmission probability [3]; targeted assessment and intervention to increase VLS is vital to sustain progressive decline in the number of new infections.

Effective monitoring of VLS should parallel high VL testing services for PLWH. Innovative interventions implemented in Nigeria such as deployment of surge members to community, improving patient contact information, and prevention of consumables stock outs facilitate VL coverage [11]. For example, community ARV therapy teams collected blood sample for VL testing in addition to facilitating the dispensing of ARV treatment. These interventions lead to improvement of viral load coverage to 88% at the beginning of 2020 [12].

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The objective of this study was to identify factors associated with VLS among PLWH on ARV therapy to inform HIV program strategies in Nigeria focused on ending the HIV epidemic.

METHODS

Survey design

The NAIIS is a nationally representative, cross-sectional household (HH) survey that was conducted in 2018. NAIIS used a two-stage cluster-based sampling design, selecting enumeration areas followed by HH as previously described [9]. The survey measured HIV prevalence, VLS, HIV incidence, HIV drug resistance (DR), ARV detection, and hepatitis B among PLWH. Laboratory specific details, blood collection, testing, and specimen management for all population-based HIV impact assessment (PHIA) surveys are described in the manuscript by Patel et al. [13]. The NAIIS survey followed similar approach, as the PHIA surveys, where participants were offered HIV testing and counseling in their homes using the national HIV rapid testing algorithm. Additionally, all HH positive participants also received their CD4 cell counts (Pima CD4; Abbott, Abbott Park, Illinois) results. All HIV-positive specimens from HH, underwent confirmatory testing using the GeeniusTM HIV 1/2 Supplemental Assay (Bio-Rad, Hercules, California, United States). Positive specimens on GeeniusTM HIV 1/2 were considered final HIV positive test result for the survey. Additionally, all confirmed HIV-positive specimens were tested for plasma HIV-1 RNA using the Roche COBAS® AmpliPrep/COBAS® TaqMan® (CAP/CTM) HIV-1 Test, version 2.0 (Roche Diagnostics, Pleasanton, CA, USA). In few cases when plasma specimen was not available, dried blood spot (DBS) VL was performed. DBS specimens were tested for the presence of ARVs; efavirenz (EFV), nevirapine (NVP), lopinavir (LPV), and atazanavir (ATV), using the qualitative high-performance liquid chromatography and tandem mass spectrometry (LC/MS-MS) assay [14]. Additional information on laboratory tests is available in the 2018 NAIIS Technical Report [9].

Eligibility

All HIV-positive adults aged 15 to 64 years who participated in the NAIIS, provided consent for biomarker testing, and either self-reported to be on ARV therapy or had detectable ARVs in their blood specimens were included in this analysis.

Variables and definitions

VLS was defined as plasma HIV-1 RNA < 1,000 cp/mL as per WHO guidelines [15]. CD4 cell count was categorized as <500 and 500 cells/mm³. Age was categorized as 15–24, 25–34, 35–44, 45–54, and 55–64 years; education as no education, primary, secondary, tertiary, and other; marital status as never married, married or living together, divorced/separated, widowed; residence as urban or rural; ARVs as detected or not detected. Asset-based wealth index was used to categorize the wealth index scores into quintiles (lowest, second, middle, and highest) [16].

Statistical analysis

The weighted prevalence and 95% confidence intervals (CI) for VLS was computed as a proportion of individuals sampled. We compared participant covariate characteristics by VLS using the Rao-Scott chi-square tests. We used bivariate and multivariable logistic regression to compute odds ratios (OR) for factors associated with VLS. Logistic regression models accounted for survey weights, stratification, and clustering in the sample design. We considered sociodemographic and other characteristics in bivariate analysis. Variables associated with the outcome at a significance level of 0.05 in bivariate analysis and variables that had been reported as biologically plausible determinants of VLS were considered in multivariable analysis. Missing data ranged from 0.08% to 1% and therefore complete case analyses was performed. All analyses were conducted in SAS 9.4 (Carey, NC).

Ethical considerations

The Nigeria National Health Research Ethics Committee, University of Maryland, Baltimore Institutional Review Board, and the United States Centers for Disease Control and Prevention Institutional Review Board approved NAIIS. Consent was obtained from participants who were 18 years or older and parental/guardian permission was obtained for minors prior to obtaining individual assent.

Results:

Of 2,739 adults, aged 15 to 64 years, who tested HIV-positive during the survey, 1,417 (51.7%) were either newly diagnosed or had no information on self-reported use of ARV therapy and no detectable ARVs and therefore excluded from this analysis (Figure 1). The final analyses included 1,322 participants of whom, 743 (56.2%) self-reported to be a PLWH and 579 (43.7%) did not self-report as a PLWH but tested HIV positive and had detectable ARVs in their blood specimens. The median age was 31 (interquartile range (IQR): 39 - 48) years. Of the study sample, 949 (71.8%) were women and 922 (69.7%) were 35 years or older. Seven hundred and sixty (57.5%) lived in urban areas and 811 (61.3%) were married or living together. Over half, 747 (56.5%) had CD4 count 500 cells/mm³ and 99 (7.5%) had hepatitis B infection (Table 1).

Characteristics of and ARV response

Overall, of 1,322 individuals included in the final analysis, 1,305 (98.7%) had detectable ARVs in the blood samples of which most (819, 62.7%) had detectable EFV, followed by NVP (417; 31.9%). Weighted prevalence of VLS was 80.6% (n=1066). The median CD4 count was 354 (IQR 545 to 765 cells/mm³).

Factors associated with VLS

Compared to participants who were 15–24 years, those who were 45–54 years had increased odds of VLS (aOR = 2.81; 95% CI, 1.14 - 6.90) (Table 2). Having higher CD4 cell count was associated with increased odds of VLS (CD4 count, 500 vs. < 500 (aOR = 5.00; 95% CI, 3.25 - 7.68). Compared to participants with detectable ARVs, those who self-report that they were on ARV therapy but not detected in their blood specimens had lower odds of

VLS (aOR = 0.24; 95% CI, 0.08-0.64). Having hepatitis B infection was associated with lower odds of VLS (aOR = 0.29; 95% CI, 0.20-0.58). Patients on non-nucleoside reverse transcriptase inhibitor-based regimen had lower odds of viral suppression (aOR = 0.34; 95% CI, 0.12-1.01) compared to protease inhibitor-based regimen, although result was not statistically significant.

Discussion

In this 2018 nationally representative population-based survey in Nigeria, 80.6% of participants on ARV treatment achieved VLS and 98.7% had ARVs detected in their specimens although the levels of ARVs was not measured. Although duration on ARV treatment was unknown, these data are encouraging, and it may indicate high level of medication adherence among Nigerian PLWH although the prevalence of viral suppression needs to be higher to attain epidemic control. While higher CD4 count, not being co-infected with hepatitis B infection, and older individuals were associated with increased odds of VLS, not having detectable ARVs was associated with lower odds of VLS.

The proportion of VLS from this survey is similar to the findings from other studies involving routinely collected data from HIV care and treatment centers [17–19]. Although there is variation in defining VLS, duration on treatment, and inclusion criteria, the range of VLS falls within what was found in the current survey. Consistent with other studies, younger individuals including adolescent and young adults are less likely to achieve VLS [20–22]. The period of mental maturation among young individuals is often associated with poor mental health and limited social support [23-25]. Prior research showed that young individual's psychosocial well-being could potentially affects VLS and retention in HIV care as well as supporting proper transition from pediatric into adult HIV care [26–28]. Addressing psychological challenges, supporting proper transitioning from pediatric to adult HIV care services and continued support to young individuals have been shown to improve HIV treatment outcomes including VLS [29,30]. ARV detection is a measure of medication adherence, an important component in achieving VLS [31]. Those with undetectable ARV were less likely to achieve VLS. The benefits of ARV treatment adherence among PLWH are substantial. Besides improvement of immune function, VLS and subsequent reduction of HIV transmission, ARV adherence is associated with good health related quality of life [32]. Different adherence interventions have been studied and adopted extensively [33], however, no one size fits all. Identification of individuals failing treatment and subsequent performance of adherence barrier analysis and implementation of interventions targeted to the identified barriers will likely improve adherence and VLS. Barrier analysis have shown to improve HIV treatment outcomes including retention in care [34]. The improved immune system indicated by higher CD4 counts in those adherent to their ARVs may explain the lower prevalence of Hep B associated with those individuals in our study.

Majority of survey participants were on non-nucleoside reverse transcriptase inhibitors (NNRTI) based regimen with 31% being on nevirapine. We noted patients on NNRTI tended to have lower odds of viral suppression. With the phasing out of nevirapine and the introduction of Dolutegravir based regimen, it is hoped that VLS will be improved.

Our study has several strengths and limitations. We used nationally representative data enabling inferences to the target population of all PLWH in Nigeria. Although some information was self-reported, collection of blood sample and testing for ARVs enabled us to identify PLWH participants who were on ARV treatment but did not self-report. The inclusion of individuals who did not self-report if they were PLWH in our analyses, limit our ability to understand their duration on ARV treatment. If most of these participants were on treatment for less than six months, our estimate on viral suppression may be underestimated. Given the cross-sectional nature of the study, inferences should be interpreted as associational and not causal.

Conclusions

As scaling up of ART coverage continues, efforts to maximize the benefits of treatment such as viral suppression should be prioritized. Young individuals and those with undetectable ARV lag-behind VLS goals. Targeted interventions to identify PLWH who do not know their status, link them to care, and improve medication adherence are needed to achieve 95-95-95 goals and reaching the target of ending HIV epidemic. In addition, our study underscores the need to develop an affordable method to monitoring levels of ARVs in treated persons to streamline targeted adherence counseling. While findings from this study are consistent with VLS observed within the HIV clinical settings among people who are on ART in Nigeria, they also underscore the need for population-based surveys to periodically assess the population-based achievement of epidemic control. Reliance solely on clinical data would overestimate population level VLS and could hinder achievement of epidemic control. The high percentage of individuals who did not report being PLWH and yet had ARVs in their blood shows that stigma associated with HIV and its treatment is still entrenched in these populations.

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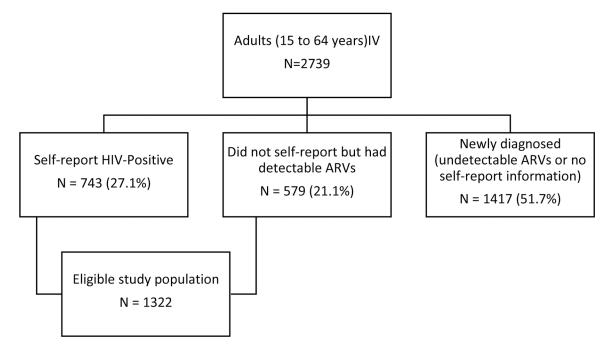


Figure 1. Description of enrolled study population

Table 1.

Percentage distribution of persons ages 15–64 years who tested HIV positive and are on ARV treatment in the NAIIS survey by viral load status and selected demographic characteristics, NAIIS 2018

	Suppressed n = 1066			Not suppressed n = 256	ъ ·
Characteristics	n	Weighted % (95% CI)	n	Weighted % (95% CI)	P-value
Gender					
Male	297	31.08 (27.8–34.36)	76	34.57 (26.96–42.18)	0.42
Female	769	68.92 (65.64–72.2)	180	65.43 (57.82–73.04)	
Age					
15–24	66	7.64 (5.26–10.02)	24	9.61 (5.25–13.96)	0.05
25–34	240	20.02 (17.02–23.03)	70	27.93 (21.18–34.67)	
35–44	355	33.6 (30.14–37.05)	92	35.12 (27.71–42.54)	
45–54	271	27.05 (23.64–30.46)	47	16.68 (11.62–21.74)	
55–64	134	11.69 (9.48–13.9)	23	10.66 (4.93–16.38)	
Education					
No education	208	16.9 (14–19.8)	43	15.56 (10.73–20.39)	0.75
Primary	265	23.57 (20.5–26.64)	58	22.8 (16.44–29.15)	
Secondary	393	40.43 (36.5–44.37)	106	42.43 (34.87–49.99)	
Tertiary	178	16.27 (13.31–19.24)	40	15.34 (9.48–21.2)	
Others	19	2.04 (0.66-3.43)	9	3.87 (0-7.81)	
Missing	3	N/A	0	N/A	
Marital Status					
Never married	104	11.4 (8.62–14.19)	47	18.24 (12.7–23.77)	0.09
Married or living together	671	61.02 (56.97-65.06)	140	56.48 (49.01-63.94)	
Divorced or separated	94	8.46 (6.29–10.62)	25	8.49 (4.85–12.14)	
Widowed	196	19.07 (16.02–22.12)	43	16.17 (11.03–21.3)	
Missing	1	N/A	1	N/A	
Type of Union					
In polygynous union	169	15.2 (12.07–18.32)	29	10.3 (5.58–15.02)	0.26
Not in polygynous union	499	45.45 (41.29–49.6)	110	46.05 (38.25-53.85)	
Not currently in union	394	38.93 (34.89-42.97)	115	42.9 (35.46–50.34)	
Missing	4	N/A	2	N/A	
Place of residence					
Urban	462	48.86 (44.03-53.69)	100	44.43 (36.54–52.32)	0.31
Rural	604	51.14 (46.31–55.97)	156	55.57 (47.68-63.46)	
Geopolitical zone					
Northwest	69	11.70 (8.46–14.95)	15	10.52 (4.98–16.05)	0.33
Northeast	192	13.36 (10.26–16.45)	64	17.59 (12.68–22.5)	
Northcentral	385	28.49 (24.9–32.08)	67	20.93 (15.78–26.08)	
Southeast	138	12.29 (9.81–14.78)	35	13.37 (8.93–17.82)	
South-south	173	17.87 (14.85–20.89)	53	21.83 (15.93–27.72)	

	Suppressed n = 1066			Not suppressed n = 256		
Characteristics	n	Weighted % (95% CI)	n	Weighted % (95% CI)		
Southwest	109	16.29 (13.33–19.25)	22	15.76 (8.69–22.83)		
Wealth quintile						
Lowest	119	9.83 (7.52–12.14)	37	12.73 (8–17.46)	0.53	
Second	204	16.99 (14.11–19.87)	40	13.51 (8.89–18.12)		
Middle	266	23.76 (20.15–27.36)	71	27.17 (20.33–34.01)		
Fourth	275	28.01 (24.14–31.87)	65	25.83 (19.17-32.49)		
Highest	202	21.42 (17.85–24.99)	43	20.76 (13.83–27.69)		
Making decisions about health care						
Self	216	20.67 (17.73-23.62)	49	24.12 (16.71–31.53)	0.28	
Spouse/partner	189	16.36 (13.51–19.22)	34	12.71 (7.45–17.97)		
Jointly	258	23.33 (20.03–26.63)	56	19.15 (13.84–24.46)		
Missing	403	N/A	117	N/A		
Hepatitis B infection						
Positive	68	5.61 (4.02–7.19)	31	14.39 (8.27–20.51)	0.0003	
Negative	996	93.77 (91.81–95.74)	225	85.61 (79.49–91.73)		
Missing	2	N/A	0	N/A		
CD4 count, cells/uL						
< 500	376	35.7 (32.08–39.33)	176	67.99 (60.59–75.38)	<.0001	
500	676	62.55 (58.87-66.24)	71	28.93 (21.61-36.25)		
Missing	14	N/A	9	N/A		
ARVs in blood specimen						
Detectable	1050	97.99 (96.69–99.28)	237	91.87 (88.19–95.55)	0.0002	
On ART but not detected in blood	16	2.01 (0.72-3.31)	19	8.13 (4.45–11.81)		
Regimen type						
PI	59	6.9 (4.8–9.0)	9	3.1 (0.5–5.7)	0.06	
NNRTI	991	93.1 (91.0–95.2)	228	96.9 (94.3–99.5)		

Abbreviations: CI, Confidence intervals; ART, antiretroviral therapy; ARV, antiretroviral; PI, Protease inhibitors; NNRTI, Non-Nuclease Reverse Transcriptase Inhibitors; NAIIS, Nigeria HIV/AIDS Indicator and Impact Survey

Table 2.

Factors associated with viral suppression, among persons ages 15–64 years who tested HIV positive and are on ART in the NAIIS survey, NAIIS 2018.

Characteristics	Univariate			Multivariate			
	OR	95% CI	P-value	aOR	95% CI	P-value	
Gender							
Male	Ref			Ref			
Female	1.17	(0.80–1.72)	0.42	1.18	(0.72–1.93)	0.52	
Age							
15–24	Ref			Ref			
25–34	0.9	(0.46–1.79)	0.768	1.12	(0.72–2.56)	0.79	
35–44	1.2	(0.63–2.30)	0.574	1.75	(0.77–3.96)	0.18	
45–54	2.04	(1.03–4.03)	0.04	2.81	(1.14–6.90)	0.02	
55–64	1.38	(0.60–3.15)	0.444	1.93	(0.62–6.00)	0.26	
Education							
No education	Ref						
Primary	0.95	(0.58–1.56)	0.845				
Secondary	0.88	(0.57–1.36)	0.557				
Tertiary	0.98	(0.55–1.74)	0.937				
Others	0.49	(0.13–1.79)	0.279				
Marital Status							
Never married	Ref			Ref			
Married or living together	1.73	(1.06–2.82)	0.029	1.27	(0.70–2.31)	0.43	
Divorced or separated	1.59	(0.82–3.11)	0.172	1.58	(0.71–3.53)	0.26	
Widowed	1.89	(1.08-3.30)	0.026	1.15	(0.56–2.37)	0.71	
Type of Union							
In polygynous union	Ref						
Not in polygynous union	0.67	(0.37–1.20)	0.179				
Not currently in union	0.61	(0.34–1.10)	0.104				
Place of residence							
Urban	Ref						
Rural	0.84	(0.59–1.18)	0.306				
Wealth quintile							
Lowest	Ref						
Second	1.63	(0.92–2.87)	0.091				
Middle	1.13	(0.66–1.95)	0.653				
Fourth	1.4	(0.82–2.39)	0.212				
Highest	1.34	(0.74–2.42)	0.34				
Hepatitis B infection							
Negative	Ref			Ref			
Positive	0.36	(0.20-0.64)	0.001	0.29	(0.20-0.58)	< 0.01	
CD4 count- cells/mm ³							

CD4 count- cells/mm3

Characteristics	Univariate			Multivariate			
	OR	95% CI	P-value	aOR	95% CI	P-value	
< 500	Ref			Ref			
500	4.12	(2.80-6.06)	0	5	(3.25–7.68)	< 0.01	
ARVs in blood specimen							
Detectable	Ref			Ref			
On ART but not detected	0.23	(0.10-0.54)	0.001	0.24	(0.08–0.67)	0.007	
Regimen type							
PI							
NNRTI	0.23	(0.10–0.54)	0.001	0.34	(0.12–1.01)	0.05	

Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, Confidence intervals; ART, antiretroviral therapy; ARV, antiretroviral; PI, Protease inhibitors; NNRTI, Non-Nuclease Reverse Transcriptase Inhibitors; NAIIS, Nigeria HIV/AIDS Indicator and Impact Survey

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