World Journal of AIDS, 2021, 11, 1-14
https://www.scirp.org/journal/wja
ISSN Online: 2160-8822
ISSN Print: 2160-8814

Viral Suppression in Adult Nigerians in a Regional Antiretroviral Therapy Programme: A Cross Sectional Descriptive Study

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How to cite this paper: Isaac, E.W., Ajani, A., Difa, A.J., Aremu, J.T., Oluwaseun, O.C. and Hassan, M.D. (2021) Viral Suppression in Adult Nigerians in a Regional Antiretroviral Therapy Programme: A Cross Sectional Descriptive Study. *World Journal of AIDS*, **11**, 1-14.
https://doi.org/10.4236/wja.2021.111001

Received: December 10, 2020
Accepted: March 12, 2021
Published: March 15, 2021

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Abstract

Background: The adult ART (antiretroviral therapy) programme started in Nigeria in 2002. After many years of ART in the country, the National implementation plan for the scale up of viral load testing was launched in 2016. Viral load estimation is the most important indicator of ART response. **Aim**: To describe viral suppression in adults on the HIV ART programme **Material & methods**: Viral load blood samples of 9450 adults on highly active antiretroviral therapy living with HIV from 4 states within Nigeria were analyzed for HIV RNA in Polymerase Chain Reaction laboratory of the Federal Teaching Hospital, Gombe between December 2017 and December 2019. **Results**: Males were 2577/9450 (27.3%) and 6873 (72.7%) females. Adults aged 26 - 45 years constituted 69.5% (6572). Viral load test was primarily routine in 96.3% (9098). ART was AZT/3TC/NVP in 52.5% (4962); TDF/3TC/EFV in 46.3% (4375). 48.3% (4568/9450) adults had received HAART for 1 - 5 years; 7.4% (699) for 6 months but <1 year; 37.6% (3551) 6 - 10 years and 6.7% (632) for >10 years. The most recent CD4 count before viral load request was ≥1000/μL in 6.5% (612) of adults; 500 - 999/μL in 38.6% (3651); 350 - 499 μL in 23.2% (2195) and <350 μL in 31.7% (2992). Viral load was ≥1000 c/ml in 22.9% (2167/9450) of adults. Viral load was >1000 c/ml in 22.8% (587/2577) males and 23.0% (1580/6873) females. Of adults aged 19 - 25 years, 28.4% (211/743) had viral load >1000 c/ml; 23.5% (1544/6572); 20.0% (294/1473); 17.8% (93/523) and 18.0% (25/139) aged 26 - 45 years, 46 - 55

years; 56 - 65 years and >65 years also had viral load >1000 c/ml (p value < 0.001) Viral load was >1000 c/ml in 26.0% (182/699) of adults on HAART for 6 months - 1 year and 21.3% (975/4568) after receiving HAART for 1 - 5 years. 24.9% (885/3551) and 19.8% (125/632) adults had viral load > 1000 c/ml after receiving HAART for 6 - 10 and >10 years respectively. (p value < 0.001) **Conclusion**: Over all viral suppression of 77% in our study is high but fell below the WHO threshold of 90%. ART programme in Nigeria requires strengthening.

Keywords

Adult, ART, Viral Load > 1000 c/ml, Nigeria

1. Introduction

The global scale-up of antiretroviral therapy (ART) under the public health approach of standardized and simplified regimens has registered significant gains, with increasing access to treatment for millions of people, and a reduction in new infections and HIV-associated morbidity and mortality and by end of 2019, 25.4 million people were receiving antiretroviral treatment worldwide [1]. Nigeria has the second largest HIV burden globally with an estimated 1,900,000 people living with the virus [2]. Of all adults aged 15 years and over living with HIV, 55% were on treatment, while only 35% of children aged 0 - 14 years living with HIV were on treatment in the country [3]. In 2018 in Nigeria: 67% of people living with HIV knew their status; 53% of people living with HIV were on treatment and 42% of people living with HIV were virally suppressed [3]. Nigeria therefore lags behind the ambitious treatment targets set by the Joint United Nations Programme on HIV/AIDS (UNAIDS), the 90-90-90 strategy by 2020. This goal stipulates that by 2020, 90% of all people living with HIV will know their HIV status; 90% of all people with diagnosed; HIV infection will receive sustained antiretroviral therapy; and 90% of all people receiving antiretroviral therapy will have viral suppression; as well as the elimination of AIDS as a public health threat by 2030 [4] [5].

Globally 59% of people living with HIV have undetectable levels of the virus and 47% are virally suppressed. In sub Saharan Africa, of the 25.7 million infected people, 60% are on ART and only 47% have achieved viral suppression [6].

World Health Organization recommended viral load testing as the preferred monitoring tool for diagnosing and confirming antiretroviral therapy failure. Plasma HIV RNA levels provide a direct measure of the efficacy of antiretroviral therapy (ART), predicting immunological and clinical outcomes and the risk of transmission [7].

Determination of virological suppression status of adults enrolled on ART is important as it allows for timely detection of treatment failures, identification of

patients in need of more intensive adherence counseling and support and minimizes development of drug resistance and unnecessary switch to expensive and limited ART regimen options [8]. WHO guidelines recommend cross-sectional studies to monitor virological efficacy and resistance to ART, or the use of cohort studies to assess one of eight early warning indicators of HIV drug resistance: viral load suppression 12 months after ART initiation [9] [10].

Sustained viral suppression, which is the key goal of cART, facilitates restoration of the immune function and significantly reduces the risk of onward HIV transmission [11]. As the availability of viral load testing grows in developing countries, the percentage of patients with virological suppression can be an important measure of overall ART clinic and program success [12].

In sub Saharan Africa, proportions of virological success were highly variable [12] [13] and viral suppression rates declined during the first 4 years of ART [14].

In Nigeria, the viral load implementation strategy and plan was launched in 2016 [15] and the National Guideline on HIV prevention and treatment [16] recommends viral load determination six months after initiating cART and then annually if viral suppression was achieved. In individuals without viral suppression, adherence counseling support is intensified followed by another viral load testing so as to differentiate poor adherence from treatment failure. Treatment failure is defined by two viral load measurements > 1000 c/ml, 3 months apart after the initial viral load determination and such individuals are switched to second-line ART [16].

ART for Nigerians living with HIV started in 2002 with 10,000 adults and by 2019, about a million people were receiving highly active antiretroviral treatment in the country [2]. The lack of routine viral load testing until 3 years ago meant suboptimal monitoring with risk for non-viral suppression and HIV drug resistance. Therefore, the aim of this study was to report viral load suppression among Adults living with HIV in a regional ART programme in Northern Nigeria.

2. Methods

2.1. Study Design

The study is descriptive cross sectional study conducted between 2017 and 2019.

2.2. Study Setting

Blood samples for HIV Viral load estimation were collected from 9450 adults aged >18 years on HAART from several health facilities including primary, secondary and tertiary health institutions in 4 states in the North of Nigeria between 2017 and 2019. The following information: age, sex, date of HIV diagnosis, date of ART start, current ART regimen, first or second line ART, date of sample collection. Viral Load results were retrieved from the RNA PCR register from the Laboratory. The sample size was the number of adult in the ART pro-

gramme in the reporting ART sites who had their samples sent to the PCR laboratory.

2.3. Inclusion Criteria

Adults with the following information age, sex, date of HIV diagnosis, date of ART start, current ART regimen; first or second line or third line, date of sample collection, together with a VL result were included. Adult was defined as age 19 years and above. Virological suppression (VS) was defined as viral load (VL) < 1000 RNA-copies/mL of blood plasma and virological non suppression (VNS) as VL ≥ 1000 RNA-copies/mL [15] [16]. Adults with incomplete data entry were excluded from this analysis.

2.4. Viral Load Determination

Viral load quantification of HIV-1 RNA was performed on plasma samples using COBAS 96 CAP//C TaqMan HIV-1 assay (Roche Diagnostics, Indianapolis, IN) at a limit of detection of 40 copies/mL. A protocol using 0.6 mL of plasma was used for RNA extraction. The lower limit of detection of the assay is <40 copies/mL of HIV-1 RNA.

The PCR laboratory, situated in the Federal Teaching Hospital Gombe, has been certified by the Federal Ministry of Health and the Pepfar CDC in Nigeria to determine HBV, HCV and HIV viral load.

Ethical clearance was received from the research and ethics committee of the Federal Teaching Hospital, Gombe.

Data was analyzed using Epi info version 3.5.1. All data were analysed with a statistical significance level set at $p < 0.05$. Frequencies, proportions, confidence interval were computed. Data were summarized using tables and figures. Hypothesis testing was performed using Pearson Chi Square and Chi Square as appropriate

3. Results

Table 1 shows that females constituted 72.7% and males 27.3% of those that had a HIV viral load test during the period. Males had 77.2% and females 77% viral suppression and distribution was statistically significant. Overall viral suppression in this sub regional adult ART programme was 77% (Figure 1). Among all age groups, viral suppression increased with increasing age with 71.6% of the age group 19 - 25 years and 82% of the >65 years age group having viral load of <1000 c/ml. Viral non-suppression was highest, 28.4% in the 19 - 25 year age group compared with 18% in the older age group. The distribution of viral suppression in the age groups was statiscally significant ($P < 0.001$).

Adults on EFV and NVP based regimen had viral load suppression of between 73% and 75.6% while viral load > 1000 c/ml was reported in between 21.2% and 24.4% of these individuals; this finding was statistically significant (Table 1). Of the adults on ART, 97.2% and 0.3% were on first and third line respectively. Viral

Table 1. Adults living with HIV and Viral suppression.

Variable	Frequency	<1000 cp/ml	>1000 cp/ml	X2
Ages				
19 - 25 yrs	743 (7.9)	532 (71.6)	211 (28.4)	<0.001
26 - 45 yrs	6572 (69.5)	5028 (76.5)	1544 (23.5)	
46 - 55 yrs	1473 (15.6)	1179 (80.0)	294 (20.0)	
56 - 65 yrs	523 (5.5)	430 (82.2)	93 (17.8)	
>65 yrs	139 (1.5)	114 (82.0)	25 (18.0)	
Sex				
Males	2577 (27.3)	1990 (77.2)	587 (22.8)	0.829
Females	6873 (72.7)	5293 (77.0)	1580 (23.0)	
ART Regimen				
AZT + 3TC + NVP	4962 (52.5)	3751 (75.6)	1211 (24.4)	<0.001
TDF + 3TC + EFV	4375 (46.3)	3449 (78.8)	926 (21.2)	
TDF + FTC + EFV	113 (1.2)	83 (73.5)	30 (26.5)	
ART Type				
1st line	9184 (97.2)	7103 (77.4)	2081 (22.6)	<0.001
2nd line	239 (2.5)	164 (68.6)	75 (31.4)	
3rd line	27 (0.3)	16 (59.3)	11 (40.7)	
Duration on ART				
1 yr	699 (7.4)	517 (74.0)	182 (26.0)	<0.001
1 - 5 yrs	4568 (48.3)	3593 (78.7)	975 (21.3)	
6 - 10 yrs	3551 (37.6)	2666 (75.1)	885 (24.9)	
> 10 yrs	632 (6.7)	507 (80.2)	125 (19.8)	
CD4 count				
<350	2992 (31.7)	1963 (65.6)	1029 (34.4)	<0.001
350 - 499	2195 (23.2)	1756 (80.0)	439 (20.0)	
500 - 999	3651 (38.6)	3051 (83.6)	600 (16.4)	
>1000	612 (6.5)	513 (83.8)	99 (16.2)	
Reason for request of viral load				
Routine	9098 (96.3)	7012 (77.9)	2086 (22.1)	<0.001
Suspected clinical failure	232 (2.5)	195 (84.1)	37 (15.9)	
Suspected immunological failure	120 (1.3)	76 (63.3)	44 (36.7)	
ART Start Year				
2000-2004	29 (0.3)	27 (93.1)	2 (6.9)	0.052
2005-2009	2214 (23.4)	1674 (75.6)	540 (24.4)	
2010-2014	4892 (51.8)	3797 (77.6)	1095 (22.4)	
2015-2018	2315 (24.5)	1785 (77.1)	530 (22.9)	

load was <1000 c/ml in 77.4% of those on first line and on second line was 68.6%. Viral non-suppression was highest in adults on third line. The distribution of viral suppression and non-suppression was statiscally significant among ART type $P < 0.001$.

In relation to the duration of ART, 85.9% of adults had received cART for between one and ten years. Viral suppression increased with the duration on ART with 80.2% suppression after 10 years on ART; viral non-suppression was 26% in those adults on ART for one year compared to 19.8% in those on cART for 10 years (Figure 2). This distribution was statistically significant $P < 0.001$ (Table 1).

The higher the CD4 count the higher the viral suppression with 65.6% at CD4 count of 350 and 83.8% viral suppression at CD4 count of 1000 (Figure 3); Viral non-suppression was 16.2% at CD4 count of 1000 and 34.4% at CD4 count at <350 and this was statiscally significant $P < 0.001$.

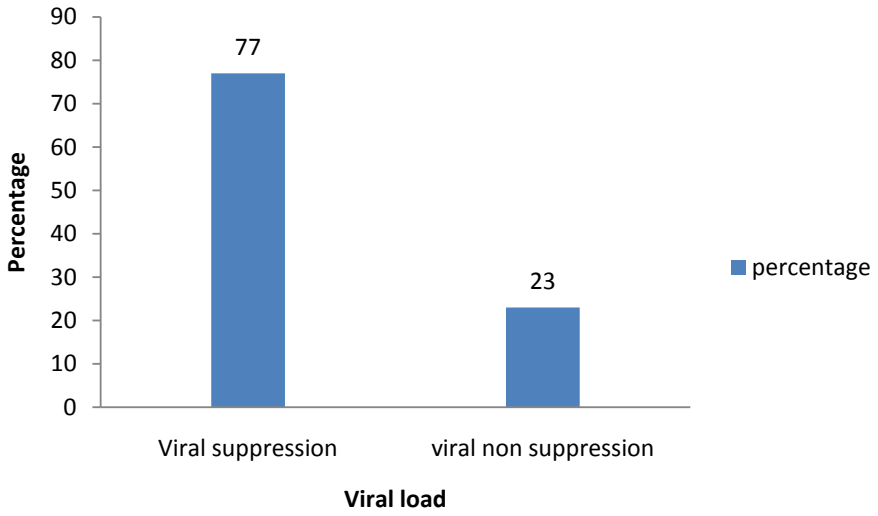

Figure 1. Viral load suppression status in Adults living with HIV/AIDS.

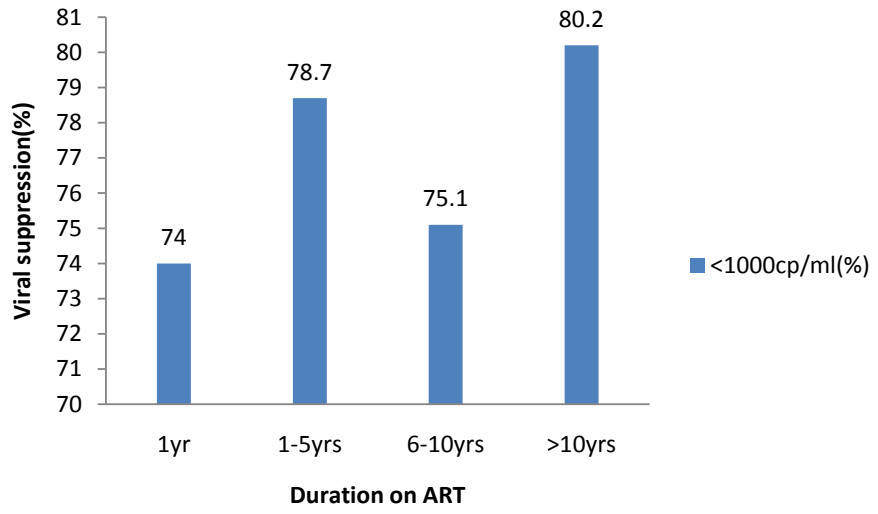

Figure 2. HIV Viral suppression rate and duration of ART in years in adults.

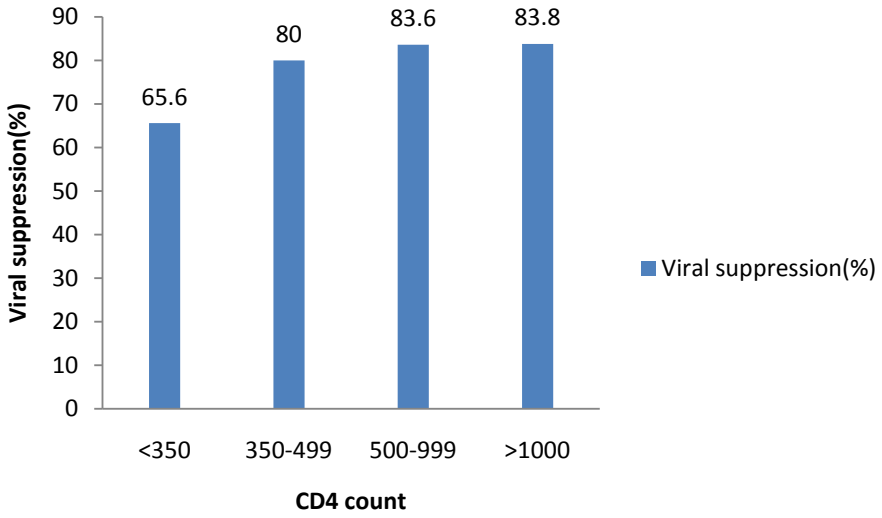

Figure 3. HIV Viral suppression rate and CD4 count in adults.

The reason for the request for a viral load test was suspected clinical failure in 2.5% and suspected immunological failure in 1.3% of adults on cART. Viral non-suppression occurred in 15.9% and 36.7% of those with suspected clinical and immunological failure respectively with statistically significant distribution. In relation to the year ART started, 85.3% of adults started cART between 2010 and 2018 (**Table 1**).

4. Discussion

Our study, determined viral load in a large number of adult Nigerians living with HIV in the national ART programme which started in 2002 [16]. Prior to 2017, ART monitoring was either clinical and /or immunological with viral load estimation for selected people living with HIV/AIDS on ART [17]. Therefore with no viral load determination as standard of care, thousands of Nigerians received NNRTI and NRTI based ART without virologic monitoring with risk for drug resistance and treatment failure. Routine regularly scheduled VL monitoring has the potential to preserve treatment options through early identification of those with non-suppression who might benefit from timely intensified adherence support to prevent treatment failure and the need for regimen changes [18] [19].

The overall viral suppression of 77% in adults in our study is higher than the 44.5% reported in adults at the national level in Nigeria [2]. In Nigeria there is wide variation in HIV prevalence between states and regions with subnational prevalence not representative [16]. While nationally representative viral suppression rates from Uganda, [20] Cameroon, [21] Kenya [22] and South Africa [23] are higher than the 44.5% reported in Nigeria, the viral suppression rates in all these countries in 2018 fall below the UNAIDS 90% recommended viral suppression threshold. Subnational viral suppression rates from Ethiopia, [24] Cameroon, [25] South Africa [26] and Ghana [27] reported various suppression

rates of 73%, 79%, 56.2% and 69% respectively. Earlier and recent systematic review of HIV viral suppression in low and middle income countries reported rates of >80% but less than the 90% UNAIDS target for ART programmes [14] [28]. While substantial progress has been made in ART programmes in sub-Saharan, the differences in VS rates are generally related to study design, population characteristics, ART type and duration of treatment and suggest substantial differences in programme performances within and across countries [12] [29].

Females constituted two third of people living with HIV in our study and were equally as virally suppressed as males. Some studies [30] [31] [32] did not find an association between gender and virologic success or failures, other reports [33] [34] [35] [36] found that males were more likely to be virally none suppressed compared to females and as a consequence they have poor HIV immuno virologic and clinical outcomes compared to females.

Younger adults were more likely to achieve viral suppression than the older adults. This is similar to reports in sub-Saharan Africa [12] [20] [24] [37] and the USA [38].

Age transition challenges, Suboptimal adherence to cART, lack of psychosocial support, stigma and fear of disclosure, substance abuse and alcohol consumption are contributor factors to low viral suppression in adolescents and younger adults [24] [39] [40] [41].

There was little difference in viral suppression rate among the main first line ART regimen in this adult population of PLHIV in our study. This difference was also small in the virally non-suppressed adult PLHIV. While reports from Uganda [24] and Nepal [42] found an association between ART regimen and viral suppression, studies from Ethiopia [43] [44] and Cameroun [21] did not find any differences. These findings may be related to differences in sample size and programme performances [12] [29]. The proportion of adults on second and third line ART regimen in this large sub national programme is low. Reports from Ethiopia, [24] Cameroun, [25] Myammar, [45] South Africa [46] showed similar finding.

In Africa, a three year incidence of switching to second line was about 2%, compared to 12% in Europe and about 30% in the United States [47]. Routine determination of viral suppression status and HIV Drug Resistance testing and surveillance in ART programmes enables early detection of treatment failure which is amenable to adherence counseling and or switching to second or third line ART regimen [8] [15] [16].

Viral suppression was higher in adults with higher CD4 count and the suppression rate increased with increasing CD4 count. This is similar to reports from Ethiopia, [24] Zimbabwe, [39] Cambodia [48] and Vietnam [49].

Low CD4 count might slow viral clearance. Sustained viral suppression, which is the key goal of cART, facilitates restoration of the immune function with resultant increase in CD4, the marker of this reconstitution [4].

Viral suppression of 74% after 12 months of ART in our study is similar to

75% from Cameroun, [25] and Cote d'Voire [50] lower than 86.4% from Congo [51] but higher than 32% from Uganda, [20] 69.2% from Togo [52] and 62% from Kenya [53].

A study from Cambodia [48] demonstrated decreasing viral suppression after 10 years of ART. Even though viral non suppression in our study is low, limited access to viral load and HIV drug resistance testing especially to NNRTI made failing and ineffective regimens being administered for many years [8] [9] [10].

Substantial progress has been made in routine viral load determination in ART programmes in sub Saharan African (96.3%).

With the recent commencement of routine Viral load monitoring in Nigeria, a large proportion of adults monitored by clinical and immunologic means are now undergoing HIV RNA quantification as recommended in the National guideline [16]. The National guideline recommends initiation of ART as soon as possible preferably within two weeks of diagnosis of HIV infection.

5. Conclusion

Viral suppression in adults in this sub national ART programme in Northern Nigeria is high but below the WHO recommended threshold for viral suppression.

Recommendations

Viral load determination according to the National Guidelines for HIV prevention treatment and care and National implementation plan for scale-up of viral load testing in Nigeria should be implemented at all level of clinical care. HIV drug resistance surveillance is important in strengthening ART especially in a large HIV programme like that of Nigeria.

Limitations

This is the first viral load results in adults with HIV in an ART programme. We therefore could not establish treatment or virologic failure especially as we did not determine level of adherence and a second viral load.

Authors' Contributions

Elon Warnow Isaac: Conceived of the study and study design, developed the first manuscript draft and critically reviewed all drafts of the manuscript.

Dr. Abubakar Joshua Difa, Ajani Ayomikun and Ms. Oyeniyi Christianah Oluwaseun: Conducted quantitative data analysis and reviewed all drafts of the manuscript.

Dr. John Tunde Aremu and **Mr. Muhammad Danlami Hassan**: Reviewed and commented on data.

Acknowledgements

We acknowledge Hajiya Fatima Y Aliyu and Hajiya Zainab Danmalam of the

data unit of paediatrics department for extracting the data. The management and staff of Centre for Integrated Health Partnership, fhi360 PEPFAR Implementing partners other non-government organisations and health care workers who are striving daily to provide quality HIV and AIDS care and treatment to children living with HIV/AIDS. We acknowledge the untiring effort of the Laboratory scientists and staff of the PCR Unit in the Federal Teaching Hospital Gombe.

Conflicts of Interest

Authors have no conflict of interest to declare.

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Abbreviations/Acronyms

ART: Anti-retroviral therapy
AZT: Zidovudine
cART: Combination Anti-retroviral Therapy
EFV: Efavirenz
HIV: Human Immunodeficiency vaccine
3TC: Lamivudine
NRTI: Nucleoside reverse transcriptase inhibitors
NNRTI: Non-nucleotide reverse transcriptase inhibitors
NVP: Nevirapine
PLHIV: People living with HIV
RNA: Ribonucleic acid
TDF: Tenofovir
UNAIDS: Joint United Nations Programme on HIV/AIDS
VS: Viral Suppression