



Prevalence and Determinants of Undetectable Viremia among Recipients of Care Receiving HIV/AIDS Care in Akwa Ibom State, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Authors RAO, DA, CI and EO developed the title, and identified the specific objectives. Authors EO, GBO and AFN pulled the data from Lafiya Management Information System (LAMIS), cleaned and validate it before importing it into SPSS, and together with author RAO conducted data analysis. Authors VNN, DI, PA and CM managed the literature searches, and together with authors RAO, OAA, PA and FIA wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background: Globally the benefits of undetectable viremia in preventing the transmission of HIV/AIDS have been established.

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Objective: The study aimed to assess the prevalence and determinants of undetectable viral load amongst HIV/AIDS clients receiving care and treatment in RISE-supported facilities in Akwa Ibom State, Nigeria.

Methods: A descriptive cross-sectional study was conducted using secondary data from a validated Retention and Audit Determination Tool (RADET) file generated in September 2021. This was cleaned, imported into, and analyzed using a statistical package for social sciences (IBM SPSS) statistical package version 25. The prevalence of undetectable viremia was determined using descriptive statistics, and factors associated with undetectable viremia were assessed using chi-square analysis. Binary logistic regression was used to identify the determinants of undetectable viremia at an alpha level of <0.05 at a 95% confidence interval.

Results: out of 47,575 recipients on care, 85.7% had undetectable viremia. Residing in rural areas ($p<0.001$, OR=1.3), respondents aged 25-49 years ($p=0.008$, OR=1.32), and those placed on Multi-Month Dispensing (MMD 6) ($p<0.001$, OR=1.45) were more likely to have undetectable viremia. While students ($p=0.035$, OR=1.2), and those employed ($p=0.001$, OR=1.102) were less likely to have undetectable viremia.

Conclusion: This study reported a high prevalence of undetectable viremia. The determinants were occupation, residing in rural areas, productive age group, and being on MMD 6. Multiple interventions that include phone reminders and behavioral models to support self-care amongst urban dwellers are imperative. Differentiated interventions that include operation Triple Zero (OTZ) and Community Adolescent Treatment Supports (CATs) targeting the pediatric age group are needed to support the adherence to ART and undetectable viremia.

Keywords: Undetectable viremia; HIV/AIDS; antiretroviral therapy; RISE; Akwa Ibom state.

1. INTRODUCTION

Human Immunodeficiency Virus (HIV) remains a pandemic in the world, with about 38 million persons living with the disease of whom 70% of these persons reside in sub-Saharan Africa [1]. Nigeria is one country in the world with the highest number of people living with the Virus [2]. About 1.9 million Nigerians are living with HIV/AIDS and a prevalence of 1.4% among 15-64 years – 1.9% amongst females and 1.1% amongst males. The prevalence of HIV among children 0-14 years was 0.2% [3]. Akwa Ibom state remains the epicenter of the disease with 5.6% of its populace living the pandemic [3].

In making HIV/AIDS cease being a disease of public health importance in 2030, in line with UNAIDS' vision 95-95-95 goals, every recipient on care should not only have seamless access to Antiretroviral therapy (ART) but have an undetectable viral load (viral load <50 copies/ml of plasma) [4]. This is needed for the achievement of Undetectable equals to Untransmittable (U=U) an important determinant toward an HIV/AIDS-free generation. Viral load is one of the most objective surrogate endpoints in measuring the progress of HIV/AIDS and treatment success, and every recipient on care need to be supported with several strategies including behavioral models to improve adherence to ART aimed at the achievement of this goal. Poor adherence to ART has serious consequences for HIV-infected patients,

including failure to prevent viral replication, an increased likelihood of developing viral resistance, the development of clinical complications, and shortened survival [5-7].

Human Immunodeficiency Virus Viral load suppression and undetectable viremia, in particular, has been shown to improve the quality of life of people living with HIV [8]. Studies have shown a strong correlation between poor adherence to ART ($<95\%$ adherence) and high viral load leading to poor clinical outcomes [9,10]. Other studies have shown significant associations between socio-demographic, psychosocial, behavioral, and clinical factors and their influence on viral load suppression [11,12]. However, a study by Silveira and colleagues indicated that there was no significant association of sex, clinical status, current immune status, and changes in treatment regimen on undetectable viral load suppression at 80 copies/ml [13]. But rather, medication adherence had the greatest effect in ensuring undetectable viral suppression [13].

A review of our data reveals that significant proportion of recipients on care in RISE-supported facilities in Akwa Ibom state have undetectable viral after six months of adherence to ART medications. Considering viral load suppression as a key attribute in reducing significantly vertical and horizontal transmission of HIV in the populace and subsequently leading to HIV/AIDS free generation, this study aimed to

assess the prevalence, associated factors, and determinants of undetectable viremia amongst recipients of care in RISE-supported facilities of Akwa Ibom State, Nigeria.

1.2 TMEC/RISE Support on HIV Epidemic Control in Nigeria

Meeting Targets Maintaining Epidemic Control, Reaching Impact Saturation and Epidemic Control of HIV/AIDS (TMEC/RISE) is a 5-year USAID-funded project that commenced in October 2019. It is managed by a consortium that comprises Jhpiego (programmatic and administrative lead) and ICAP (technical lead) and supports five states in Nigeria namely – Akwa Ibom, Adamawa, Niger Cross River, and Taraba States in supporting the UNAIDS vision 95-95-95 aimed at preventing HIV/AIDS as a public health threat by 2030. RISE Akwa Ibom state supports sixty-two (including a quaternary facility) health facilities located in the northern part of the state across ten (10) local government areas (LGAs).

2. METHODOLOGY

Akwa Ibom state, the study center, is located in South-southern Nigeria. The study utilized a descriptive cross-sectional design carried out in September 2021. The study population comprised recipients of care attending the ART clinic across 62 supported health facilities. Every recipient of care (RoC) have access to viral blood sample and analysis after having being on antiretroviral (ART) for at least six (6) months.

In RISE Akwa Ibom State, viral load evaluation among HIV recipients of care is done by collecting 10ml of whole blood through venipuncture into an EDTA vacutainer. RNA is preserved for amplification and detection using real-time polymerase chain reaction (PCR) methodology to ensure the integrity of the HIV. Samples collected are centrifuged at 4000 rpm for 10 minutes and plasma separated into a 1.8ml cryovial within 6 hours of sample collection. Plasma samples for HIV VL assay are stored at +2 to +8oC for onward shipment to the PCR molecular laboratory for analysis. However, for long term storage, plasma samples are sorted and preserved at -20oC to -70oC in the PCR laboratory until when samples are ready for analysis. The VL assay assesses patient prognosis by measuring the baseline HIV-1 RNA level or to monitor the effects of antiretroviral therapy by measuring changes in HIV-1 RNA

levels during the course of antiretroviral treatment.

In Nigeria, VL testing services are coordinated within PEPFAR funded programs in a laboratory network comprising 17 PCR laboratories. University of Uyo Teaching Hospital (UUTH) PCR laboratory which is within the PEPFAR funded laboratory network, is the main site where these HIV VL samples are referred following the National Integrated Specimen Referral Network (NiSRN) guideline. The UUTH PCR laboratory utilizes 2 major PCR equipment – the COBAS® AmpliPrep and COBAS® TaqMan® 48/96 (CAP-CTM) and the Abbot m2000sp/rt instruments.

COBAS AmpliPrep/COBAS TaqMan 48/96 HIV assay is an in-vitro nucleic acid amplification test for the quantitation of HIV-1 group M and HIV-1 group O RNA in human EDTA plasma. Though dried plasma spot collected on a Cobas Plasma Separation Card (PSC) and dried whole blood spot (DBS) sample could be used for this test, but plasma samples collected in an EDTA vacutainer was used. A sample volume of 0.85mL of 1.10mL plasma loaded on the instrument is processed in an automated magnetic system (Magnetic glass Particle technology) to wash and dye (dual label) the target RNA material. The COBAS TaqMan Analyzer amplifies and detects the HIV-1 RNA count in logscale or in copies/ml. The test can quantify HIV-1 RNA over the range of 20 - 10,000,000 copies/mL in EDTA plasma, hence CAP-CTM has a limit of detection of 20 copies/mL of EDTA plasma. The basic operating principle of COBAS AmpliPrep/COBAS TaqMan HIV-1 RNA Test is based on three major processes including an automated specimen preparation to isolate HIV-1 RNA; reverse transcription of the target RNA to generate complementary DNA (cDNA); and the simultaneous PCR amplification of target cDNA and detection of cleaved dual labeled oligonucleotide detection probe specific to the target.

The Abbott RealTime m2000 sp HIV-1 RNA assay provides up to 4 sample volume options (0.2mL, 0.5mL, 0.6mL, and 1.0mL). However, the UUTH PCR laboratory uses 1.0mL and 0.6mL (based on sample volume available) sample volume procedure with a limit of Detection of HIV-1 assay at 40 copies/mL and an Upper Limit of Quantification at 10,000,000 copies/mL. Sample preparation procedure is done along with calibrators, controls and the specimen from

which potential inhibitors of amplification are removed and HIV-1 RNA targets are extracted and concentrated for subsequent amplification. The Abbott mSample Preparation System (4 x 24 Preps) uses magnetic particle technology to capture nucleic acids and washes the particles to remove unbound sample components.

The Abbott m2000sp uses a master mix reagent which is a combination of the Abbott RealTime HIV-1 amplification reagents comprising HIV-1 Oligonucleotide Reagent, Thermostable rTth Polymerase Enzyme, and Activation Reagent. The Abbott m2000sp dispenses the master mix to the Abbott 96-Well Optical Reaction Plate along with aliquots of the nucleic acid samples extract. The plate is ready after manual application of the optical seal for transfer to the Abbott m2000rt for HIV-1 RNA amplification and fluorescent detection of amplified products as the HIV-1 and IC probes anneal to the highly conserved pol integrase region of the HIV-1 genome (real-time fluorescence detection). The HIV-1 probe has a fluorescent moiety that is covalently linked to the 5' end. A short oligonucleotide (quencher oligonucleotide) is complementary to the 5' end of the HIV-1 probe and has a quencher molecule at its 3' end. In the absence of HIV-1 target, the HIV-1 probe fluorescence is quenched through hybridization to the quencher oligonucleotide. In the presence of the HIV-1 target sequence, the HIV-1 probe preferentially hybridizes to the target sequence, dissociating from the quencher oligonucleotide, allowing fluorescent detection.

A secondary data was generated from a validated Retention and Audit Determination Tool (RADET) file. All recipients of care in RISE-supported facilities for at least six (6) months were included in the study. The generated RADET file was cleaned and imported into and analyzed using the statistical package for social sciences (IBM SPSS) statistical package version 25. Analysis of data included descriptive statistics using mean and standard deviation for quantitative variables like age, duration on ART, and viral load copies, counts, and frequencies for qualitative variables like sociodemographic variables. Factors associated with undetectable viremia were assessed using chi-square analysis. Binary logistic regression was used to identify the determinants of undetectable viremia at an alpha level of <0.05 at a 95% confidence interval.

3. RESULTS

Majority 35,795 (77%) of the respondents were between 25 and 49 years most of whom were females 30,429 (64%). Over half 27, 158 (57.1 %) of them were married, and the majority 30,331 (63.8%) of the respondents reside in rural settings. The majority 32,957 (69.7%) of the respondents had secondary education. Unemployed category 23,725 (51.4%) accounted for over half of the respondents (Table 1).

Majority of the respondents had undetectable viremia 35,996 (85.7%) and are placed on MMD6 38,395 (80.7%). Half 24,101 (50.7%) of the respondents were enrolled in the Community and only 39 (0.1%) were enrolled through the Laboratory Clinical Platform and almost all 46,671 (98.1%) respondents were on TDF-3TC-DTG (Table 2).

Table 1. Sociodemographic characteristics of respondents

Sociodemographic characteristics	Frequency (%)
Age (years)	
0-9	661 (1.4)
10-24	3524 (7.7)
25-49	35795 (77.9)
50-64	5228 (11.4)
≥65	755 (1.6)
X ± SD	37.09 ± 11.3
Sex	
Male	17,146 (36.0)
Female	30,429 (64.0)
Marital status	
Single	17,506 (36.8)
Married	27,158 (57.1)
Separated	586 (1.2)
Divorced	315 (0.7)
Widowed	2,010 (4.2)
Population setting	
Rural	30,331 (63.8)
Urban	17,244 (36.2)
Education	
None	2,042 (4.5)
Primary	8,837 (19.3)
Quranic	73 (0.2)
Junior Secondary	865 (1.9)
Senior Secondary	31,092 (67.8)
Post Secondary	2,922 (6.4)
Occupation	
Unemployed	23,725 (51.4)
Student	2,133 (4.6)
Employed	20,131 (43.6)
Retired	143 (0.3)

Table 2. ART parameters of respondents

Variables	Frequency (%)
ART regimen^a	
TDF-3TC-DTG	46,671 (98.1)
ABC-3TC-LPV/r	612 (1.3)
TDF-3TC-NVP	245 (0.5)
AZT-3TC-ABC	1 (0.0)
AZT-3TC-LPV/r	7 ((0.0)
AZT-3TC-NVP	3 (0.0)
AZT-3TC-TDF	5 (0.0)
TDF-3TC-ATV/r	4 (0.0)
TDF-3TC-EFV	4 (0.0)
TDF-3TC-LPV/r	18 (0.0)
MMD Status	
MMD<3	9,143 (19.2)
MMD3-5	37 (0.1)
MMD6	38,395 (80.7)
ART Enrolment Setting	
Clinical Platforms (Chemists/PMVs/Dispensary)	6,135 (12.9)
Clinical Platforms (Laboratories)	39 (0.1)
Clinical Platforms (PHCs/Private Clinics/Nursing Homes)	170 (0.4)
Community	24,101 (50.7)
Community-Based Organization	99 (0.2)
Facility	17,030 (35.8)
Viral load status (undetectable status)	
Undetectable (≤ 50 copies/ml)	35,996 (85.7)
Detectable (>50 copies/ml)	6,028 (14.3)
Viral load status (status of suppression)	
Suppressed ($<1,000$ copies/ml)	40,438 (96.2)
Unsuppressed ($\geq 1,000$ copies/ml)	1,586 (3.8)
<i>ART regimen: TDF-3TC-DTG – Tenofovir Disoproxil Fumarate-Lamivudine-Dolutegravir; ABC-3TC-LPV/r – Abacavir-Lamivudine-Lopinavir/ritonavir boosted; TDF-3TC-NVP – Tenofovir Disoproxil Fumarate-Lamivudine-Nevirapine; AZT-3TC-ABC – Zidovudine-Lamivudine-Abacavir; AZT-3TC-LPV/r – Zidovudine-Lamivudine-Lopinavir/ritonavir boosted; AZT-3TC-NVP – Zidovudine-Lamivudine-Nevirapine; AZT-3TC-TDF – Zidovudine-Lamivudine-Tenofovir Disoproxil Fumarate; TDF-3TC-ATZ/r – Tenofovir Disoproxil Fumarate- Lamivudine-Atazanavir/ritonavir boosted; TDF-3TC-EFV – Tenofovir Disoproxil Fumarate-Lamivudine-Efavirenz; TDF-3TC-LPV/r – Tenofovir Disoproxil Fumarate-Lamivudine-Lopinavir/ritonavir boosted</i>	

Over half of the respondents with undetectable viremia were unemployed ($\alpha^2 = 13.97$, $p = 0.003$) and those that reside in rural areas were 1.33 times more likely to have undetectable viremia ($\alpha^2 = 101.43$, $OR = 1.33$, $p < 0.001$). Majority (76.6%) of the respondents with undetectable viremia were between the age group 25-49 years ($\alpha^2 = 43.13$, $p < 0.001$). Almost (90%) all the respondents with undetectable viremia were placed on MMD6 ($\alpha^2 = 156.17$, $p < 0.001$) Table 3.

Students ($p=0.035$, $OR=1.154$) and those employed ($p=0.001$, $OR=1.102$) were more likely to have detectable viremia and this was statistically significant. Respondents that reside in rural areas were 1.26 times more likely to have

undetectable viremia, and this was statistically significant ($p < 0.0001$, $OR = 1.26$, $95\%CI [1.187 - 1.335]$). Similarly, those 25-49 years ($p=0.008$, $OR=1.32$) were 1.32 times more likely to have undetectable viremia, and this was statistically significant. Respondents on MMD 6 were 1.45 times more likely to have undetectable viremia, and this was statistically significant ($p < 0.001$, $OR = 0.688$, $95\%CI [0.636 - 0.745]$) Table 4.

5. DISCUSSION

WHO targets to end HIV/AIDS as a public health problem by 2030 with the introduction of the ambitious “95-95-95” strategy to attain this target, and the third 95 (at least 95% of the recipient of care are virally suppressed) being one of the key

Table 3. Factors associated with undetectable viremia amongst respondents

Variables	Viral load		Chi-square statistics p-value
	≤ 50 copies/mls Freq (%)	>50 copies/mls Freq. (%)	
Occupation of respondents			
Unemployed	18,640 (53.3)	2,963 (51.5)	$\alpha^2 = 13.97$ p = 0.003*
Student	1,641 (4.7%)	319 (5.5)	
Employed	14,576 (41.7)	2,456 (42.7)	
Retired	115 (0.3)	12 (0.2)	
Population Setting			
Rural	23,330 (87.0)	3,501 (13.0)	$\alpha^2 = 101.43$; OR = 1.33 p <0.001*
Urban	12,666 (83.4)	2,527 (16.6)	
Age of respondents (years)			
0-9	542 (1.5)	141 (2.3)	$\alpha^2 = 43.13$ p <0.001*
10-24	3235 (9.0)	595 (9.9)	
25-49	27,544 (76.7)	4417 (73.4)	
50-64	4,008 (11.2)	751 (12.5)	
≥65	578 (1.6)	110 (1.8)	
MMD Status			
MMD<3	4,410 (12.3)	1,092 (18.1)	$\alpha^2 = 156.17$ p <0.001*
MMD3-5	31 (0.1)	4 (0.1)	
MMD6	31,555 (87.7)	4,932 (81.8)	

*p<0.05

Table 4. Determinants of undetectable viremia amongst respondents

Variables	Regression coefficient (B)	p-value	OR	95% CI	
				Lower	Upper
Occupation – unemployed					
Student	0.143	0.035**	1.154	1.010	1.318
Employed	0.097	0.001**	1.102	1.039	1.170
Retired	-0.713	0.26	0.49	0.261	1.020
Population setting - Rural	0.230	<0.001**	1.259	1.187	1.335
Age in categories- 0-9yrs^a					
10 – 24 yrs.	-0.154	0.169	0.857	0.688	1.068
25 – 49 yrs.	-0.279	0.008**	0.757	0.615	0.931
50 - 64 yrs.	-0.115	0.309	0.892	0.715	1.112
≥65 yrs.	-0.50	0.738	0.951	0.709	1.276
MMD status - <MMD 3^a					
MMD 3-5	-0.515	0.337	0.598	0.209	1.709
MMD 6	-0.373	<0.001**	0.688	0.636	0.745

*binary logistic regression; **p=0.05; a - reference categories

determinants towards this goal [14]. The quantification of the viral load in the plasma is a predictor of the progression of the disease [15-17] and, along with CD4 lymphocyte counts, has been used to monitor therapeutic responses [17, 18].

The findings of this study are consistent with other studies that have shown that the female sex is more prone to getting infected with HIV. A study conducted in Akwa Ibom suggests that the high rate of HIV among women who have sex with their partners is worrisome, therefore

suggesting the need for comprehensive HIV prevention programs to include the use of pre-exposure therapy (PrEP) and other methods [19]. Also, in a three population-based studies, it was consistently found that women are more likely to be infected with HIV than men. These results suggest that the higher incidence of HIV in women is due to several reasons that include a higher rate of transmission, as well as longer survival among infected women [20]. Other studies also suggest that the onset of AIDS in women is earlier than in men [21].

This study reported that 96.2% of recipients on care had suppressed viral load (<1,000 copies/ml) with 85.7% having undetectable viremia six (6) months after ART initiation. This is significantly higher than the 43.1% suppression reported by the Nigeria HIV/AIDS and Impact Survey (NAIS) [3]. This is also significantly higher than undetectable viremia of 48.4% reported by Silveira and colleagues [13] in Brazil but similar to 92% reported by a recent study by Mogosetsi and colleagues in South Africa [8]. This was possible since almost all the respondents were on TDF-3TC-DTG which is the recommended first-line ART regimen that has been proven to be very effective with fewer side effects and pills.

The determinants of undetectable viremia were respondents 25-49 years residing in rural areas and those placed on MMD 6. This is consistent with previous studies that reported increasing age and adherence to ART as the predictor of undetectable viremia [13]. This study reported that those residing in the rural areas were more likely to have undetectable viremia compared with those residing in the urban areas and this was statistically significant. On a contrary, students and the employed were more likely to have detectable viremia and this was statistically significant. Although this study did not assess adherence to ART, being busy is a determinant of forgetfulness, the commonest reason for poor adherence to ART. However, the association between occupation, population setting and undetectable viremia is weak, evident by the odds ratio. This may be due to the fact that secondary data was used for the study that had a very large sample size. Socioeconomic status could impact virologic outcomes by delays in receiving a timely HIV diagnosis [19], low CD4 count at ART initiation [20], differences in experiences or quality of health care, and pharmacokinetics (e.g., nutrition deficiencies) [21]. The findings in this study is in contrast with recent study from South Carolina, USA that reported that beneficiaries of care who were employed full-time were more likely to be virally suppressed [22]. This is consistent with previous studies reported in the United Kingdom [23] and USA [24]. Another study noted that unemployment was associated with twice the adjusted risk of virologic failure [25].

Almost all the respondents between the age group 25-49 years had undetectable viremia at bivariate analysis. Respondents within the age group 25-49 years were more likely to have undetectable viremia and this was statistically

significant at multivariate analysis. This is consistent with other studies that reported that the prevalence of undetectable viral load increased with age [26,27]. Other more recent studies also corroborated that the older age group (> 40 years) was associated with better viral load suppression among patients on ART [28,29]. Adults are more likely to imbibe the right behavior needed for self-care to support good adherence to ART compared with pediatric clients whose care and treatment are more dependent on caregivers or their parents.

Respondents placed on MMD 6 were 1.45 times more likely to have undetectable viremia compared with those on MMD3-5 and MMD3. Multi-month dispensing 6 (MMD 6) is a type of Differential Service Delivery (DSD) Model where stable clients – adherent to ART with fewer or no signs and symptoms, are placed on antiretrovirals (ARVs) for six (6) months thereby reducing the clinic visits and burden on healthcare providers. This allows healthcare workers to focus on newly enrolled and virally unsuppressed clients that will need more extensive and specific interventions to support their care and treatment. It is imperative to report that despite being placed on ARVs for six months with clinic visits limited to twice a year and virtual adherence support, a significant number of them had undetectable viremia compared with other MMD statuses.

This study on undetectable viremia is the first to be conducted in Akwa Ibom State, Nigeria. Another strength of this study is the large sample size that gives it adequate power to detect a difference if it exists. However, it utilized secondary data and it did not assess adherence to ART – the most important determinant of undetectable viremia. Subsequent studies should preferably utilize primary data where several variables can be captured in the tools of data collection that can include an assessment of adherence to ART – both by self-report and the use of a nonjudgmental method like Morisky Medication Adherence Assessment (MMAS 8).

6. CONCLUSION AND RECOMMENDATIONS

This study reported a high prevalence of undetectable viremia. The determinants of undetectable viremia were residing in rural areas, respondents between 25 and 49 years, and being on MMD 6. Interventions to increase undetectable viremia among the recipients of care that are employed and residing in urban

areas are highly imperative. These should include a behavioral model aimed at improving the client's self-care. Differentiated interventions that include operation triple zero (OTZ) and community adolescent treatment support (CATs) targeting the pediatric age group are needed to support adherence to ART and undetectable viremia. I hereby recommend that future studies use primary data for a more comprehensive assessment of adherence to ART and undetectable viremia – both by self-report and the use of a nonjudgmental method like Morisky Medication Adherence Assessment (MMAS 8).

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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