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FACTORS ASSOCIATED WITH VIRAL NON-SUPPRESSION AMONG HIV-POSITIVE PATIENTS ON ANTIRETROVIRAL THERAPY IN SIERRA LEONE, JANUARY 2018–JUNE 2019

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ABSTRACT

Despite the growing number of people on antiretroviral therapy (ART), there is limited information about viral non-suppression and its determinants among HIV-positive individuals enrolled in HIV care in many resource-limited settings. We estimated the proportion of virally non-suppressed patients, and identified the factors associated with viral non-suppression. We conducted a descriptive cross-sectional study using routinely collected program data from viral load (VL) samples collected across the country for testing at the Central Public Health Reference Laboratories (CPHRL) in Sierra Leone. Data were generated between January 2018 and December 2019. We extracted data on socio-demographic, clinical and VL testing results. We defined viral non-suppression as having ≥1000 copies of viral RNA/ml of blood for plasma or ≥5000 copies of viral RNA/ml of blood for dry blood spots. We used logistic regression to identify factors associated with viral non-suppression. This study consisted of 8,657 patients, of whom 4224 (74%) were male, and 94.3% were older than 15 years old. Of the total, 7619 (88%) patients routinely monitored, 659(8%) were suspected treatment failure and 379(4%) were repeat testers after suspected failure. The proportion of non-suppression was 22%, of which 876 (71%) were female. viral non-suppression proportion was 26% for suspected treatment failures and 23% for patients routinely monitored after suspected failure (23%). Factors associated with viral non-suppression included patient adhered to ARV treatment (aOR= 0.03, 95%CI = 0.23-0.36), aged <15 years (aOR = 0.22, 95%CI = 0.19-0.27) and young adolescents (aOR = 0.22 95%CI = 0.21-0.29), and patients receiving second-line regimens (aOR= 0.1, 95%CI = 0.03-0.17).Viral non-suppression was relatively low among patient on ART in Sierra Leone. ARV treatment adherence, being adult and patient receiving first-line treatment were protective factors against viral suppression. We recommend to close follow-up for children and to intensify adherence support for patients suspected with treatment failure.

Key word: Antiretroviral treatment (ART), viral non-suppression, HIV, Sierra Leone

BACKGROUND

There is a marked increase in the number of people accessing antiretroviral therapy (ART) worldwide (*Antiretroviral Therapy (ART)*, 2021). Given the high numbers of patients on ART, it is important to sustain treatment success and limit development of treatment failure (Boyd *et al.*, 2019). However, ART management is challenging in people living in Low-and-middle income countries due to reduced access to ART and viral load monitoring (Grinsztejn *et al.*, 2019). Additionally, limited access to both virological and immunological regular monitoring was observed not only in limited-resources country, but even in well-resource settings (Pham *et al.*, 2017). In July 2013, the world health organization (WHO) recommended the use of viral load testing as the gold standard to monitor patients response to ART, to allow timely detection of treatment failures (Reid, Fidler and Cooke, 2013; Bulage *et al.*, 2017a). Determining the viral suppression status for individuals on ART is critical for the timely detection of treatment failures, identification of patients in need of more intensive adherence support and minimization of the development of drug resistance and unnecessary switch to expensive and limited ART regimen options(Bulage *et al.*, 2017a).

The Sierra Leone guidelines recommend that viral load testing should be done 6 months after initiating ART and thereafter annually for people who have achieved viral suppression (Ministry of Health and Sanitation, Sierra Leone, 2018). Individuals with detectable viral loads must undergo targeted intensified adherence support for 6 months followed by confirmatory viral load testing in order to differentiate poor adherence from treatment failure. Those with treatment failure as defined by two detectable viral load measurements above the threshold are switched to second-line ART (Amstutz *et al.*, 2020).

A number of factors have been found to be associated with viral suppression, including individuals in WHO clinical staging 4 who are more likely to be non-suppressed. A study has demonstrated patients who are regularly and routinely evaluated by physicians on each clinic visit are less likely to develop viral failure (Bastard *et al.*, 2012) , while children and adolescents on ART are more likely to have high viral loads (Nasuuna *et al.*, 2018). Other factors found to be associated with viral non-suppression have included suboptimal adherence, poor tolerability, and drug and food interactions, CD4 cell count, treatment history and drug-resistance. Patient-related factors such as co-morbidities, incomplete medication adherence and missed clinic appointment and interruption of or intermittent access to ART can also cause viral non-suppression (Bulage *et al.*, 2017a). In addition, ARV regimen related factors such as drug adverse effects, suboptimal pharmacokinetics, suboptimal viral potency and food requirements, amongst other factors cause viral non-suppression (Bulage *et al.*, 2017a). in Sierra Leone, a qualitative study identified stigma, frequency of medication, use of traditional medicine, lack of money and long distance to treatment centers as factors influencing adherence to ART among people livening with HIV (Lahai *et al.*, 2022). An other study conducted in Sierra Leone identified gap in HIV care and no adherence support were independent predictors for viral failure (Lakoh *et al.*, 2021).

In December 2020, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set new targets towards elimination of HIV, including diagnosis of 95% of HIV infected individuals, access to treatment for 95% of identified HIV infected persons, and 95% viral suppression among those initiated on

treatment by 2030 (Frescura *et al.*, 2022). These targets have since been adopted by several countries including Sierra Leone. Thus, viral load is a critical indicator for HIV treatment quality and tracking of progress towards national and global indicators. According to the 2017 Sierra Leone HIV and AIDS Country Progress Report, 61,000 people were living with HIV (Ellie *et al.*, 2019). Of these, 32,002(43% coverage) were active on ART by Dec 2020. The number of patients receiving ART in Sierra Leone was 46445 in 2021 (*Sierra Leone*, 2021). According to the viral load testing request form version for Sierra Leone, the three main reasons for viral load testing are including routine testing, suspected failure, and repeat viral load testing after suspected treatment failure for patients who were virally non-suppressed on first time testing and underwent enhanced adherence support for 6 months and submitted a follow-up sample at the end of 6 months. Despite the increasing number of HIV positive patients accessing ART(*Antiretroviral Therapy (ART)*, 2021), there is limited information about non-suppression rates amongst the different groups of people enrolled in care in Sierra Leone and many resource limited settings in general. Studies that have highlighted the factors associated with viral suppression in most developed countries and resource limited settings have used lower cut-offs to determine non-suppression. The thresholds used range from 300 to 500 copies/ml of blood(Bulage *et al.*, 2017a). However, since several clinical and epidemiological studies have highlighted the risk of HIV transmission being very low when the viral load is lower than 1000 copies/ml, WHO recommends using 1000 copies/ml as the threshold when using plasma and 5000 copies/ml for dry blood spots (DBS) (Sawadogo *et al.*, 2014). Sierra Leone using the WHO recommended thresholds. Few s studies were conducted in Sierra Leone that have assessed viral suppression and associated factors. The aim of this study was to estimate the proportion of virally non-suppressed HIV positive patients who had been on ART for at least 6 months and identify factors associated with viral non-suppression using a large national dataset of routinely collected program data at the Central Public Health Reference Laboratories (CPHRL) in Sierra Leone.

METHODS

Study design

This was a descriptive cross-sectional study using a large national dataset of routinely collected program data that were submitted to the CPHRL at Lakka from all health facilities in Sierra Leone.

Study setting

The study was conducted at CPHRL where the centralized VL testing is done in Sierra Leone. Centralized monitoring of response to ART using viral load as a gold standard started in Sierra Leone in November 2016 (Ministry of Health and Sanitation, 2018). The samples come from all over the country from both private and government health facilities offering HIV ART services. Sierra Leone is located within the Western African region with a population of 7.5 million (BAILEY and MAKANNAH, 1996) and a general HIV prevalence of 1.7%(Yendewa *et al.*, 2018).

Study participants and data collection

A total number of 8657 patients receiving ART were included in this study. We used VL testing data for HIV positive patients who had been on ART for at least 6 months. Data were extracted from the VL testing at CPHRL for period from January 2018 to June 2020. Variables with missing values were 16% of all the variables in the data set. Missing values were dropped automatically from each variable and analysis.

Measures

The primary outcome was viral non-suppression, defined as having ≥1000 copies of viral RNA/ml of blood for plasma or ≥5000 copies of viral RNA/ml of blood for dry blood spots. Any measurement more than ≥1000 copies of viral RNA/ml of blood for plasma or ≥5000 copies of viral RNA/ml of blood for dry blood spots will be considered as high viral non-suppression. (World Health Organization, 2020). We abstracted data on viral load testing results (for plasma and DBS) measured in terms of viral RNA copies/ml of blood. We defined viral load testing as routine monitoring, suspected treatment failure, and repeat VL test after suspected treatment failure. The laboratory analysis was based on the qualitative Nucleic Acid Amplification assay, which is polymerase chain reaction (PCR) test for HIV1. PCR is a molecular method for amplifying and finding particular HIV-1 RNA, proviral DNA, anticoagulated whole blood in plasma and dried blood spots. Test was done using the COBAS Ampliprep/Taq man 48 analyzers (Roche Molecular Diagnostic Assay, automated PCR)

Data analysis

We analyzed ART data set to estimate the proportion of patients with viral non-suppression, among patients receiving ART. We analyzed demographic, clinical characteristics, and proportions of patients with viral non-suppression. Variables included in the analysis were age group, gender, duration on treatment, reported adherence levels, having active TB, treatment line, reason for VL test.

We used bivariate analysis to determine variables associated with outcome variable (viral non-suppression). Crude odds ratios (OR) and 95% confidence intervals were calculated. Variables had significant association at bivariate level were identified. We used multivariate to control for confounding and identify factors independently associated with viral non-suppression. Adjusted odds ratios (aOR) and 95% confidence intervals were calculated. Statistical significance was considered at *p*-value <0.05 (two-sided). Data were entered into Excel 2007 and analyzed using Epi-info version 7.

Ethical consideration

We used secondary data collected for routine patient care at all health facilities in Sierra Leone and submitted to the CPHRL. No personal identifiable information was included this study. The data were not accessible by any other third parties other than the main investigators. Permission to use the data was sought from the Sierra Leone Ministry of Health and Sanitation and from the CPHRL.

RESULTS

Table 1: **Socio-demographic and clinical characteristics of HIV patients on ART, January 2018 – June 2020 (N = 5680)**

Variable	General-*N* (%)	Routine monitoring, *n* (%)	Suspected treatment failures, *n* (%)
Age group (years)			
< 15	438 (7.7)	21 (13.9)	225 (14.6)
15 – 35	2575 (47.3)	59 (39.1)	684 (44.2)
≥ 36	2667 (47.0)	71 (47.0)	638 (41.2)
Sex			
Female	1456 (25.6)	1195 (24.5)	79 (27.9)
Male	4224 (74.4)	3674 (75.5)	204 (72.1)
Duration on treatment			
6 months - <1 year	980 (17.2)	964 (19.8)	11(3.9)
1year -< 2 years	1405 (24.7)	1302 (26.7)	51 (18.0)
2 years - < 5 years	1804 (31.8)	1495 (30.7)	119 (42.1)
≥ 5 years	1491 (26.3)	1108 (22.8)	102 (36.0)
Treatment Line	5427 (95.5)	4675 (96.0)	269 (95.0)

First line Second line Other regimen	134 (2.4) 119 (2.1)	103 (2.1) 91 (1.9)	7 (2. 7 (2.
ARV adherence Poor <85% Fair 85-94% Good >95	 151 (2.7) 1547 (27.2) 3982 (70.1)	 121 (2.5) 1286 (26.4) 3462 (71.1)	 5 (1. 75 (2 203 (
TB status			
Yes No	109(1.71%) 6248(98.3%)	138 (1.1) 5723 (46.0)	7(1.0 603 (

The study was composed of 8,657 HIV patients, 4224 (74%) were male, and 94.3% were more than 15 years old. The overall proportion of non-suppression was 22%, and majority of them found in the age group between 15 -35 which accounted for 9531 (43%). Female accounted for 876 (71%) of the non-suppressed patients. Of the total, 7619(88%) patients were under routine monitoring, 659(7%) in suspected treatment failures while 379(4%) patients were repeat testers after suspected failure. Out of the total, 32% of patients under for a period between 2 years and less than five years, while those who received treatment for five years and more accounted for 26%. Only 109(2%) HIV patients co-infected with tuberculosis (Table 1).

A total of 1,226 (26.6) HIV patients enrolled on ART treatment. Patient involved in first-line ART treatment had non-suppression which accounted for 1156 (94%). Majority of non-suppressed patients, 1156 (94%) were receiving first-line ART treatment. Viral non-suppression was accounted for 531 (43.3) among patients aged between 15 -35 years, while it was 495 (40.4) for patients older than 35 years.

Table 2: Proportion of HIV patients on ART with virologic non-suppression (N=1226)

Variable	Non-suppression status n (%)
Overall	1,226 (26.6)
Age (years)	
< 15 15 – 35 ≥ 36	200 (16.3) 531 (43.3) 495 (40.4)
Sex	
Male	350 (28.6)
Female	876 (71.4)
Duration on treatment	
6 months - <1 year 1year -< 2 years 2 years - < 5 years ≥ 5 years	174 (14.2) 296 (24.1) 402 (32.8) 354 (28.9)
Treatment Line	
First line	1156 (94.2)
Second line	35 (2.9)
Other regimen	35 (2.9)
Indication for viral load testing	
Routine monitory	1045 (85.2)
Suspected treatment failure	51 (4.2)
Repeat testing	130 (10.6)
ARV adherence	
Poor <85%	74 (6.0)
Fair 85-94%	466 (38.0)
Good >95	686 (56.0)
TB status	
Yes	14 (1.1)
No	1212 (98.9)

Patients on repeat testing registered the lowest proportion, (20%), of non-suppressed patients. Viral non-suppression was accounted for 1045 (85%) among patients on routine monitory after suspected failure, while accounted only 51 (4.2) for patients under suspected treatment failure (**Error! Reference source not found.**). Tuberculosis was accounted for only 14 (1.1) among HIV patients with viral non-suppression.

Table 2: **Factors associated with viral non-suppression among HIV patients on ART, January 2018 - June 2020**

Variable	Supressed	Not suppressed	aOR(95% CI)	P-Value
Duration on treatment				
6 months - <1 year	8061	174	Ref	**0.173**
1yr -< 2 years	1109	296	-0.02(-0.06-0.01)	**0.039**
2 years - < 5 years	1402	402	-0.03 (-0.07-(-0.00)	**0.001**
≥ 5 years	1137	354	-0.06 (-0.09-(-0.02)	
ARV adherence				
Poor <85%	771	746	Ref	**<0.001**
Fair 85-94%	1081	686	0.19 (0.12-0.26)	**<0.001**
Good >95	3296		0.30 (0.23-0.36)	
Indication for viral load testing				
Routine monitory	3824	1045	Ref	0.111
Repeat testing	232	513	0.34(-0.01-0.09)	0.094
Suspected treatment failure	398	130	0.01(-0.03-0.05)	
Treatment line				
First line	4271	1156	Ref	**0.008**
Second line	9984	3584	0.10 (0.03-0.17)	0.934
Other regimen			0.00 (-0.07-0.08)	
Age				
Under 15	2382	200	Ref	**<0.001**
15-35	2044		0.22(0.19-0.27)	
Above 36	2172	531495	0.25 (0.21-0.29)	**<0.001**

Patient adhered to ARV treatment were less likely to have viral non-suppression (aOR= 0.03, 95%CI = 0.23-0.36). The odds of viral non-suppression was decreased with age increase for both children aged <15 years (aOR = 0.22, 95%CI = 0.19-0.27) and young adolescents (aOR = 0.22 95%CI = 0.21-0.29). Patients receiving second-line regimens (aOR= 0.1, 95%CI = 0.03-0.17) protected against viral non-suppression (Table 2).

DISCUSSION

In this study we estimated the proportion of patients with viral non-suppression and identifies risk factors associated with non-suppression. The overall proportion of viral non-suppression was 23.1%, which is relatively low compared to a system review study which reported 50% (Ford *et al.*, 2019), but was higher than the proportion reported in Uganda (11%) (Bulage *et al.*, 2017b). Our finding was lower than a results of study conducted in Ghana, where the viral non-suppression was 41% (Anito *et al.*, 2022). We observed that patients among age group 15-35 years, those who on routine monitoring treatment, patients receiving first-line treatment, and those with good adherence had high non-suppression proportions.

Despite that our study observed high non-suppression among age group 15-35 years, study conducted in Ghana concluded that that the prevalence of non-suppression was high among children less than 15 years (Afrane *et al.*, 2021). We observed high non-suppression proportion among patients in first-line treatment which in discordance with study conducted in Uganda, where viral suppression was high (Crawford *et al.*, 2015). Based on our finding, children up to 15 years were less likely to be non-

suppressed compared to the rest of the age groups. Study conducted in Rwanda found that viral suppression was less likely among young people between 15 – 24 years (Ross *et al.*, 2020). ARV treatment for children and adolescents has several challenges such as pediatric care provision and complexity of the ARV dosing. Other factors that might affect the children treatment include type of caretakers for children, transition to adolescence, stigma, and schooling environment. Study conducted in USA among children and adolescents indicated that challenges such as caregiver literacy can affect the proper treatment administration which can lead to viral non-suppression (Lee *et al.*, 2021). In a hospital-based study conducted in India to assess factors affecting adherence in children, concluded that caretaker's forgetfulness and momentary problem were the factors contribution on the viral non-suppression. Other factors affecting adherence to HVI treatment in children included long distance to the treatment center and unavailability of parents or caretakers (Verma *et al.*, 2020).

We observed that patients adhered to ART were less likely to have non-suppression. This finding was supported by systematic review results in Sub-Sharan Africa where low adherence as associated for viral failure (Agegnehu *et al.*, 2022). Our finding indicated that viral non-suppression was decreased when age increased and it was statistically significant. On contrary, study conducted in Ethiopia among HIV patients receiving first-line treatment found that adult age is associated with viral failure (Mengistu *et al.*, 2022). Our finding revealed that patients involved in second-line regimens were less likely to suffer fromviral non-suppression. Astudy conducted in China reported that patients shifted from first-line regimen to second-line had better viral response as compared to the period before shifting from first-line regimen (Cao *et al.*, 2018). We found that good adherence to ARV treatment was associated with the viral non-suppression. Our finding was in agreement with results of study conducted in Ethiopia where poor adherence to ART was associated with viral failure (Agegnehu, Merid and Yenit, 2020).

The main strength of this study is, we analyzed national data which is adequate to inform decision making. Despite this strength, this study had some limitations. Firstly, the study analyzed secondary data of ART patients and the data had missing records which might have led to bias. In cross-sectional study design, we cannot establish causality between outcome and exposure variables.

Conclusion

Viral non-suppression was relatively low among patient on ART in Sierra Leone. ARV treatment adherence, being adult and patient receiving first-line treatment were protective factors against viral suppression. We recommend close follow-up for children and to intensify adherence support for patients suspected with treatment failure.

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