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90-90-90 Ambitious Targets: Achieving the Last 90 of the UNAIDS Targets in Western Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Authors SOU, OO, GPO, AA, FA, GBA and OA' designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors SOU, OO, GPO, FA, TA, OA, MO and AA managed the analyses of the study. Authors SOU, OO, GPO, TA, GBA and MO managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: In resource-limited settings, where genotypic drug resistance testing is rarely performed and poor adherence is regarded as the most common reason for treatment failure, programmatic approaches to handling treatment failure are essential. This study is thus aimed at determining and monitoring HIV/AIDS disease progression using viral load to provide prognostic information and evaluate all patients for viral suppression using the World Health Organization (WHO) guideline strategies.

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Methods: This study was an observational longitudinal prospective study of subjects living with HIV already initiated on antiretroviral (ARV) therapy for at least six months, with a minimum of two CD4 cell count test done, enrolled at PEPFAR-supported health facilities Ekiti State, Western Nigeria. All data were statistically analysed, using statistical package for the social sciences (SPSS) and statistical test of significance was performed with Chi-Square test while multiple comparisons were done using Post Hoc Bonferonni test.
Results: A total of 910 subjects eligible for the study were recruited. Most of them were in the age range of 30 – 44 years, with a mean age ± SD of 40.75 ± 10.33 years. There was a significant increase in the average cell count of the subjects while 787 (86.5%) & 490 (53.9%) of the subjects had viral suppression of <1000 RNA copies per ml and <50 RNA copies per ml respectively on all tests during the period of observation. 96% of the subjects with <50 RNA copies per ml, are currently on first line regimen.
Conclusion: HIV treatment intensive adherence counselling is key to the reduction of virologic treatment failure, thus, routine monitoring of viral load alongside CD4 cell count will ultimately reduce treatment failure tendencies thereby helping more patients stay on first line regimen and prolong their life expectancy, indicating that the UNAIDS 90-90-90 targets are achievable in resource-constrained settings.

Keywords: Adherence; viral load; Nigeria; target.

1. INTRODUCTION

HIV RNA (viral load), along with CD4 T-lymphocyte (CD4 cell count) are two markers of antiretroviral treatment (ART) responses and the HIV/AIDS disease progression used to manage and monitor the infection in patients living with virus. The magnitude of the viral load after ART initiation provides prognostic information about the disease progression. The key goal of ART is to achieve and maintain durable viral suppression. Optimal viral suppression is defined generally as a viral load persistently below the level of detection (usually < 20 - 75 copies/mL, depending on the assay used) [1,2,3]. The guidelines of the World Health Organization (WHO) for the treatment of Human Immunodeficiency Virus (HIV) infection recommend that, where possible, the viral loads of individuals receiving ART be measured every month to detect viral replication and confirm treatment failure whenever it occurs [4]. Although, the viral load tests are currently unaffordable for routine use in many low and middle income countries (LMICs), including Nigeria, the potential for increased access to such tests exists as costs decrease and countries prioritize this method of patient monitoring [3].

According to the WHO's strategy for the surveillance and monitoring of HIV drug resistance in Low & Middle Income Countries (LMICs), a viral load of <1000 RNA copies per ml should be taken as evidence of viral suppression [5]. Guidelines for the treatment of HIV infection in high-income countries stipulate that a viral load of <50 RNA copies per ml or a load below the limit of detection of the most sensitive assay available, be taken as evidence of viral suppression [6,7,8]. According to a study in Botswana from Harvard T.H Chan school of Public Health & Colleagues, Botswana was reported to have achieved very high rates of HIV diagnosis, treatment and viral suppression, even much better than most Western Nations. The country was reported to have 96.5% viral suppression [9]. In another 2016 research, 78.5% of HIV patients in care were reported to have a suppressed viral load based on a single test while 65.9% were virally suppressed based on a minimum of two or more rounds of test done [10].

In a 2015 study carried out on the scale- up of HIV viral load monitoring across seven Sub-Saharan African countries revealed that South Africa, for instance, initiated viral load monitoring in 2004 and scale up for routine viral load monitoring in 2014 on the basis of the 2013 WHO HIV treatment recommendations. Thus, the proportion of viral load monitoring scale up was 78% in South Africa, 83% in Kenya, 84% in Malawi, 86% in Namibia, 94% in Uganda, 53% in Cote d'voire and 72% in Tanzania [11]. In another Uganda study, 6% of the patients were reported to have experienced virological failure, which was defined as two consecutive viral loads >500 copies/ml occurring more than three months after the start of ART [12]. The aim of the study was to determine and monitor the

HIV/AIDS disease progression using viral load to provide prognostic information and evaluate all patients for viral suppression, with intensive adherence counselling, using the World Health Organization (WHO) guideline strategies.

1.1 Research Hypothesis

1) Current antiretroviral (ARV) therapy regimen does not significantly have impact on viral load outcome.
2) Antiretroviral (ARV) therapy adherence does not significantly have impact on viral load outcome.
3) WHO clinical staging does not significantly have impact on viral load outcome.

2. METHODS

This study was an observational longitudinal prospective study of subjects living with HIV already initiated on antiretroviral (ARV) therapy for at least six months and who have done viral load test, enrolled at various secondary and tertiary level hospitals supported by donor/funder (PEPFAR) on HIV/AIDS program across Ekiti State during a 12-month observation period starting January 2016 till December 2016. The study populations were adult and paediatric patients living with HIV already initiated on antiretroviral (ARV) therapy for at least six months, with a minimum of two CD4 count test results and viral load test done. Relevant data such as age, sex, functional status, WHO clinical staging, CD4 cell count, ARV regimen at start and current, ARV adherence level, among others were obtained and analysed. The CD4+ count was carried out using a flow cytometry technique through a Cyflow counter (Partec GmbH Görlitz, Germany) while viral load was done using Cobas Taqman 48 Analyzer.

The data analysis was done using statistical package for the social sciences (SPSS) for windows version 23.0 software (SPSS Inc; Chicago, IL, USA). Frequency counts were generated for all variables and statistical test of significance was performed with chi-square test. Other data were expressed as Mean ± Standard Deviation and analysed with Analysis of Variance (ANOVA) while multiple comparisons were done using Post Hoc Bonferonni test. Significance was fixed at $P < 0.05$ and highly significance if $P < 0.01$.

3. RESULTS

3.1 Socio-demographic Data

A total of 910 subjects eligible for the study were recruited. The mean age ± SD of the subjects was 40.75 ± 10.33 years. 752 (82.6%) were recruited from tertiary hospitals within the state while 158 (17.4%) were from secondary facilities.The mean number of active years ± SD of subjects is 4.34 ± 2.44 years.

The functional status of all the subjects who were on ART was working, that is, able to work, do housework and other day-to-day activities while they all did not have signs or symptoms of tuberculosis during the review period. The WHO clinical staging of the subjects used was as the time subjects were on ART while the viral load was performed for subjects living with HIV already initiated on antiretroviral (ARV) therapy for at least six months. Using the WHO strategy, those having viral load <1000 RNA copies per ml, were 701 (77.0%), out of which 430 (47.3%) were having viral load <50 RNA copies per ml, while 209 (23.0%) had viral load >1000 RNA copies per ml. The 209 went through intensive adherence counseling for three months and viral load test repeated three further months after. 86 of the subjects (41.1%) had viral load <1000 RNA copies per ml, from which 60 (28.7%) were <50 RNA copies per ml. Thus, 787 (86.5%) & 490 (53.9%) of the subjects had <1000 RNA copies per ml and <50 RNA copies per ml respectively on all tests during the period of observation.

4. DISCUSSION

The outcome of this research reveals that 77.0% of the subjects had a suppressed viral load based on a single test and using the WHO's strategy for the surveillance and monitoring of HIV drug resistance in Low & Middle Income Countries (LMICs), which indicated that a viral load of <1000 RNA copies per ml should be taken as evidence of viral suppression [5]. The virally unsuppressed subjects went through a period of intensive adherence counselling on therapeutic medication regimen in order to control viral replication and improve immune system function, for three consecutive months and viral load repeated three further months after. This adherence counselling process increased the virally suppressed in this category to 86.5% based on all tests done during the period of observation.

Meanwhile, in comparison with high-income countries where the guidelines stipulate that a viral load of <50 RNA copies per ml or a load below the limit of detection of the most sensitive assay available, be taken as evidence of viral suppression [6, 7, 8] and on the basis of a single test done, 47.3% of the subjects achieved viral suppression, however, after the period of intensive adherence counselling for the unsuppressed subjects, the proportion moved up to 53.9%. These outcomes are slightly similar to a study that reported 78.5% viral suppression [10], but differ slightly from a Botswana study that reported 96.5% viral suppression [9]. This generally however shows that more subjects exhibited improvement, as they went from unsuppressed to suppressed status, within a short period of adequate drug adherence. The CD4 cell count monitored showed significant increase in the average cell count of subjects, indicating better clinical outcomes, with majority of the subjects having their CD4 cell count increased over the course of treatment. Thus, routine monitoring of viral load alongside CD4 cell count will ultimately reduce treatment failure tendencies thereby helping more patients stay on first line regimen.

The rejection of the first hypothesis on the impact of current ARV therapy regimen on viral load outcome, shows that the particular regimen a patient is placed on, significantly have effect on the viral load outcome. This is given credence by the fact that an estimated 96% of the subjects with <50 RNA copies per ml, are currently on first line regimen, mainly of the combinations Tenofovir, Lamivudine & Efavirenz (1E) and Zidovudine, Lamivudine & Nevirapine (1B), which is a sign of drug efficacy and reduced tendency of drug switch. This is thus an indication for treatment success. Moreover, the rejection of the second hypothesis on the influence of ARV therapy adherence on viral load outcome, indicates that drug adherence significantly determines outcome of viral load, evident by the ART adherence of all subjects with <50 RNA copies per ml having ≥ 95% (good) drug adherence, which shows that they have either not missed any dose or few missed ≤ 3 doses, also indicating treatment success. However, the acceptance of third hypothesis on the impact of WHO clinical staging on viral load outcome, shows that it does not necessarily determine the outcome, though , majority of the subjects with viral suppression were classified to be stage I.

Table 1. Socio-demographic & treatment data

Variables	Frequency (%)
Age group (years)	
< 15	7(0.8)
15 – 19	2 (0.2)
20 – 24	12 (1.3)
25 – 29	67 (7.4)
30 – 34	165 (18.1)
35 – 39	198 (21.8)
40 – 44	165 (18.1)
45 – 49	108 (11.9)
50 – 54	88 (9.7)
55 – 60	57 (6.3)
> 60	41 (4.5)
Sex	
Male	181 (19.9)
Female	729 (80.1)
Hospital facility	
Tertiary	752 (82.6)
Secondary	158 (17.4)
Antiretroviral Therapy (ART) taken at start of treatment	
Zidovudine, Lamivudine & Efavirenz (1A)	2 (0.2)
Zidovudine, Lamivudine & Nevirapine (1B)	580 (63.7)
Tenofovir, Emtricitabine & Efavirenz (1C)	2 (0.2)
Tenofovir, Lamivudine & Efavirenz (1E)	326 (35.8)

Variables	Frequency (%)
Antiretroviral Therapy (ART) currently used	
Zidovudine, Lamivudine & Nevirapine (1B)	144 (15.8)
Tenofovir, Emtricitabine & Efavirenz (1C)	2 (0.2)
Tenofovir, Lamivudine & Efavirenz (1E)	734 (80.7)
Tenofovir, Lamivudine &Nevirapine (1F)	1 (0.1)
Tenofovir, Emtricitabine & Lopinavir/Ritonavir (2A)	2 (0.2)
Tenofovir, Lamivudine & Lopinavir/Ritonavir (2B)	22 (2.4)
Tenofovir, Lamivudine & Atazanavir/Ritonavir (2D)	1 (0.1)
Zidovudine, Lamivudine & Lopinavir/Ritonavir (2E)	4 (0.4)
Antiretroviral Therapy (ART) Adherence	
Fair (85 – 94%) / (4 – 8 doses missed per month)	46(5.1)
Good (≥ 95%) / (≤ 3 doses missed per month)	864 (94.9)
Cotrimoxazole Adherence	
Fair (85 – 94%) / (4 – 8 doses missed per month)	13 (1.4)
Good (≥ 95%) / (≤ 3 doses missed per month)	897 (98.6)
CD4 cell count at treatment commencement(cells/µL)	
< 50	93 (10.2)
50 – 100	144 (15.8)
101 – 200	242 (26.6)
201 – 300	195 (21.4)
301 – 400	208 (22.9)
401 – 499	28 (3.1)
CD4 cell count done before the last(cells/µL)	
< 50	45 (5.0)
50 – 100	43 (4.7)
101 – 200	171 (18.8)
201 – 300	181 (19.9)
301 – 400	178 (19.6)
401 –500	152 (16.7)
501 – 600	58 (6.4)
>600	82 (9.0)
Last CD4 cell count done(cells/µL)	
< 50	31 (3.4)
50 – 100	31 (3.4)
101 – 200	150 (16.5)
201 – 300	166 (18.2)
301 – 400	127 (14.0)
401 – 500	140 (15.4)
501 – 600	111 (12.2)
>600	154 (16.9)
Number of years active on treatment	
1 year	85 (9.3)
2 years	182 (20.0)
3 years	153 (16.8)
4 years	109 (12.0)
5 years	103 (11.3)
6 years	75 (8.2)
7 years	62 (6.8)
8 years	67 (7.4)
9 years	74 (8.1)

Table 2. Comparison of CD4 cell count results at treatment commencement and the last two done six months apart

Groups	Parameter
	CD4 count (cells/µL)
CD4 count at treatment commencement	194.28 ± 113.83
CD4 count before the last	329.61 ± 219.42
Last CD4 count	394.03 ± 240.30
F-value	238.761
P-value	0.001*
POST HOC	
a/b	0.001*
a/c	0.001*
b/c	0.001*

KEY: a – CD4 count at treatment commencement
b – CD4 count before the last
c – Last CD4 count
** = Results compared are significantly different at P-value < 0.05 (P < 0.05)*

Table 3. Chi square result showing influence of current ARV therapy regimen, ARV therapy adherence & WHO clinical staging on viral load outcome

Variables	χ^2	df	Critical value	Decision
Current ARV therapy regimen influence on viral load outcome	68.585	24	36.415	Rejected
ARV therapy adherence influence on viral load outcome	15.141	6	11.070	Rejected
WHO clinical staging influence on viral load outcome	13.046	9	16.919	Accepted

The null hypothesis is rejected when the test statistic (χ^2) is greater than the critical value

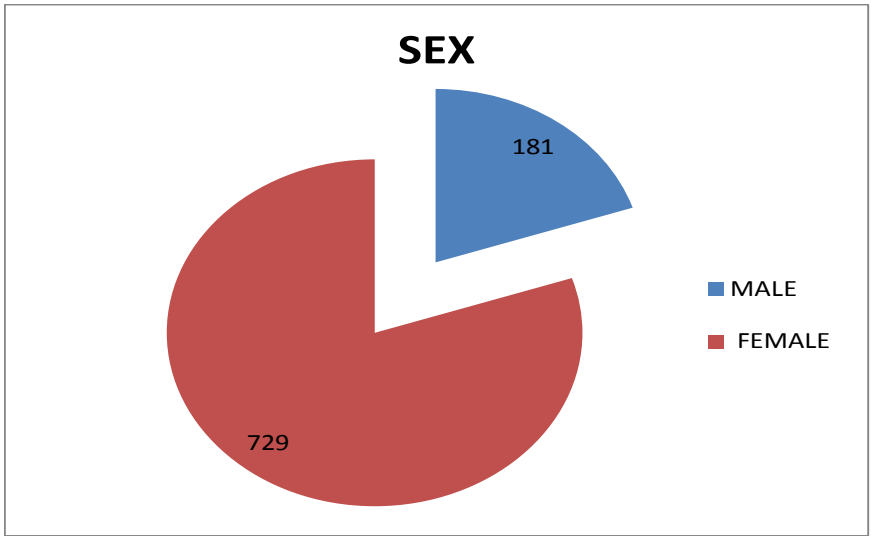

Fig. 1. Sex of the subjects

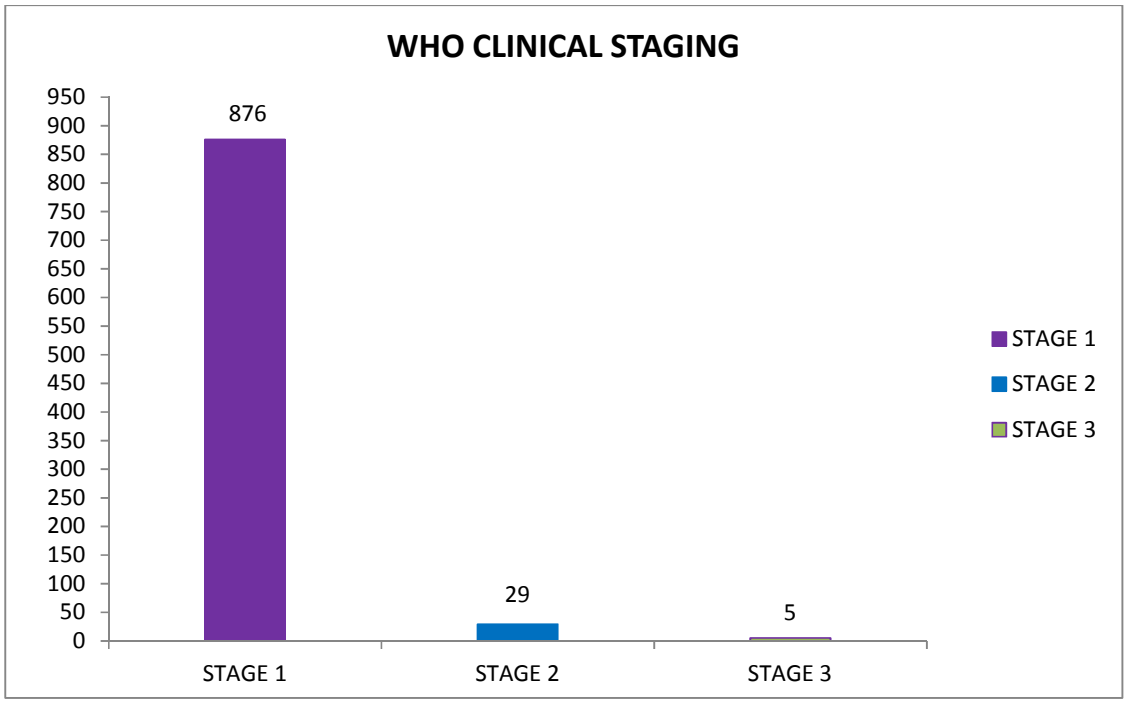

Fig. 2. WHO clinical staging of the subjects

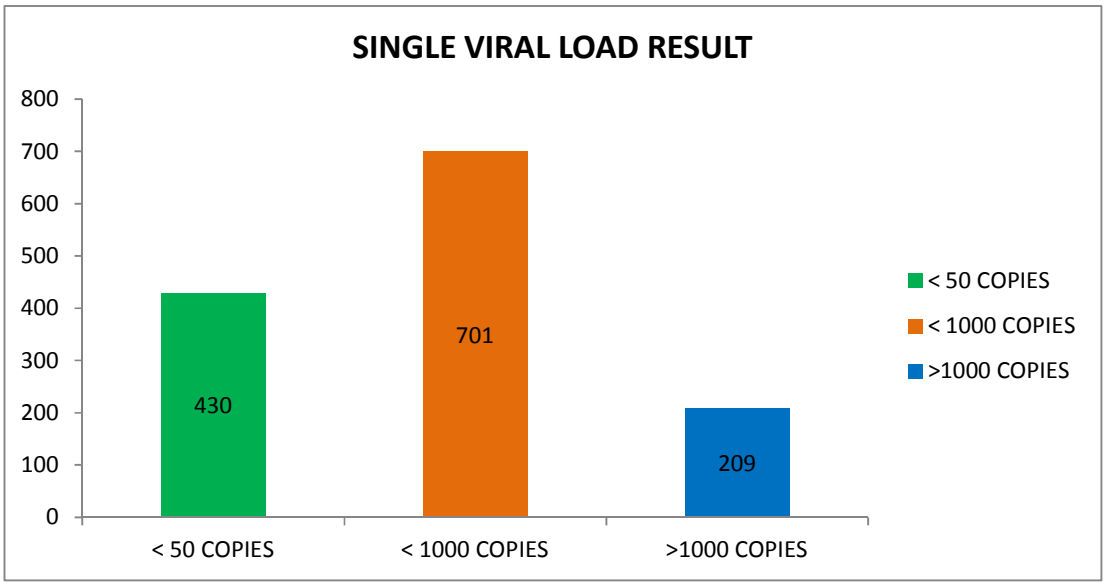

Fig. 3. Viral load results of the subjects

5. CONCLUSION

With a 53.9% viral load suppression based on a viral load of <50 RNA copies per ml suppression level, HIV treatment intensive adherence counselling is key to the reduction of virologic treatment failure, thus, routine monitoring of viral load alongside CD4 cell count will ultimately reduce treatment failure tendencies thereby helping more patients stay on first line regimen and prolong their life expectancy, indicating that the UNAIDS 90-90-90 targets are achievable in resource-constrained settings especially with well controlled intervention, which will be required to

determine the optimal approach to improve first-line regimen outcomes and reduce the need for regimen switch.

CONSENT

All authors declare that 'written informed consent was obtained from the subjects and other approved parties for publication of this paper and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee (the ethical review committee of the Federal Teaching Hospital, Ido Ekiti, Nigeria) and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki."ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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