Magna Scientia Advanced Biology and Pharmacy

eISSN: 2582-8363

Cross Ref DOI: 10.30574/msabp

Journal homepage: https://magnascientiapub.com/journals/msabp/

(RESEARCH ARTICLE)

The Impact of Highly Active Antiretroviral Therapy (HAART) on Viral Load and CD4 Count amongst HIV-1 infected Subjects in Federal Medical Center Lokoja, Nigeria

Emeje Paul Isaac [1,*], James Garba Damen [2] and Oyibo Saidu Silas [3]

[1] *Department of Medical Laboratory Science, Faculty of Allied Health Sciences, College of Health Sciences, Federal University Lokoja, Kogi State, Nigeria.*

[2] *Department of Medical Laboratory Science, Faculty of Health Sciences and Technology, College of Health Sciences, University of Jos, Jos, Plateau State, Nigeria.*

[3] *Department of Nursing Sciences, Faculty of Allied Health Sciences, College of Health Sciences, Federal University Lokoja, Kogi State, Nigeria.*

Magna Scientia Advanced Biology and Pharmacy, 2024, 13(02), 017–026

Publication history: Received on 08 October 2024; revised on 19 November 2024; accepted on 21 November 2024

Article DOI: https://doi.org/10.30574/msabp.2024.13.2.0066

Abstract

This study was aimed at evaluating the role of antiretroviral drug monitoring, viral load, and CD4 counts amongst HIV-1 infected individuals in FMC, Lokoja, Nigeria, that randomly recruited 154 participants within the age range of 18 and 65 years with a population- based sample of males and females divided into three groups designated A to C; comprising of 40 HIV-1 seropositive individuals on HAART (TDF + 3TC + EFV) designated as group A, 35 HIV-1 seropositive individuals on HAART (AZT + 3TC +NVP) designated as group B, and 79 HAART naïve HIV-1 seropositive individuals designated as control group C. Two points blood samples were taken for group A and group B participants for the measurement of drugs(HAART) using HPLC, HIV-1 RNA Load using PCR and CD4 counts using flow cytometry while one point samples were taken for group C for the measurement of HIV-1 RNA Load and CD4 counts. Data were expressed as mean ± standard deviation and Chi-square analysis. The results showed a significant difference in HIV-1 RNA Load and CD4 counts in group A when compared to group B and group C ($p<0.05$). There was also a significant difference in HIV-1 RNA Load and CD4 counts in group B when compared with group C ($p<0.05$). Plasma drug concentrations were higher at 12 months of therapy when compared with plasma drug concentrations at 6 months ($p<0.05$) with 17.4% virologic failure in participants on nevirapine based regimen and 7.5% virologic failure amongst participants on efavirenz based regimen; this showed the superiority efficacy of efavirenz based regimen to nevirapine based regimen.

Keywords: HAART; HIV-1 RNA Viral Load; CD4 Count; Therapeutic level; Sub-therapeutic level

1. Introduction

About 20 million death were due to drug failure in HIV/AIDS patients globally in 2005 [30, 31]. It is well documented that drug toxicity happens commonly among patients with supra-therapeutic drugs level than among patients with therapeutic drug concentrations. Also, non-virologic suppression is common among patients with sub-therapeutic drugs level. Therefore, it is important to develop early indicators of drugs failures that are reliable as this will determine switch in drug combination [4].

Determination of viral load remains gold standard in determining the viraemia in HIV infected individuals. However, monitoring of drug concentrations in resource-limited countries also has a strong potential due to its alignments with the viral loads.

* Corresponding author: Emeje Paul Isaac

Not all the health care giving centres has the facility for determining HIV viral loads. Since the major successful intervention in HIV/AIDS management now is the administration of HAART, considering measurement of plasma antiretroviral drug concentrations is imperative due to good association between virologic suppression and therapeutic drugs level [30, 31].

The HIV/AIDS pandemic has severely affected health development and eroded improvements in life expectancy, particularly in developing countries with the highest prevalence of infection [32]. Expanding access to antiretroviral therapy in resource-limited settings along with close monitoring is needed for successful treatment outcomes [1]. In high income settings, this is achieved by performing quantitative viral load monitoring every 3-6months [1]. However,in resource limited settings, patient evaluation is based on CD4+ T-cell count, clinical findings, neither of which accurately predicts viral suppression [17]

2. Material and methods

2.1. Study Site

The study was carried out on HIV-1 infected individuals at Federal Medical Centre, Lokoja, Kogi State, Nigeria.

2.2. Study Design

In this study, 154 participants aged between 18 and 64 (37 ± 11.4) years were randomly recruited. This was a longitudinal study in which 40 individuals on antiretroviral drugs (efavirenz, Lamivudine and tenofovir) served as test participants designated on group A, 35 individuals on antiretroviral drugs (nevirapine, Lamivudine and zidovudine) also served as test participants designated as group B while 79 HIV-1 seropositive HAART naïve individuals served as control designated as group C. Two point blood samples were collected from each test participants (group A and group B) at 6 months and 12 months exposure to antiretroviral drugs while one point sample was taken from the control participants (group C) for the determination of HIV-1 viral load and immunologic marker (CD_4^+ cells count).

2.3. Inclusion and exclusion criteria

Inclusion criteria were adult HIV-1 seropositive individuals diagnosed using Nigeria national algorithm, aged between 18 and 64 (37 ± 11.4) years without virologic and immunologic failure. HIV-1 seropositive individuals on first-line antiretroviral drugs not exceeding 6 months of therapy were included in the study. HIV-1 seropositive individuals that had co-morbidity such as renal disease, heart diseases, diabetes were excluded. HIV-1 pregnant women on antiretroviral drugs and HIV-1 seropositive individuals co-treated with anti-tuberclosis medications were excluded. HIV-1 seropositive individuals on first line regimen above 12 months of therapy were also excluded. HIV-1 seropositive individuals on contraceptives, alcoholics and smokers were excluded from the study. HIV-1 seropositive individuals on first-line regimen other than efavirenz based regimen (efavirenz, lamivudine and tenofovir) and nevirapine based regimen (nevirapine, lamivudine and zidovudine) were excluded from the study.

2.4. Sample Collection

Eight milliliters of venous blood was collected from each subject at point of joining the research and six months after joining the research. 4ml of blood was dispensed into Ethylene diamine tetra-acetic acid (EDTA) bottle and was used for CD_4 count, viral load and antiretroviral drug concentrations, 4 ml of blood was dispensed into another EDTA bottle for drug concentrations, sample for drugs when taken, were centrifuged immediately at 3000rpm for 3 minutes, plasma obtained were stored at -20^{0}C before analysis. For CD^+_4 counts; whole blood samples was used to measure the CD_4+ count immediately after samples were collected.

2.5. Methods

2.5.1. HIV viral load assay by polymerase chain reaction (RT PCR using COBAS ampliprep/COBAS Taqman) [5]

Principle

The principle of viral load was based on RNA extraction, amplification and quatification of amplified RNA using RT-PCR. The principle involves primers mediated enzymatic amplification, involving the ability of DNA polymerase to use primers to synthesize new strand of deoxyribonucleic acid or ribonucleic acid complementary to a given template.

2.5.2. CD^{+}_{4} count assay by flow cytometry using BD facscount [1].

Principle

When whole blood is added to the reagent tubes containing fluorochrome-labeled antibodies, the fluorochrome-labeled antibodies bind specifically to the antigens on the surface of lymphocytes, these surface antigens produces photons of light at excitation which is translated as CD_4^+ cells count.

2.5.3. ARVs (Antiretroviral drugs) measurement by high performance liquid chromatography [30]

Principle

The principle of high performance liquid chromatography is based on separation of mixtures of compounds due to differences in their distribution equilibrium between two phases: the stationery phase packed inside columns and the mobile phase, delivered through the columns by high pressure pumps.

2.6. Statistical Analysis

Values obtained were expressed as mean ± standard deviation (SD) using SPSS version 25.0. All numerical results were analyzed with one-way ANOVA with post hoc multiple comparisons test, paired student t-test was used to compare means from the same group at different times while qualitative variables analyzed using Chi-square. P≤0.5. Were considered statistically significant

3. Results

3.1. Characteristics of the Study Population

The characteristics of the study population (mean age, sex and residential status) are shown in table 1. The mean values of age in group A subjects on TDF + 3TC + EFV was 37± 9.73 years, while that of group B subjects on AZT + 3TC + NVP was 38 ± 10.63 years were significantly higher (P<0.01) than similar value in the controls (36 ± 8.71 years). However, women were the majority of subjects (71.43%). In total 108/154 (70.13%) of subjects were living in rural areas

Table 1 Characteristics of the Study Population

Variables	All subjects N = 154	Group A (TDF + 3TC + EFV) n = 40	Group B (AZT + 3TC + NVP) n = 35	Group C those not on drugs (control) n = 79	P values
Mean age in years (±SD)	36.68 (±11.4)	37.3 (±9.73)	38.11 (±10.63)	35.86 (±8.71)	0.005
Male	44 (28.57%)	11 (27.5%)	9 (25.71%)	24 (30.38%)	0.001
Female	110 (71.43%)	29 (72.5%)	26 (74.29%)	55 (69.62%)	0.001
Residential Status:					
(i) Semi-urban	46 (29.87%)	13 (32.5%)	12 (34.29%)	21 (26.58%)	0.05
(ii) Rural	108 (70.13%)	27 (67.5%)	23 (65.71%)	58 (73.42%)	0.001

*Values differ significantly from controls (P<0.05) C: Control group not on drugs ; N: Total Sample Size; AZT: Zidovudine; A: TDF + 3TC + EFV ; TDF: Tenofovir; n: Group Sample Size ; EFV: Efavirenz; B: AZT + 3TC + NVP; 3TC: Lamivudine; NVP: Nevirapine ; %: Percent; SD: Standard Deviation

3.2. Mean values of parameters in those on drug combinations (group A and B) at 12 Months and HIV-seropositive controls (group C) (mean ± SD)

The mean values of viral load and CD_4 cells count are shown in table 2. The values for participants in group A (efavirenz based regimen group) are 94±18 cp/ml and 515±81 cell/µl. The values for participants in group B (nevirapine based regimen group) are 160±30 cp/mland 579±53 cells/µl. The values for controls (group C) are 17429±1351 cp/ml and 584±27 ccells/µl. The values of viral load were significantly lower for the test participants (group A and group B) than in the controls (group C) ($p<0.05$). The CD_4^+ cells count values showed no significant difference between the test participants (group A and group B) and controls (group C) ($p>0.05$).

Table 2 Mean values of parameters (mean ± SD) in those on drug combinations (Group A and B) at 12 months and HIV-positive Controls (Group C)

GROUP	N	VL (copies/ml)	CD4 (cell/µl)
A	40	94±18	515±81
B	35	160±30	579±53
C	79	17429±1351	584±27
f-value		117.541	0.218
p-value		0.001*	0.804
A vs B		0.037*	1.000
A vs C		0.008*	1.000
B vs C		0.001*	1.000

*Significant; A: TDF + 3TC + EFV drug combination group; SD: Standard Devia ; B: AZT + 3TC + NVP drug combination group; VL: Viral load C: Control group not yet on drugs; N: Group Sample Size; CD: Cluster of Differentiation

3.3. Mean values of HAART, viral load and CD4 Count in HIV-1 infected individuals at 6 months and 12 months on antiretroviral therapy (tenofovir, lamivudine and efavirenz) in group A subjects

The mean values of viral load, CD_4 cells count, TDF, 3TC and efavirenz at 6 months and 12 months of therapy are shown in table 3. The values at 6 months are 9490±184 cp/ml, 509±30 cells/µl, 54.61±25.69 µg/ml, 17.39±5.89 µg/ml and 1182.70±488.38 ng/ml. The values at 12 months are 94±3 cp/ml, 520±40 cells/µl, 97.30±21.27 µg/ml**,** 22.83±2.42 µg/ml and 1573.26±487.45 ng/ml. The values of viral load at 12 months of therapy were significantly lower compared with viral load at 6 months of therapy ($P<0.05$). Similarly, the mean values of drug concentrations were significantly higher for the test participants (group A and group B) than in the controls (group C) ($p<0.05$). No significant difference in CD_4^+ cells count values at 12 months and 6 months of therapy ($P>0.05$).

3.4. Mean values of HAART, viral load and CD4 Counts in HIV-1 infected individuals at 6 months and 12 months on antiretroviral therapy (zidovudine, lamivudine and nevirapine) in group B

The mean values of viral load, CD_4 cells counts, AZT, 3TC and NVP at 6 months and 12 months of therapy are shown in table 4. The values at 6 months are 18036±83 cp/ml, 551±53 cells/µl, 1944.18±68.71 ng/ml, 12.17±4.97 µg/ml and 40.46±9.15 ng/ml. The values at 12 months of therapy are 160±21 cp/ml, 571±30 cells/µl, 2085.56±63.27 ng/ml, 14.64±5.07 µg/ml, and 35.93±6.60 ng/ml. The values of viral load were significantly lower at 12 months of therapy that the values of viral load at 6 months of therapy ($p<0.05$). The values of 3TC were significantly higher at 12 months of therapy than the values of 3TC at 6 months of therapy ($p<0.05$). The values of NVP at 12 months of therapy were significantly lower than the values of NVP at 6 months of therapy ($p<0.05$). No significant difference in CD_4^+ cells count and AZT values at 12 months and 6 months of therapy ($p>0.05$).

Table 3 Mean values of HAART, viral load and CD_4 Count in HIV-1 infected individuals at 6 months and 12 months on antiretroviral therapy (tenofovir, lamivudine and efavirenz) in group A subjects

Parameters	N	6 months	12 months	t-test	p-value
Viral load (copies/ml)	40	9490±184	94±3	2.948	0.005*
CD4 (cell/µl)	40	509±30	520±40	-5.541	0.211
TDF (µg/ml)	40	54.61±25.69	97.30±21.27	-9.454	0.001*
3TC (µg/ml)	40	17.39±5.89	22.83±2.42	-5.144	0.001*
EFV (ng/ml)	40	1182.70±488.38	1573.26±487.45	-4.158	0.001*

* Significant, TDF(Tenofovir): 80 – 160 µg/ml; N: Group Sample Size; 3TC(Lamivudine): 6 – 24 µg/ml; EFV(Efavirenz): 1000 – 4000 ng/ml

Table 4 Mean values of HAART, viral load and CD4 Counts in HIV-1 infected individuals at 6 months and 12 months on antiretroviral therapy (zidovudine, lamivudine and nevirapine) in group B

Parameters	N	6 months	12 months	t-test	p-value
Viral load (copies/ml)	35	18036±83	160±21	6.672	0.001*
CD_4^+ (cell/µl)	35	551±53	571±30	-3.147	0.063
AZT (ng/ml)	35	1944.18±68.71	2085.56±63.27	-.872	0.389
3TC (µg/ml)	35	12.17±4.97	14.64±5.07	-4.212	0.034*
NVP (ng/ml)	35	40.46±9.15	35.93±6.60	2.294	0.028*

* Significant; AZT(Zidovudine): 925 – 2,187 ng/ml; 3TC (Lamivudine): 6 – 24 ug/ml; B = AZT + 3TC + NVP drugs combination; NVP(Nevirapine): 34 – 80 ng/ml; N: Group Sample Size

3.5. Proportion of HIV-1 infected individuals with serum drug levels within or outside the therapeutic range among participants on efavirenz based regimen in group A

The efavirenz based regimen used in this group A was TDF + 3TC + EFV (Tenofovir, Lamivudine and Efavirenz respectively) as shown in table 5. Two point samples were taken and analyzed with the initial samples taken after 6 months of therapy designated as TDF_1 + $3TC_1$ +EFV_1 while second samples were the samples taken at 12 months of therapy from the same subjects designated as TDF_2 + $3TC_2$ + EFV_2.

Of the 40 participants enrolled; the sub-therapeutic, therapeutic and supra-therapeutic plasma antiretroviral drug concentrations at 6 months for TDF were 32/40 (80%), 8/40 (20%) and (0%) respectively. The sub-therapeutic, therapeutic and supra-therapeutic plasma antiretroviral drug concentrations at 6 months for 3TC were 2/40 (5%), 37/40 (92.5%) and 1/40 (2.5%) respectively while that of 6 months for EFV were 12/40 (30%), 28/40 (70%), and (0%) respectively.

The sub-therapeutic, therapeutic and supra-therapeutic plasma antiretroviral drug concentrations at 12 months for TDF were 4/40 (10%), 36/40 (90%) and (0%) respectively. The sub-therapeutic, therapeutic and supra-therapeutic plasma antiretroviral drug concentrations at 12 months for 3TC were (0%), 40/40 (100%) and (0%) respectively while that of EFV at 12 months were 4/40(10%), 36/40(90%) and 0% respectively.

3.6. Proportion of HIV-1 infected individuals with serum drug levels within or outside the therapeutic range among participants on Nevirapine based regimen in group B

The nevirapine based regimen used in this group B was AZT + 3TC + NVP (Zidovudine, lamivudine and nevirapine respectively). Two point samples were taken and analyzed with the initial samples taken after 6 months of therapy designated as AZT_1 + $3TC_1$ + NVP_1 while second samples taken at 12 months of therapy from the same subjects were designated as AZT_2 + $3TC_2$ + NVP_2.

Of the 35 participants enrolled; the sub-therapeutic, therapeutic and supra-therapeutic plasma antiretroviral drug concentrations at 6 months for AZT were 0%, 28/35 (80%) and 7/35 (20%) respectively as shown in table 6. The sub-therapeutic, therapeutic and supra-therapeutic plasma antiretroviral drug concentrations at 6 months for 3TC were 0%, 35/35 (100%) and (0%) respectively while that of nevirapine at 6 months were 9/35 (25.71%), 26/35 (74.29%) and (0%) respectively.

The sub-therapeutic, therapeutic and supra-therapeutic plasma antiretroviral drug concentrations at 12 months for AZT were 0%, 23/35 (62.71%) and 12/35 (34.29%) respectively. The sub-therapeutic, therapeutic and supra-therapeutic plasma antiretroviral drug concentrations at 12 months for 3TC were 0%, 31/35 (88.57%) and 4/35 (11.43%) respectively while that of nevirapine at 12 months were 13/35 (37.14%), 22/35 (62.86%) and 0% respectively. From this table 4.6, lamivudine in group B accounted a better therapeutic level than zidovudine and nevirapine.

Table 5 Proportion of HIV-1 infected individuals with serum drug levels within or outside the therapeutic range among participants on efavirenz based regimen in group A (n=40)

ARV Regimen	Duration	Sub- therapeutic	Therapeutic	Supra-therapeutic
TDF_1	6 months	32 (80%)	8 (20%)	0 (0%)
TDF_2	12 months	4 (10%)	36 (90%)	0 (%)
$3TC_1$	6 months	2 (5%)	37 (92.5%)	1 (2.5%)
$3TC_2$	12 months	0	40 (100%)	0
EFV_1	6 months	12 (30%)	28 (70%)	0
EFV_2	12 months	4 (10%)	36(90%)	0
Total		54(22.5%)	185(77.08%)	1(0.42%)

1: Initial result at 6 months; 2: Follow-up result at 12 months; %: Percent

Table 6 Proportion of HIV-1 infected individuals with serum drug levels within or outside the therapeutic range among participants on Nevirapine based regimen in group B (n=35)

ARV Regimen	Duration	Sub-therapeutic	Therapeutic	Supra-therapeutic
AZT_1	6 months	0 (0%)	28 (80%)	7 (20%)
AZT_2	12 months	0 (0%)	23 (62.71%)	12 (34.29%)
$3TC_1$	6 months	0 (0%)	35 (100%)	0 (0%)
$3TC_2$	12 months	0 (0%)	31 (88.57%)	4 (11.43%)
NVP_1	6 months	9 (25.71%)	26 (74.29%)	0 (0%)
NVP_2	12 months	13 (37.14%)	22 (62.86%)	0 (0%)
Total		22 (10.48%)	165 (78.57%)	23 (10.95%)

1: Initial result at 6 months; 2: Follow-up result at 12 months; %: Percent

3.7. Index of HIV-1 antigenic suppression in group A and B participants at 12 months of therapy

The antigenic suppression in group A participants were significantly higher than the antigenic suppression in group B participants ($\chi 2 = 9.857$, $p = 0.015$)as shown in table 7. In group A participants, 92.5% of the participants were viroligically suppressed and 7.5% of the participants were non-virologically suppressed. In group B participants, 82.9% of the participants were virologically suppressed while 17.1% of the participants were non-virologically suppressed

Table 7 Index of HIV-1 antigenic suppression in group A and B participants at 12 months of therapy

Group	Suppressed	Non-Suppressed	Total	Chi-square	p-value
Group A (n=40)	37(92.5%)	3(7.5)	40	9.857	0.015*
Group B (n=35)	29(82.9%)	6(17.1%)	35		
Total = 75	66	9	75		

* Significant; n= Group Sample Size

3.8. Figure 1: Proportions of participants with virologic and non-virologic suppression at 12 months of antiretroviral therapy.

Out of 75 participants on treatment; 40 participants are on efavirenz based regimen, 35 participants are on nevirapine based regimen. Out of 40 participants on EFV based regimen, 37 participants (92.5%) were virologically suppressed while 3 participants (7.5%) were non-virologically suppressed. Out of 35 participants on NVP based regimen; 29 participants (82.9%) were virologically suppressed while 6 participants (17.1%) were non-suppressed virologically.

From these results, 66 participants (88%) were virologically suppressed while 9 participants (12%) were non-suppressed virologically in this study amongst the subjects on antiretroviral therapy (table 4.7).

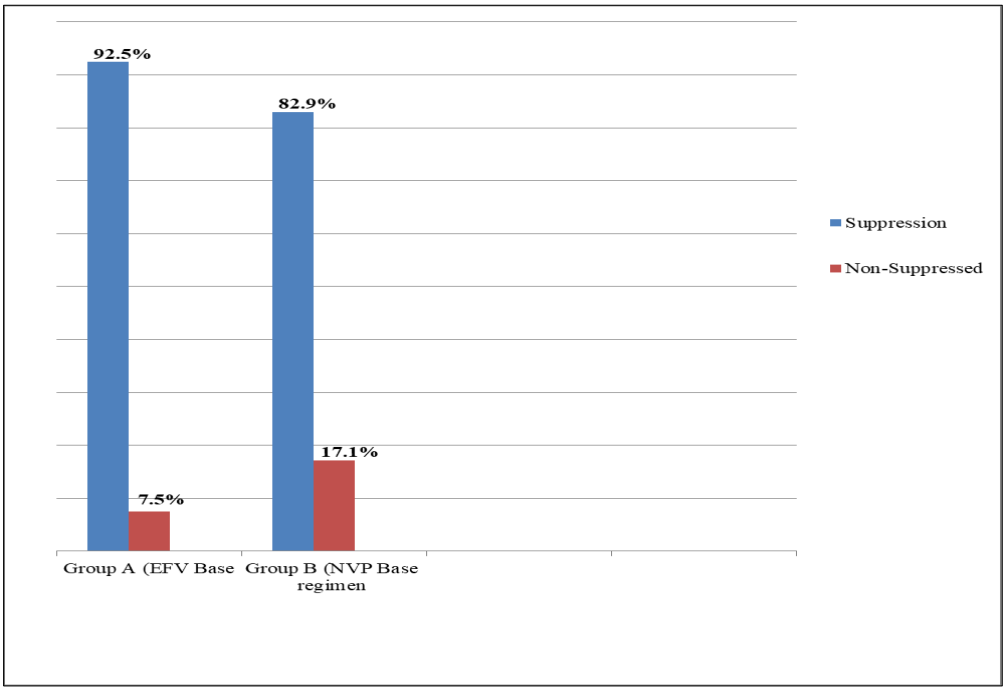

Figure 1 Proportions of participants with virologic and non-virologic suppression at 12 months of therapy

- Group A: Efavirenz based drug combinations (Tenofovir + Lamivudine + efavirenz)
- Group B: Nevirapine based drug combinations (Zidovudine + lamivudine + nevirapine)s

4. Discussion

In this study, the HIV-1 viral load in participants on antiretroviral drugs was significantly lower when compared with HAART naïve participants. The low viral load at 12 months of therapy is an indication of efficacy and suitability of the regimen for individual client. In this study, viral load was predominantly undetectable in participants on efavirenz and nevirapine based regimens. This result is similar to that predicted by UNAIDS,[30, 31] that with a successful therapy, a fall of $1.5\log_{10}$ to $2\log_{10}$ in plasma viral load occurs within 4 – 6 weeks. And with successful HAART treatment, viral load should become undetectable in 4 – 6 months of therapy. However, about 7.5% to 17.14% of the participants on efavirenz and nevirapine based regimen did not experience significant drop in viral load respectively, although, the treatment failure was more with nevirapine based regimen than efavirenz based regimen.

For the participants with viral load suppression; it means the virus is being suppressed by the current antiretroviral drugs (efavirenz and nevirapine based regimens). Undetectable or suppressed viral load does not mean that HIV-1 virus has disappeared completely from the body but that the virus is present in an amount too low to be measured or hiding in "Sanctuary sites" (cerebrospinal fluid or brain, genital fluids, gut or lymph nodes) [30, 31].

For the participants with non-virologic suppression; this means the virus is not properly controlled by the current antiretroviral drugs. However, there are two possibilities: the first possibility could be lack of adherence (adherence problem) and the second possibility could be that the antiretroviral drugs are no longer working due to resistance. These possible reasons are resolved by repeating viral load after enhanced counseling. If the results of the viral load repeated after 6 months of enhanced adherence counseling returns to less than 1000 copies/ml (or undetectable); it means the participants was not adherent initially, but if the results of the repeated viral load is greater than 1000 copies/ml (or detectable); considering logarithm drop of not greater than $0.5\log_{10}$ between the first viral load and the repeated viral load; then the patient has failed antiretroviral therapy regimen and need to be switched to second-line drugs [30, 31]. From these findings, it could be suggested that HIV-1 viral load is not just a monitoring tool to switch patients to second-line but it also helps participants to stay on first-line therapy.

The study observed no statistical difference in CD_4^+ cells counts at 12 months for participants on antiretroviral drugs when compared with treatment naïve participants. Since the CD_4^+ T cell count was same between those on drugs and those not on drug; this is an indication of CD_4^+ count limitation in the monitoring of patients on antiretroviral therapy. This finding is supported by the work of Onyenekwe *et al.,* [23] that CD_4^+ count depletion is not bizarre to HIV-1 infection but retention of circulating immune complexes which is great burden to HIV/AIDS individuals. Onyenekwe *et al.,* [23] research findings further revealed that, one would expect from 70 participants who do not have HIV, up to 99% of them should have CD_4^+ count above 500cells/mm^3. However, only 55.7% have CD_4^+ count above 500cells/mm^3. There may be other factors other than HIV viral infection, adversely affecting CD_4^+ count. It was hypothesized that malaria reduces the CD_4^+ count more than HIV infection [7]. In a similar development, Onyenekwe *et al.,* [23] reported that after antimalarial treatment, the median CD_4 count at day 28 of follow-up increased from 468 to 811cells/µl in HIV-1 negative and from 297 to 447cells/µl in HIV-positive patients, and that after successful treatment, the proportion of patients with CD_4^+ count <200/µl at day 45 decreased from 9.6% to 0% in HIV-1 negative and from 28.7% to 13.2% in HIV-1 positive malaria patients. Hence CD_4^+ T-lymphocytopenia is caused majorly by circulating immune complexes due to malaria parasite, Salmonella species and other microbial agents than HIV-1 infection [23].

The study also observed that the plasma antiretroviral drug concentrations (efavirenz based regimen) were significantly higher at 12 months of therapy when compared with plasma antiretroviral drug concentrations (efavirenz based regimen) at 6 months of therapy. These differences in plasma antiretroviral drug concentrations in this study showed that the higher duration of therapy may be associated with good therapeutic concentrations that are effective for virologic suppression. However, the plasma nevirapine based regimen concentrations were not significantly different at 12 months of therapy when compared with the plasma nevirapine based regimen concentrations at 6 months of therapy. This is probably due to short half life of zidovudine and lamivudine (0.5 to 3 hours for zidovudine and 5 to 7 hours for lamivudine). Whereas, the drop in plasma concentrations of nevirapine at 12 months of therapy could be due to effective permeability and excretion by kidney; this was probably possible due to its low molecular mass (263g/mol). The reduced plasma concentrations of nevirapine leads to sub-therapeutic drug concentrations as observed in the study participants. Sub-therapeutic nevirapine based regimen concentrations were observed with high viral load (≥1000copies/ml). In a similar study by Kasany *et al.,* (2013) that sub-therapeutic nevirapine based regimen concentrations could be due to non-compliance, low potency and discontinuation of medications. In another study by Ana *et al., [21]* that treatment failure was more frequent among participants with low plasma antiretroviral drug concentrations than among patients with adequate antiretroviral drug concentrations. This finding is supported by reports by Veldkamp *et al.,* [32] and Ana *et al.,* [21] that plasma efavirenz based regimen is associated with better virological response in HIV-1 infected participants than nevirapine based regimen. It could be hypothesized from these findings that optimization of efavirenz and nevirapine based regimens might be used as a tool to improve virologcal response in HIV-1 infected participants

5. Conclusion

The therapeutic antiretroviral drug concentrations was observed in 93% and 72% of participants on efavirenz and nevirapine based regimen respectively. Sub-therapeutic antiretroviral drug levels was associated with low antigenic suppression while therapeutic drug concentration was associated with high antigenic suppression. This finding may indicate potential usefulness of plasma antiretroviral drug measurement in the prediction of treatment failure or success in HIV-1 infected participants on highly active antiretroviral therapy (HAART).

Compliance with ethical standards

Acknowledgments

Authors wish to acknowledge all the HIV-1 infected individuals who voluntarily agreed to participate in this study.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The ethical approval was obtained in accordance with the principles of declaration of Helsinki from the board of ethics committee of Kogi State Ministry of Health, Kogi State, Lokoja, Nigeria.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Becton Dickson and Company, 2005. Flow Cytomeric Enumeration of T-cells specific antigens. New York Journal of Immounology, 1:258 - 259.

[2] Bryant, L., Smith, N. and Keiser, P.A. (2013). A model for reduced HIV Viral Load monitoring in resource limited setting. Journal of international association of providers of AIDS care, 12: 67 – 71

[3] Chargelegue, D. and OToole, C.M. (1992). Development of a sensitive ELISA for HIV-1 p24 antigen using a fluorogenic substrate for monitoring HIV-1 replication in vitro. Journal of Virology Methods, 38(3): 323 – 332.

[4] Chargelegue, D., Stanley, C.M., OToole, C.M., Colvin, B.T. and Steward, M.W. (1995). The affinity of IgG antibodies to gag p24 and p17 in HIV-1 infected patients correlates with disease progression. Journal of Translational Immunology, 99(2): 175 - 181.

[5] Daniel, W.G., Christa, K., Benson, R.K., Rodrick, K., Stephen, E.M., Jeremiah, K., Samuel, E.K., Gilbert, W.K and Hartwig, K., (2013). Plasma concentrations of efavirenz and Nevirapine among HIV-infected patients with immunological failure attending a tertiary hospital in North-Western Tanzania. Journal of Public Library of Science 8(9): 75118.

[6] Easley, C.J. (2006). Development & application of microfluidic genetic analysis systems. Charlottesville: University of Virginia. American Journal of Virology, 103(51): 19272-19277.

[7] Enzensberger Doerr, H.W., Preiser, W. and Storkel, F. (1988). Kinetics IV antigen and antibodies in HIV infected haemophiliacs. Abstracts of the International AIDS congress, Stockholm, Sweden, 4(1): 1623

[8] Erikstrup, C., Kallestrup, P., Zinyama, R.B., Gomo, E., Lüneborg, M., Gerstoft, J., Schupbach J., Ullum, H. and Katzenstein, T.L. (2008). P24 as a predictor of mortality in a cohort of HIV-1-infected adults in rural Africa. Journal of Acquired Immune Deficiency Syndrome, 48(3): 345 – 349.

[9] Ezeugwune, I.P., Onyenekwe, C.C., Ahaneku, J.E., Ifeanyichukwu, M., Meludu, S.C., Onwurah, O.W. and Osuji, F.N. (2012). Serum hormonal levels in HIV/AIDS infected male subjects on antiretroviral therapy (ART) in Nnewi, Nigeria. International Journal of Biological and Chemical Sceinces, 6(4): 1409 – 1418.

[10] Farzadegan, H. (1996). Virologic and serologic markers of rapid progression to AIDS after HIV-1 seroconversion. Journal of Acquired Immune Deficiency Syndrome, 1(13): 448-455.

[11] Idoko, J. (2016). The status of HIV and AIDS Control in Nigeria. Institute of Public Health, 1(7): 30 -39.

[12] Iqbal, H.S., Balakirishnan, P. and Cecelia, A.J. (2007). Use of an HIV reverse transcriptase enzyme activity assay to measure HIV Viral Load as a potential alternative to nucleic acid based assay for monitoring antiretroviral therapy in resource-limited setting. Journal of Medical Microbiology, 56: 1611-1614.

[13] Johnston, L.G., Sabin, M.L., Prybylski, D., Sabin, K., Macfarland, W. and Baral, S. (2016). Policy and practice; the importance of assessing self-reported HIV status in bio-behavioral surveys. World Health Organization, 94: 605-612.

[14] Jorg, S., Jurg, B., Markus, F., Zuzana, T., Helen, J. and Milos, O. (2001). Antiretroviral treatment monitoring with an improved HIV-1 p24 antigen test: an alternative to test for viral RNA. Journal of Medicine, 65(2): 225 – 232.

[15] Kahl, C.A., Marsh, J., Fyffe, J., Sanders, D.A. and Cornetta, K. (2004). HIV p24 Enzyme Linked Immunosorbent Assay (ELISA). Journal of Virology, 78(3): 1421 – 1430.

[16] Mallet, S., Halligan, S., Thompson, G.S. and Altman, D.G. (2012). Interpreting diagnostic accuracy studies for patient care. British Medical Journal, 2(345): 3999.

[17] Marzolini, C., Telenti, A., Decosterd, L.A., Greub, G. and Biollaz, J. (2001). Efavirenz plasma levels can predict treatment failure and central nervous system sideeffects in HIV-1-infected patients. AIDS, 15(1): 71 – 75.

[18] Mazzaferro. E.M., Rudloff, E. and Kirby, R. (2002). The role of albumin replacement in the critically ill veterinary patient. Journal of veterinary emergency critical care, 12(2): 113 – 124.

[19] Meng, J. (2015). Screening of HIV-1 protease using a combination of an ultra-high throughput fluorescent-based assay and Rapid Fire mass spectrophotometry. Journal of Biomolecular diagnostics, 20(4): 606-735.

[20] Miranda, S., Suzanne, M.C. and Johnson, M. (2001). Maintenance of the Gag/Gag-pol Ratio is important for Human Immunodeficiency Virus Type 1 RNA dimerization and viral infectivity. Journal of Virology, 75(4): 1834 – 1841.

[21] Neogi, U., Heylen, E. and Shet.A. (2013). Long term efficacy of first line antiretroviral therapy in Indian HIV-1 infected patients: A longitudinal cohort study. American Journal of Virology. 8: 55-60.

[22] Nosyk, B., Zang, X., Min, J.E., Krebs E., Lima, V.D. and Milloy, M.J. (2017). Relative effects of antiretroviral therapy and harm reduction initiatives on HIV incidence in British Columbia, Canada. Lancet HIV, 4(7): 303-310.

[23] Oneyenekwe, C.C., Ukibe, N., Meludu, S.C., Ezeani, M., Ofiaeli, N., Onochie, A., Ilika, A., Ifeanyi, M., Aboh, N. and Ele, P. (2008). Serum Levels of anti-BCG, Albumin and packed cell volume and White Blood Cell Count in subjects with HIV and Malaria Co-morbidity. Journal of Tropical Medicine and health, 36(1): 17 – 22.

[24] Peterson, M., Balzer, L., Kwarsiima, D., Sang, N., Chamie, G. and Ayieko, J. (2017). Association of implementation of a universal testing and treatment intervention with HIV diagnosis, receipt of antiretroviral therapy, and viral suppression in East Africa. Journal of American Medical Association, 317(21): 2196-2206.

[25] Rawizza, H.E. Chaplain B. and Meloni S.T (2011). Immunologic criteria are predictors of virologic outcome: implications for treatment monitoring in resource limited setting. Journal of infectious diseases, 53(12): 1283-1290.

[26] Stevens, W.S., Scoh L.E. and Crowe, S.M. (2010). Quantifying HIV for monitoring antiretroviral therapy in resource-poor settings. Journal of infectious diseases, 201(1): 16-26.

[27] Stowell, L.H., Sharman, L.E. and Hamel, K. (1991). An enzyme linked Immunosorbent Assay (ELISA) for prostate specific antigen. Journal of Forensic Science, 50(1): 125-138.

[28] Swanson, P., Hotzmayer, V., Huang, S., Hay, P., Adebiyi, A. and Rice, P. (2006). Performance of the automated Abott Realtime HIV-1 assay on a genetically diverse panel of specimens from London. Journal of Virology Methods, 137(2): 184-192.

[29] Tehan, P., Bray, A., Keech, R., Rounsley, R., Carruthers A. and Chuter, V.H. (2015). Sensitivity and specificity of the toe brachial index for detecting peripheral arterial disease. Journal of Ultrasound Medicine, 34(10): 1737 – 1743.

[30] The Joint United Nations Programme on HIV/AIDS (2015). Guildelines for national human immunodeficiency virus case surveliance, including monitoring for human immunodeficiency virus infection and acquired immunodeficiency syndrome. Global AIDS Response Programme Report, 48(13): 1 – 15.

[31] The Joint United Nations Programme on HIV/AIDS (2017). HIV/AIDS case definitions for surveliance and reverse clinical staging and immunological classification of HIV-related disease in adult and children. Geneva, 2000 – 2015.

[32] Veldkamp, A.I., Weverling, G.J., Lange, J.M., Montaner, J.S. and Reiss, P. (2001). High exposure to Nevirapine in plasma is associated with an improved virological response in HIV-1-infected individuals. AIDS, 15(9): 1089 – 1095.

[33] Vibhuti, K., Vivet, A., Chandrabose, K. and Piyush, T. (2009). Simultaneous quantitative determination of zidovudine and nevirapine in human plasma using isocratic, reverse phase high performance liquid chromatography. Tropical Journal of Pharmaceutical Research. 8(1): 79-86.

[34] World Health Organization (2013). Consolidation guidelines on the use of antiretroviral drugs for treating and preventing HIV infections. Recommendations for a public health approach. Geneva.

[35] World Health Organization 2014. Towards universal access: Scaling up priority HIV/AIDS interventions in the health sector. Progress report, Geneva