**Utilization of Mobile Phone for Routine Enhanced Adherence Counselling Intervention**

**Abstract**

**Objectives**: To determine outcome of routine utilization of mobile phone based EAC intervention among ART non-adherers

**Methods**: This was a single centre hospital-based retrospective cohort study of antiretroviral therapy (ART)-experienced adult (≥18 years) people living with HIV (PLHIV) that had EAC at the ART outpatient clinic Federal Teaching Hospital (FTH) Gombe, Nigeria.

**Result**: A total of 321 non-adherers identified with viral load VL of >1000 copies/ml completed the required EAC sessions/ interventions. The mean age and duration on ART of the participants were 40.78±10.81 and 9.6±4.17 (years) respectively. Majority (69.2%) of the participants were females, but male participants were older than their female counterparts (45.81±10.95 vs 38.23±10.78, *p*=0.001). The pre EAC VL was <10,000 copies/ml in 134 (42%) participants, between 10,000- 100,000 copies/ml in 106 subjects, and >100,000 copies/ml in 79 (24.8%) participants. The proportion of VL re-suppression (<1000 copies/ml) among those that completed EAC was 66.6%. The pre EAC VL of participants with unsuppressed VL significantly exceeded those with suppressed VL (*p*=0.001). Participants that achieved VL suppression after the EAC intervention had gained significant weight (66.17±15.22 vs 61.80±15.33, *p*<0.001), while those with unsuppressed VL had a significant decrease in weight (63.40±14.96 vs 62.45±14.72, *p*<0.001).

**Conclusion**: This study showed that VL suppression target of 70% after EAC intervention as recommended by WHO is unmet and further highlights the need for more rapid objective assessment of adherence and prompt intervention

**Keywords**: Mobile phone, adherence,

**Introduction**

As at the end of 2017, 15.3 million people living with HIV (PLHIV) in Africa had access to antiretroviral (ARV) drugs. The success of human immunodeficiency virus (HIV) treatment owing to widespread availability of ARV drugs requires monitoring of people on ARV drugs to limit the development of treatment failure and further guide switch of regimen. Viral load testing was approved by the WHO as monitoring approach to diagnose treatment failure. Routine monitoring viral load among patients enrolled on ART is important for timely detection of treatment failures, identification of patients in need of more intensive adherence support and minimizes development of drug resistance and unnecessary switch to expensive and limited ART regimen options. Adherence to ART reduces the transmission rates of HIV and HIV-related morbidity and mortality. Suboptimal adherence is a major cause of regimen discontinuations and virologic failure. The WHO recommends enhanced adherence counselling (EAC) for those with high viral load. EAC is a continual and repeated process that involves a structured assessment of the current level of adherence, explore the specific barriers the patient must overcome, assisting patients to identify solutions, and address barriers and develop an individualized adherence interventional plan which improve viral load suppression and reduces subsequent treatment failure.

The growing use of mobile phones in resource poor settings has highlighted the potential adoption and utilization of mobile phone applications for adherence intervention. The ease of immediate contact is particularly appealing to address the time lag in commencing physical EAC intervention considering the fact that transport logistic is a major barrier to ART adherence in resource poor settings. This study evaluated the outcome of routine utilization of mobile phone based EAC intervention among non-adherers with the aim of identifying measures for individualized and holistic treatment of PLHIV to improve their quality of care.

The 2019 NAIIS report showed that the prevalence of HIV in North East Nigeria is 1.1%.

HIV RNA virological suppression requires adherence to therapy of more than 95% and routing viral load monitoring is the gold standard for measuring ART progress.3

**Methods**

*Study design and setting*

This study retrospectively reviewed data of ART-experienced non-adherers at the ART outpatient clinic Federal Teaching Hospital (FTH) Gombe, Northeast Nigeria. Data was manually retrieved from the EAC register for non-adherers identified with viral load of ≥1000 copies/ ml. Initial viral load testing in people with HIV should be after 6 months of initiating ART and every 12 months thereafter routinely. Targeted viral load testing are offered for those on follow up with suspected clinical or immunological failure. The ART regimen Tenofovir (TDF)/ Lamivudine (3TC)/ Dolutegravir (DTG) was rolled out from 2019 according to the Nigerian national guidelines as preferred First-line regimen to replace the older TDF/3TC/ Efavirenz (EFV) regimen. Hence, participants on follow up had their regimen replaced to DTG-containing ART. Participants that had failed the initial first-line regimen had their ART substituted to second-line ART that is protease inhibitor based (TDF/3TC/ Atazanavir boosted with ritonavir (AZVr). Resistance testing is done for those that failed second-line regimen prior to switch to third-line therapy.

PLHIV on routine clinic visits have their weight and blood pressure checked regularly and venous blood samples for VL testing is collected when due. Results for the VL is retrieved by team and those with high VL (>1000 copies/ml) qualifying for EAC intervention are sent to the EAC unit. The registered telephone contact of the EAC eligible person is electronically retrieved for commencement of the EAC session in the ensuing work free day (weekend). The intervention strategies include: education, counselling, peer group support, direct observed therapy (DOT), SMS, frequent phone calls and utilization of alarms as reminders after identifying possible barriers for non-adherence. Participants that completed the EAC sessions/ intervention are asked to present for a repeat VL.

Data was collected on the number of active patients receiving ARV drugs from the electronic patient monitoring system (EPMS). Information on the number who underwent viral load testing from the laboratory records of the hospital. We then line-listed all patients with high viral loads from the laboratory records and obtained individual client level information from the ART registers, individual patients ART booklets and EAC registers. Additional information that will be obtained Are ART number, name, age, sex, date of ART enrolment/ initiation, dates of viral load testing, reason for doing viral load testing (routine or for confirmation of treatment failure) ART regimen, EAC enrolment and the number of EAC sessions attended. By using the date of ART initiation and last clinic visit date the duration on ART will be derived.

*Data analysis*

Data obtained from the study was analysed using SPSS (version 26; SPSS Inc., Chicago, IL, USA). Demographic variables like age and sex were represented using mean (SD) for continuous variables and proportions/percentages for categorical variables. Independent student t test and paired t test were used to compare mean differences between the same and different groups. Mann-Whitney U test was used to determine pre EAC VL difference between various groups. Log binomial regression was done to identify predictors of viral re-suppression after EAC. All tests were considered statistically significant at P values <0.05.

**Result**

A total of 634 PLHIV with routine VL screening of >1000 copies/ ml was enrolled to the EAC session over the study period and 321 completed the required EAC sessions. The mean age and duration on ART of the participants were 40.14±10.65 and 9.48±4.16 (years) respectively. Majority (69.2%) of the participants were females, but male participants were older than their female counterparts (45.81±10.95 vs 38.23±10.78, *p*=0.001). there was statistical association in duration on ART between participants on second- and first-line ART (10.34±3.52 vs 9.3±4.37, *p*=0.047) The pre EAC ART regimen of the participants were TDF/3TC/DTG in 148 (46.1%), TDF/3TC/AZVr in 90 (28%), and TDF/3TC/EFV in 83 (25.9%) as shown in figure 1 below. The pre EAC VL was <10,000 copies/ ml in 134 (42%) participants, between 10,000- 100,000 copies/ ml in 106 subjects, and it was >100,000 copies/ml in 79 (24.8%) participants. The proportion of VL suppression after EAC intervention was 66.6%. An extended EAC session was done to participants with unsuppressed VL after failing the first session, amongst which 58 had available repeat VL and 27(46.6%) had suppressed VL. There was no statistical difference in age and duration on ART between those that had suppressed and unsuppressed VL after the first EAC intervention as shown in table 1. Similarly, there was no gender difference in those that had suppressed and unsuppressed VL load after the first EAC session. Participants that achieved VL suppression after the EAC intervention had gained significant weight after the EAC intervention (63.28±14.84 vs 66.34±14.67, p<0.001), while those with unsuppressed VL had a significant decrease in weight (64.41±14.33 vs 62.81±13.88, p<0.001).

A Mann-Whitney U test indicated that, on average, the pre EAC VL of participants with unsuppressed VL (mean Rank =186.54, n =107) significantly exceeded participants with suppressed VL (mean Rank =147.4, n =213), U =8605.0 z =-3.574, *p*= 0.001, two tailed. Male participants had higher pre EAC VL (mean Rank=182.5 n= 99) compared with females (mean Rank= 151.43, n= 222) U= 8865.0 z= -2.766 *p*= 0.006. Participants on second-line ART pre EAC intervention had higher pre EAC VL (mean Rank= 183.16, n= 90) compared with those on first-line ART regimen (mean Rank= 152.37, n=231) U= 8401.0 z= -2.670 *p*=0.008.

Number that had unsuppressed VL after EAC = 107 (33.4%)

Number that had suppressed VL after EAC intervention = 213 (66.6%)

Total number that had 3 EAC sessions and included in the study = 321

Adult cases =603

Total number of participants enrolled to EAC = 634

Paediatric cases =31

Participants on EFV containing regimen =83

Participants on DTG containing regimen =148

Participants on 2nd line regimen = 90

Number that had extended EAC with repeat VL = 58

Participants that had suppressed VL after extended EAC session = 27 (46.6%)

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Fig 1. Management of people living with HIV on ART with high viral load >1000 copies/ml

Table 1. Relationship between pre EAC VL levels with demographic factors and outcome

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Pre EAC VL** | | | | | |
| **Variables** | **Mean rank** | **n** | **U/H** | **Z** | ***p*-value** |
| **Age** |  |  |  |  |  |
| <40 | 162.41 | 141 | 12491.5 | -.241 | 0.810 |
| ≥40 | 159.9 | 180 |  |  |  |
| **Sex** |  |  |  |  |  |
| Male | 182.45 | 99 | 8865.0 | -2.766 | **0.006\*** |
| Females | 151.43 | 222 |  |  |  |
| **Duration on ART** |  |  |  |  |  |
| <10 | 164.07 | 142 | 11136.5 | -1.260 | 0.208 |
| ≥10 | 151.13 | 171 |  |  |  |
| **Outcome** |  |  |  |  |  |
| Suppressed VL | 147.2 | 213 | 8562.0 | -3.514 | **0.001\*** |
| Unsuppressed VL | 185.73 | 107 |  |  |  |
| **ART regimen** |  |  |  |  |  |
| First-line | 152.37 | 90 | 8401.0 | -2.670 | **0.008**\* |
| Second-line | 183.16 | 231 |  |  |  |
| **Pre EAC ART** | 152.37 | 90 |  |  |  |
| TDF/3TC/EFV | 144.45 | 83 | 8.071 |  | **0.018\*a** |
| TDF/3TC/AZVr | 183.16 | 90 |  |  |  |
| TDF/3TC/DTG | 156.81 | 148 |  |  |  |

Key: ART; antiretroviral therapy, EAC; enhanced adherence counselling, U; Mann-Whitney U, H/a; Kruskal Wallis test, \*; statistically significant (*p*<0.05),

Table 2. Relationship between baseline characteristics and VL re-suppression of the participants

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **Suppressed VL n(%)** | **Unsuppressed VL n(%)** | **x2** | ***p*-value** |
| **Age** |  |  |  |  |
| <40 | 95(67.4) | 46(32.6) | 0.042 | 0.838 |
| ≥40 | 118(66.3) | 60(33.7) |  |  |
| **Sex** |  |  |  |  |
| Male | 61(62.9) | 36(37.1) | .948 | 0.366 |
| Female | 152(68.5) | 70(31.5) |  |  |
| **Duration on ART** |  |  |  |  |
| <10 | 102(72.3) | 39(27.7) | 2.729 | 0.063 |
| ≥10 | 108(63.5) | 62(36.5) |  |  |
| **ART regimen** |  |  |  |  |
| First-line | 171(74) | 60(26) | 19.864 | **<0.001\*** |
| Second line | 42(47.7) | 46(52.3) |  |  |
| **Pre EAC ART** |  |  |  |  |
| TDF/3TC/EFV | 60(72.3) | 23(27.7) | 20.04 | **<0.001\*** |
| TDF/3TC/AZVr | 42(47.7) | 46(52.3) |  |  |
| TDF/3TC/DTG | 111(75) | 37(25) |  |  |

Key: ART; antiretroviral therapy, EAC; enhanced adherence counselling, x; chi square \*; statistically significant (*p*<0.05),

A logistic regression (table 3 below) was performed to ascertain the effects of age, sex, duration on ART, and pre EAC VL and ART regimen (first- or second line) on the likelihood that participants will have unsuppressed VL. The logistic regression model was statistically significant, χ2 = 27.954, *p* < .0005. The model explained 12.0% (Nagelkerke *R2*) of the variance in VL suppression and correctly classified 70.6% of cases. Participants with pre EAC VL of >100,000DTG-containing regimen were 2.5 times more likely to have unsuppressed VL than those with pre EAC VL of <10,000. Similarly, participants on second-line ART were also 2.5 times more likely to have unsuppressed VL after the EAC interventions.

Table 3. log binomial regression analysis

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **variables** | **B** | **S.E.** | **Wald** | **df** | **Sig.** | **Expo(B)** | **96% CI** | |
| **Age** | .002 | .013 | .022 | 1 | .882 | 1.002 | .977 | 1.027 |
| **Sex (1)** | .129 | .297 | .188 | 1 | .665 | 1.137 | .636 | 2.034 |
| **Duration on ART** | .049 | .032 | 2.341 | 1 | .126 | 1.050 | .986 | 1.119 |
| **Pre EAC VL cat** |  |  | 8.498 | 2 | .014 |  |  |  |
| **Pre EAC VL (1)** | .114 | .302 | .141 | 1 | .707 | 1.120 | .620 | 2.026 |
| **Pre EAC VL (2)** | .897 | .323 | 7.691 | 1 | **.006\*** | **2.452** | **1.752** | **4.622** |
| **ART regimen (1)** | .955 | .274 | 12.187 | 1 | **.000\*** | **2.599** | **1.520** | **4.443** |
| **Constant** | -1.925 | .719 | 7.173 | 1 | .007 | .146 |  |  |

Key: ART; antiretroviral therapy, EAC; enhanced adherence counselling, \*; statistically significant (*p*<0.05),

**Discussion**

The study evaluated the outcome of mobile phone based EAC intervention among PLHIV in a tertiary outpatient ART clinic in Nigeria. Majority (69.2%) of the participants were females, but male participants were older than their female counterparts. The results of the study showed that the proportion of VL re-suppression (<1000 copies/ml) after EAC was 66.6%. The pre EAC VL of participants with unsuppressed VL significantly exceeded those with suppressed VL, and participants that achieved VL suppression after the EAC intervention had gained significant weight, while those with unsuppressed VL had a significant decrease in weight. Male participants had higher pre EAC VL compared with females. Participants on second-line ART regimen and those with higher pre EAC VL were 2.5 times more likely to have unsuppressed VL compared with those on first-line and lower pre EAC VL.

The VL suppression rate found in our study was similarly reported in a study from Northeast Ethiopia (66.4%) after the recommended physical EAC intervention in their cohorts.12 But it is much higher than the previously reported rates of 52.9% and 23% in Zimbabwe and in Uganda respectively.13,14 The aforementioned re-suppression rates are short of the recommended 70% by WHO, the consequence of which threatens the successes of newly adopted regimens and transmission of ART-resistant strains. When compared with the previous studies that utilized physical EAC, the use of phone-based EAC has shorter EAC onset time as presented in our results. However, even though timely completion of the EAC session was aided by telemedicine, the challenge still remains for prompt repeat of VL for evaluation of intervention which will guide subsequent care.

Our finding of the association between baseline pre EAC VL with the outcome is in keeping with previous reports showed initial VL levels may be a good determinant of VL suppression in patients with high VL.13,14 Contrary to previous reports of females having higher baseline VL, our results showed that males had higher baseline pre EAC VL. While more studies are needed to further clarify the role of gender in VL re-suppression among non-adherers,

Our report of participants on second-line regimen were more likely to have unsuppressed VL after the EAC intervention raises valid concerns for subsequent care. While it has been shown that virologic suppression is easily achieved with a lower adherence threshold for newer generation ART just like in the case of this study having most participants on DTG-containing regimens,15

The results of our results showed that participants that achieved VL suppression gained more weight while those with unsuppressed VL lost weight on subsequent visit after the EAC intervention. This finding has important clinical significance considering the significant delay from VL testing to enrolment into EAC as reported in previous studies. Weight is routinely measured for , in identifying non-adherers while on clinic visits and prompt initiation of EAC intervention.

Limitations of the study is its retrospective design the analysis and interpretation of the data were restricted to only those variables that are available and captured in the patient records. Some of the important variables like socio-economic status, educational level of the participants, distance of patients’ residence to the ART centres, patients’ clinical condition, which could have played a major role in initial viral load testing, enrolment for EAC, repeat viral load testing and viral suppression, were not available. Since we did not measure these other variables, we are unable to account for the influence of these factors in our analysis. The strength of this study is in its demonstration of the

In conclusion, this study showed that VL suppression target of 70% after EAC intervention as recommended by WHO is unmet and further highlights the need for more rapid objective assessment of adherence and prompt intervention

**Author’s contributions**

MWA

**Funding**

There was no funding for this study

**Conflict of interest**

The author declared none

**Ethical approval and consent to participate**

Approval for the study was obtained from the ethics and research committee FTH Gombe (approval no: NHREC/25/10/2013) prior to commencement of the study. The research was performed in accordance with the Declaration of Helsinki.

**Availability of data and material**

All datasets on which the conclusions of the manuscript rely; to be made available from the corresponding author on reasonable request from the editors

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Even though timely completion of the EAC session was aided by telemedicine, the challenge still remains for prompt repeat of VL for evaluation of intervention which will guide subsequent care.

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