Virological Non-suppression among HIV-Positive Patients on Antiretroviral Therapy in Northwestern Nigeria: An eleven-year experience of a tertiary care Centre, January 2009–December 2019

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Abstract:

Background: Human Immuno-Deficiency Virus (HIV) remains one of the world’s significant public health challenges. Viral suppression is the key indicator for treatment success in People living with HIV (PLHIV). We determined the level of viral non-suppression and its associated factors among PLHIV attending Federal Medical Centre Katsina (FMC Katsina), Nigeria.

Methods: This retrospective descriptive study was conducted on 913 HIV positive adults enrolled in care between January 2009 and December 2019. Information on socio-demographics, clinical, immunological, Viral Load (VL) and other relevant parameters were extracted from the patients’ care Centre Katsina estimated frequencies/proportions, performed bivariate and multivariate analysis to determine factors associated with VL non-suppression using p<0.05 as significant level.

Results: Records of 831 registered patients were analyzed using Epi-info 7. During the period, 751 (90.4%) achieved viral suppression, 426 (51.3%) had CD4 counts of ≥500 and 477 (57.4%) were on HAART for ≥5 years. Majority, 793 (95.4%) were on first-line and 809 (97.4%) in the non-advanced stage (WHO stages 1 and 2). The independent predictors of viral non-suppression included being on the second line HAART [Adjusted OR (AOR) 6.5; 95% CI 3.02-13.89], being employed [AOR 0.26; 95% CI 0.15-0.44] and baseline CD4 count less than 500 [AOR 0.35; 95% CI 0.21-0.61].

Conclusions: Our study demonstrated a good viral suppression among PLHIV on HAART. Low baseline CD4 counts and being on second-line HAART are predictive of viral non-suppression while being unemployed seems to be protective against viral non-suppression.

Key words: Viral Non-suppression, HIV-Positives, Antiretroviral Therapy, Nigeria.
**Background:**

Human Immuno-Deficiency Virus (HIV) is a leading cause of infections worldwide despite the success of highly active antiretroviral therapy (HAART) [1]. It remains one of the world’s most significant public health challenges, affecting about 38 million of the world’s population majority of whom are living in low and middle income countries [2]. Nigeria shares a chunk of this estimate with a recent national prevalence of 1.4%. With varying prevalence across the country, Katsina state has the lowest prevalence of 0.3% while Akwa-Ibom state has the highest prevalence of 5.6% [3,4].

The 90-90-90 target by UNAIDS envisages that by 2020, 90% of PLHIV will know their HIV status, 90% of people who know their HIV-positive status will be accessing treatment and 90% of people on treatment will have suppressed viral loads⁵. However, in 2018 Nigeria has only 67% of PLHIV that knew their status, of which 53% were on treatment and only 42% were virally suppressed⁵. The northwest zone of Nigeria also reflects similar statistics as only 9 out of 20 PLHIV on HAART achieved viral suppression [5,6].

Viral load (VL) measurement is the gold standard for monitoring treatment success. PLHIV on HAART with unsuppressed viral load have a higher risk of disease progression, transmission, and mortality [7]. Available statistics have shown that Nigeria is far behind the target of ‘UNAIDS 90-90-90 aspirations’ despite the recent downward trend in prevalence and incidence. Within the limits of our literature search on major databases- PubMed, Medline, Scopus, Google scholars, and Web of Science-there was no research that has evaluated viral suppression among HIV patients in the north-western part of Nigeria.
The objective of this study was to determine the level of viral suppression and factors associated with viral load non-suppression among HIV positive adults attending the HIV clinic at FMC Katsina.

Methods:

This retrospective cross-sectional descriptive study was conducted from January 2009 to December 2019 at FMC, Katsina. The hospital is a 1000 bed capacity, tertiary health facility. It serves as a referral center for both private and other public health facilities in the state, neighboring states, and the Niger Republic. The HIV clinic otherwise refers to as Action Aid clinic was established in 2006 and provides services for the diagnosis, treatment, and prevention of HIV, inclusive of free counseling and testing. It can accommodate about two hundred patients per clinic day and further subdivided into units. The HIV clinic units included the adult ART clinic, Paediatrics ART unit, the Prevention of Mother-to-Child Transmission (PMTCT) unit, HIV/TB co-infection unit, Pharmacy unit and the laboratory.

Study participants and data collection

The source of data was from the database of the HIV clinic obtained from all PLHIV enrolled in ART care from January 2009 to December 2019 at FMC Katsina. The database provided information on socio-demographics, clinical, immunological, virological and other relevant parameters of patients. A total number of 913 adult clients were enrolled within the study period and they were all considered as the study subjects. We excluded children and adolescents less than 18 years. We used VL testing data for samples corresponding to HIV positive patients who had been on HAART for at least 6 months. Where there were more than one VL results, the most recent (not more than 12 months in line with the country’s national guideline for HIV) was used.
for the data. We abstracted data on VL testing results (for plasma and DBS) measured in terms of viral RNA copies/ml of blood.

**Outcome Measures**

The primary outcome was virological 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. The secondary outcome was factors predictive of virological non-suppression.

**Laboratory Testing Methods**

The laboratory analysis was carried out by the CDC accredited laboratory of the Aminu Kano Teaching Hospital, Kano. For each sample collected from the patients, RNA was extracted and plasma VL determined using Polymerase chain reaction (PCR).

**Data Quality Assurance**

One of the authors extracted the data into Microsoft Excel spreadsheet and this was verified independently by two other co-authors to ensure accuracy of the data.

**Data analysis** This was done using Epi-info version 7. to estimate the proportion of patients with virological non-suppression. Univariate analysis was used to describe the demographic characteristics and clinical indices of the patients using frequencies and proportions. Bivariate analysis was performed to identify factors associated with viral load non-suppression. Factors found to be significant at bivariate analysis were included in the unconditional logistic regression model used for multivariate analysis at a significance of p <0.05.
Results:
During the study period, out of 913 enrolled subjects, 831 (91.0%) were included in the final data analysis due to incomplete information in 82 clients. The ages ranged from 18 to 77 years. The mean age (standard deviation) of the subjects was 34.5±9.3 years. Most of the subjects were below the age of 50 years (782; 94.1%). There were more females, 578 (69.6%). A total of 709 (85.3%) were unemployed while 78.6% were married as shown in Table 1.

Table 1. Socio-demographic profile of the study participants (n=831)

| Variables              | Frequency(n) | Percentage (%) |
|------------------------|--------------|----------------|
| Current Age (Years)    |              |                |
| 18 – 27                | 56           | 6.7            |
| 28 – 37                | 295          | 35.5           |
| 38 – 47                | 305          | 36.7           |
| 48 – 57                | 138          | 16.6           |
| 58 – 67                | 34           | 4.1            |
| 68 – 77                | 2            | 0.2            |
| ≥78                    | 1            | 0.1            |
| Gender                 |              |                |
| Male                   | 253          | 30.4           |
| Female                 | 578          | 69.6           |
| Occupation             |              |                |
| Business               | 7            | 0.8            |
| Employed               | 114          | 13.7           |
| Retired                | 1            | 0.12           |
| Unemployed             | 709          | 85.3           |
| Marital Status         |              |                |
| Divorced               | 56           | 6.7            |
| Married                | 653          | 78.6           |
| Single                 | 56           | 6.7            |
| Widowed                | 66           | 7.9            |
| Educational level      |              |                |
| Qur'anic               | 12           | 1.4            |
| Primary                | 163          | 19.6           |
| Secondary              | 536          | 64.5           |
| Tertiary               | 104          | 12.5           |
| None                   | 16           | 1.9            |
| Location               |              |                |
| Far (>100Km from *FMCK) | 63          | 7.6            |
| Near (≤100Km from FMCK) | 768         | 92.4           |

* FMCK-Federal Medical Centre, Katsina
Out of the 831 subjects, 751 (90.4%) achieved viral suppression while 426 (51.3%) had baseline CD4 counts of 500 and above. Based on the duration of the HAART, 477 (57.4%) were on drugs for five years and more. Most of the subjects 793 (95.4%), were on first-line HAART, and 809 (97.4%) in the non-advanced stage of HIV (WHO stages 1 and 2). The tuberculosis status was known in 21 (2.7%) of the subjects’ while 11.3% were obese. Furthermore, 20 out of 578 females were pregnant (3.5%) as shown in Table 2.
Table 2: Clinical and Laboratory Parameters of the Study Participants (n=831)

| Variables                        | Frequency | Percentage (%) |
|----------------------------------|-----------|----------------|
| Viral Load (cp/ml)               |           |                |
| Suppressed                       | 751       | 90.4           |
| Unsuppressed                     | 80        | 9.6            |
| Baseline CD₄ (umol/L)            |           |                |
| <500                             | 404       | 48.7           |
| ≥500                             | 426       | 51.3           |
| Body Mass Index (Kg/m²)          |           |                |
| Obese                            | 94        | 11.3           |
| Not Obese                        | 737       | 88.7           |
| Years on HAART                   |           |                |
| <5years                          | 354       | 42.6           |
| ≥5years                          | 477       | 57.4           |
| Current HAART Regimen            |           |                |
| First Line                       | 793       | 95.4           |
| Second Line                      | 38        | 4.6            |
| TB Status                        |           |                |
| Yes                              | 21        | 2.7            |
| No                               | 731       | 97.3           |
| Disease stage                    |           |                |
| WHO stages 1 and 2               | 809       | 97.4           |
| WHO stages 3 and 4               | 22        | 2.6            |
| Pregnancy Status (n=580)         |           |                |
| Not Pregnant                     | 560       | 96.5           |
| Pregnant                         | 20        | 3.5            |
The sex, age, year of commencement of HAART, body mass index (BMI), educational status, distance from the facility, pregnancy status, and disease stages were not associated with non-viral suppression. However, CD4 count at the start of the treatment was associated with non-viral suppression (CD4 less than 500 at the start of the treatment had a higher risk of non-suppression (odds ratio [OR] of 3.3; 95% CI 1.96-5.51). The employment status (OR 0.23, 95% CI 0.14-0.38), and the HAART regimen (OR 7.30; 95% CI 3.63-14.68) were also related to viral non-suppression as shown in Table 3.
Table 3: Bivariate analysis of some selected variables and Viral load status (n=831)

| Variables                              | Viral Load (cp/ml) | OR  | 95% CI       | P-value |
|----------------------------------------|--------------------|-----|--------------|---------|
|                                        | Suppressed (<1000) |     |              |         |
|                                        | Unsuppressed (≥1000)|     |              |         |
| Gender                                 |                    |     |              |         |
| Male                                   | 233                | 20  | 1.35         | 0.79-2.28 | 0.266  |
| Female                                 | 518                | 60  |              |         |
| Age at Start of HAART (Years)          |                    |     |              |         |
| <35                                    | 390                | 49  | 0.68         | 0.43-1.10 | 0.112  |
| ≥35                                    | 361                | 31  |              |         |
| BMI (Kg/m²)                            |                    |     |              |         |
| Not Obese                             | 666                | 71  | 0.99         | 0.48-2.06 | 0.985  |
| Obese                                  | 85                 | 9   |              |         |
| Years on ART                           |                    |     |              |         |
| ≤5                                     | 325                | 29  | 0.62         | 0.384-1.004| 0.050  |
| >5                                     | 355                | 51  |              |         |
| CD4 at start of care                   |                    |     |              |         |
| <500                                   | 345                | 59  | 3.3          | 1.96-5.51 | <0.001 |
| ≥500                                   | 405                | 21  |              |         |
| Educational status                     |                    |     |              |         |
| Not Educated                           | 13                 | 3   | 0.45         | 0.13-1.62 | 0.194a |
| Educated                               | 738                | 77  |              |         |
| Employment Status                      |                    |     |              |         |
| Employed                               | 91                 | 30  | 4.35         | 2.63-7.20 | <0.001 |
| Not Employed                           | 660                | 50  |              |         |
| Current HAART regimen                  |                    |     |              |         |
| First Line                             | 728                | 65  | 7.30         | 3.63-14.68| <0.001 |
| Second Line                            | 23                 | 15  |              |         |
| Location                               |                    |     |              |         |
| Far (>100Km from FMCK)                 | 60                 | 3   | 2.29         | 0.68-7.28 | 0.263a |
| Near (<100Km from FMC)                 | 691                | 77  |              |         |
| TB Status                              |                    |     |              |         |
| Yes                                    | 19                 | 2   | 0.99         | 0.23-4.34 | 1.000a |
| No                                     | 662                | 69  |              |         |
| Pregnancy Status                       |                    |     |              |         |
| Not Pregnant                           | 503                | 57  | 1.56         | 0.44-5.48 | 0.451a |
| Pregnant                               | 17                 | 3   |              |         |
| Disease Stage                          |                    |     |              |         |
| WHO stages 1 and 2                     | 732                | 77  | 1.50         | 0.43-5.19 | 0.461a |
| WHO stages 3 and 4                     | 19                 | 3   |              |         |

*a Fischer’s exact*
After adjusting for confounders, the independent predictors of non-viral suppression included being on the second line HAART regimen (Adjusted OR [AOR] 6.5; 95% CI 3.02-13.89), being employed (AOR 0.26; 95% CI 0.15-0.44) and having a baseline CD4 count greater than 500 (AOR 0.35; 95% CI 0.21-0.61) as shown in Table 4 below.

Table 4: Logistic Regression Analysis: Predictors of Viral Non-suppression in the study subjects (n=831)

| Variables                        | AOR   | CI       | P-value |
|----------------------------------|-------|----------|---------|
| Current HAART Regimen            |       |          |         |
| Second Line                      | 6.5   | 3.02-13.89 | <0.001  |
| First Line                       |       |          |         |
| Years on HAART                   |       |          |         |
| >5 years                         | 1.1   | 0.62-1.79 | 0.833   |
| ≤5 years                         |       |          |         |
| Occupational Status              |       |          |         |
| Not Employed                     | 0.26  | 0.15-0.44 | <0.001  |
| Employed                         |       |          |         |
| Baseline CD4 count (umol/L)      |       |          |         |
| ≥500                             | 0.35  | 0.21-0.61 | <0.001  |
| <500                             |       |          |         |
Discussion:
The level of non-viral suppression in this study is low and falls within the global target set of 90% viral suppression among PLHIV on HAART by USAID [5]. This study also showed that the level of viral suppression in this cohort is one of the highest levels of viral suppression in the low-middle income country. This level of viral load suppression is higher compared with the national level of viral suppression of 44.4% in the north-western part of Nigeria [6]. The value of viral suppression in this study is also higher compared with 79% in a multi-center Nigerian study [8], and 84% in Borno state in north-eastern Nigeria [9], 69% in Ghana [10] and 73% in northern Ethiopia [11]. Our findings of a high level of viral suppression are comparable with the reports from Uganda where a level viral suppression of 95% was observed after 12 months of HAART among PLHIV [12]. Similarly, the level of viral non-suppression obtained in this study is comparable to 9.0% reported in the African cohort study [13], and 7.0% reported in Vietnam [14] after at least 12 months of HAART. The high levels of viral suppression observed in this study compared to the other studies may be due to several reasons; for instance, the cut off used for the viral suppression in our study was VL < less 1000 compared with a low value of 400 used in the earlier Nigeria study that evaluated viral suppression after test and treat protocols [8] and after six months of initiation of first-line of HAART in a Moroccan study [15]. Besides, our centre is also a tertiary health care centre with a dedicated unit for PLHIV and patients routinely undergo adherence counselling during their clinic visits which could have enhanced their compliance with their medications [16]. Our findings also suggest that the goal of achieving a 90% level of viral suppression is achievable in a resource-limited country like ours and the current approach in the management of HIV should be sustained.
Our study also showed the factors associated with viral load non-suppression to include low baseline CD4 counts, employed people, and being on second-line HAART. The study in Ethiopia also found that low baseline CD4 count and 2nd line HAART regimen were associated with viral load non-suppression [11]. In contrast, the study in Borno State, north-eastern Nigeria found the age group and marital status to be associated with viral load non-suppression [9]. A study in South Africa also identified low CD4 count to be associated with high viral load [17]. The CD4 cells are one of the prime targets of HIV, hence it’s fall corresponds to increasing viral loads. Although not the main marker of monitoring HIV in the recent, low CD4 counts at the beginning of treatment calls for closer monitoring of the PLHIV as they have a higher chance of having viral load non-suppression.

This study showed the independent predictors of non-viral suppression among the cohorts as being on the second line HAART, with an odds ratio of six and half times compared with those on the first-line. This is consistent with the observation in Borno State, northeast Nigeria where being on the second line HAARTs was associated with viral load non-suppression [9]. The African cohort study also found that being on the second line HAART was predictive of viral load non-suppression [13]. The higher level of non-suppression of viral load in those on the second line HAART may indicate a high level of resistance as patients are moved to second-line following the failure of first-line. This is also a source of concern as non-viral suppression on second-line may necessitate consideration for the commencement of third-line HAART which are presently limited. Besides, being unemployed seems to be protective against viral load non-suppression with odds of 0.22. A study in Ghana that included occupations among factors that may predict non-suppression of viral load, did not observe any significant relationship [10]. Several factors may account for a higher level of non-suppression of viral load among the
employed people in this study. The work schedules may affect their compliance and adherence levels. Also, those that work in the formal sectors may not be regular at clinic follow up due to their work schedules and the need for frequent permission for clinic attendance. Our study also showed that baseline CD4 counts greater or equal to 500 are protective against non-suppression of viral loads with odds of 0.35. Similarly, a study in Ethiopia also observed low CD4 count to be predictive of viral load non-suppression [18]. In Vietnam, low CD4 counts were also found to be predictive of non-viral suppression [14]. The findings of low baseline CD4 counts as predictive of viral load non-suppression affirms the previous observation that patients with high viral loads tend to have low CD4 counts and suggests a slow viral clearance.

In conclusion, our study demonstrates a low level of viral non-suppression among PLHIV on HAART and the target of 90% viral suppression in the PLHIV on HAART by the USAID is achievable in the resource constraint settings. Also, having low baseline CD4 count and being on second-line HAART are predictive of viral load non-suppression, while being unemployed seems protective against non-suppression of viral load.

**Limitations:** The study used secondary data, hence the analysis might have missed some important variables that can significantly determine the VL status in the study participants.

**Abbreviations:**

AIDS: Acquired Immune Deficiency Syndrome; AOR: Adjusted Odds Ratio; ART: Antiretroviral therapy; CD-4: Cluster of Differentiation 4; CDC: Centers for Disease Control and Prevention; CI: Confidence Interval; OR: Odds Ratio; HIV: Human Immunodeficiency Virus PEPFAR: President’s Emergency Plan For AIDS Relief; PLHIV: People Living With HIV/AIDS; P-value: Precession value UNAIDS: United Nations Programme on HIV and AIDS; VL: Viral Load; WHO: World Health Organization; FMC Katsina: Federal Medical Centre, Katsina.
Declarations:

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Authors’ contributions:

SBA conceptualized and designed the study, involved in data analyses, acquisition of data, tabulating the data, interpretation of data, preparing tables and figures, drafting the initial manuscript and critically revising the manuscript. ORI has involved in interpretation of data, drafting the initial manuscript, and critically revising the manuscript. ABO, RIY, IB, SH, SAI, OTIA, SBM, MY and MKA have contributed in interpretation of the data, initial draft synthesis, and revising the manuscript. MKA and MBS have primary responsibility for final content and involved in final review. All authors read and approved the final manuscript.

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Availability of data and materials:

The data that support the findings of this study are available from the Federal Medical Centre, Katsina HIV clinic. Data are available from the authors upon request and with permission of Federal Medical Centre, Katsina management. Request for permission to access this data should be directed to the Medical Director, Federal Medical Centre, Katsina-Nigeria.

Ethics approval and consent to participate: Ethical clearance and approval were obtained from Federal Medical Centre, Katsina Health Research Ethics Review Committee with the registration number FMCNHREC.REG.003/082012. All methods and procedures in this study were performed in accordance with approved guidelines of the research ethics committee. Permission to use the data was obtained from the Medical Director, Federal Medical Centre Katsina. The data were from a secondary database on HIV infected patients for VL monitoring while on treatment. Informed consent was gotten from all adults enrolled in care in the HIV clinic of the Hospital that information generated in the course of their care could be used for research purposes. The data were not accessible by any other third party other than the study team.

Consent for publication: Not applicable
Competing interests: Authors’ declare that there are no competing interests.

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