

Sex Differences in Response to Antiretroviral Therapy Among People Living With HIV/Aids Attending Art Clinic in Federal Medical Centre, Abuja

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Abstract

To assess gender differences in response to antiretroviral therapy among people living with HIV/AIDS attending ART Clinic in Federal Medical Center (FMC), Abuja. A retrospective cross-sectional study was conducted among 595 HIV-positive adult patients attending HIV clinic in FMC Abuja between January 2021 and December 2022. Data was retrieved from the database of ART Clinic, FMC Abuja, for patients who have been on TDF/3TC/DTG regimen for at least six months before viral load testing. A total of 1,150 registered People Living with HIV Aids (PLWHA) received care between January 2021 and December 2022 in FMC Abuja. Only 595 had viral load test within the study period, comprising of 205 (34%) males and 390 (66%) females in a ratio of 1:1.9. The viral load of the study participants ranged from 0 to 3,970,000.00 copies/ml with a standard deviation of 310,099.63 copies/ml. 571 (96%) of the total study participants had viral load less than 1,000 copies/ml, and 200 (35%) of them were males whereas 371 (65%) were females. The remaining 24 (4%) of the study participants who had viral load greater than 1,000 copies/ml were 8 (34%) males and 16 (66%) females. The differences in the means of viral load between males and females were not statistically significant, with a p-value of 0.054. This study found a very high viral suppression and females were equally virally suppressed as the males.

Keywords: Abuja, Assessment, ART clinic, Federal Medical Centre, Gender differences, HIV/AIDS, Response to ART.

Introduction

In 1981, the Acquired Immune Deficiency Syndrome (AIDS) was discovered, and the Human Immunodeficiency Virus (HIV) was identified as the causative agent [1]. HIV exists in two forms: HIV-1 and HIV-2. HIV-1 is the predominant type and widely distributed with high genetic diversity and mutation potentials¹. HIV transmission occurs mainly through sexual routes, contact with infected blood, and vertical transmission from mother to child [1].

A total of 84.2 million people have been infected with HIV and 40.1 million people died from AIDS-related illnesses since it was discovered in 1981. In 2021, 38.4 million

people were living with HIV and 1.5 million people were newly infected with 650,000 deaths from AIDS-related illnesses [2]. Comparatively, there were 2 million deaths in 2004 and 1.4 million deaths in 2010. Out of the 38.4 million living with HIV in 2021, 36.7 million (96%) of them were adults (15 years or older), 1.7 million (4%) were children (0–14 years), and 54% were women and girls⁵. Only 28.7 million (75%) people accessed antiretroviral therapy in 2021, against 7.8 million in 2010. In the same period, 70% and 80% of adult males and females respectively accessed treatment [2].

70% of HIV infections in 2021 were attributed to sex workers, gays, injection drug

users, and transgender. The risk of acquiring HIV [3]:

1. 30 times higher for female sex workers.
2. 28 times higher among gay men.
3. 35 times higher among people who inject drugs.
4. 14 times higher for transgender women.

Nigeria's current HIV prevalence is 1.4% with varying prevalences across the states. Katsina state has the lowest prevalence of 0.3% while Akwa-Ibom state has the highest prevalence of 5.6% [4].

Hormones modulate different biochemical processes in the body and the differences in the hormonal profile of male and female are quite profound. Such difference has been exhibited in the immune response. It has been demonstrated that oestrogen plays a significant role in regulating the innate immune system. Oestrogen mediates the formation of complexes involved in gene regulation and promotes transcription and epigenetic changes. Oestrogen is also involved in the cellular signalling system for rapid cell response by promoting the production of interferon and pro-inflammatory cells whose effects may be potentiated or depressed by the activity of oestrogen receptors. The relationship between estradiol and oestrogen receptor activity has been known to be dose-dependent. Sex differences in immune response are the function of innate immune system regulation by oestrogen receptors [5].

The AIDS epidemic has had a unique impact on women and has been exacerbated by their role within society and their biological vulnerability to HIV infection [6]. Frequently, in developing countries women with HIV infection encounter great difficulty in accessing health care and carry a heavy burden of caring for children and other family members who may also be HIV-infected [6-7]. Women often lack social support and face other challenges that might interfere with their ability to adhere to treatment regimens [7].

Viral load testing is the preferred monitoring tool for antiretroviral therapy failure (ART) as recommended by the World Health Organization (WHO). Plasma HIV ribonucleic acid (RNA) levels provide a direct measure of the efficacy of antiretroviral therapy, predicting immunological and clinical outcomes and the risk of transmission [8]. The National Guideline on HIV prevention and treatment recommends viral load testing at six months at six months after initiating ART, then annually if virally suppressed. However, individuals who are not virally suppressed will undergo intensive adherence counseling, after which viral load testing can be repeated, in order to differentiate poor adherence from treatment failure [9].

The overall objective of this study is to determine sex differences in response to antiretroviral therapy among people living with HIV/AIDS (PLWHIV) attending the ART Clinic at Federal Medical Centre, Abuja, Nigeria. However, the specific objectives of this study include the determination of the percentage of viral suppression among PLWHIV attending ART Clinic in FMC Abuja, as well as the difference in viral suppression between the males and females.

This research considers the following questions:

1. Is there a sex difference in antiretroviral therapy (ART) response among people living with HIV/AIDS (PLWHIV) attending ART Clinic at Federal Medical Centre (FMC), Abuja, Nigeria?
2. What is the percentage of viral suppression among PLWHIV in the ART Clinic at FMC Abuja?
3. What is the proportion of viral load suppression between males and females attending the ART Clinic in FMC Abuja?

In the statement of problem for this research, it is important to note that statistics have adequately proven that Highly Active Antiretroviral Therapy (HAART) improved the lives of HIV-infected people by reducing

morbidity and mortality [10]. However, certain factors related to the host may influence the success of HAART. Gender is one of such factors that may affect disease progression and treatment outcome. Hence, HIV affects men and women differently based on differences in sexual configuration. The innate immune system can be influenced by hormones, especially oestrogens [11]. Even though oestrogen may appear to put women at some advantage, the untoward experience of likely stronger side effects by women on antiretroviral drugs may lead to low adherence to antiretroviral drugs. Oestrogen may play a significant role in the expression of such high levels of side effects [11].

The justification for this research hinges on the fact that different aspects of HIV disease progression and treatment outcomes have been studied with varying findings. Although the differences were attributed to different factors, biological and social differences between males and females play a key role in immune modulation and response to antiretroviral drugs. Additionally, it has been established that sex influences disease processes as well as the outcome of treatment. Some studies in other regions of the country showed conflicting results about sex differences in response to antiretroviral therapy. Furthermore, to the best of my knowledge, no research has been done which assessed gender differences in response to antiretroviral therapy among HIV-positive patients in Abuja. This study, therefore, aims to determine sex differences in response to ART among PLWHIV attending the ART Clinic in FMC Abuja. Findings from this research will add to the body of knowledge as well as become the base for further studies.

Literature Review

The introduction of highly active antiretroviral therapy (HAART) ushered in a considerable reduction in morbidity and mortality in HIV-infected individuals [12].

Some studies reported different rates of HIV disease progression and virological and immunological responses to antiretroviral therapy to the sex of the infected people. Some studies provided evidence that clinical progression of HIV appeared to be more rapid among women than men and attributed it to the fact that women were less likely to be started on antiretroviral drugs [7].

The clinical course in HIV-infected men and women also differ because of frequent gynecologic morbidity, pregnancy, pretreatment anaemia and older age at the time of HIV acquisition [6].

Psychosocial factors such as violence, discrimination and other stressful conditions have been attributed to a high risk of adverse health outcomes in women with HIV [15]. While some studies showed that plasma HIV-RNA levels are significantly lower in women than men [13], more recent studies have shown that there are no significant gender differences concerning the clinical progression of the disease as well as hospitalization rate [10-14].

Baseline clinical and immunologic status are predictors of HIV-related mortality and morbidity in HIV outcome studies conducted in both high-income and low-income countries.

Loss to follow-up and non-adherence to antiretroviral therapy have been reported in some studies to be higher in males than females [15]. Some studies also reported that biological differences between males and females accounted for the differences in immunologic response to antiretroviral therapy. This may result from the physiological changes associated with ovulation where HIV-RNA level decreases in the luteal phase of the ovulatory cycle [15].

Nicastroi et al, in Italy, conducted a longitudinal observational multicentre cohort study to assess gender differences in the clinical progression of HIV-1-infected individuals during long-term highly active antiretroviral therapy and recruited 2,460

participants who must have been on protease inhibitor regimen for 43 months. The result showed no differences between male and female participants with regard to virologic and immunologic outcomes during the long period of follow-up. However, the female participants have been reported to have a slightly lower risk of clinical progression of the disease [16].

A multicentre observational cohort study involving all HIV-infected patients seen at the Danish HIV clinics showed that in a setting with free access to healthcare and HAART, there are no gender differences in both virologic and immunologic responses to HAART [17].

Suba in Budapest reported the findings of an experiment that proved the role of estrogen receptors in innate and adaptive immune responses as well as in tissue repair processes during respiratory virus infection. In the experimental study of mice infected by the respiratory virus, the results showed increased morbidity and mortality among mice with weaker oestrogen receptor functioning in both male and female mice [18]. In animal experiments, estrogen treatment improved inflammatory reactions and decreased virus titers leading to improved survival rate [18].

A series of mixed studies by Gandhi et al. in San Francisco, USA, assessed viral load among men and women infected with HIV. A total of 13 studies were conducted. In seven of the nine cross-sectional studies, there was a reduction in the viral load of women by 2-fold compared to that of men. All four longitudinal studies showed a reduction in the viral load of women than men by 2-6 folds. There was no change in the outcome after adjustment for possible confounders such as race, mode of virus transmission, age, and antiretroviral therapy use [19].

Fausta Mosha [20] conducted a cohort study in Dar es Salaam, Tanzania, to assess gender differences in HIV disease progression and treatment outcomes after one year of ART. He

observed some differences in clinical disease progression between males and females before starting antiretroviral therapy and after one year of antiretroviral therapy. The males were observed to have delayed commencement of antiretroviral therapy and most of them started in an advanced stage of HIV infection, depicting increased mortality. The study showed that more females survived, and more females had undetected viral load compared to the males. However, after one year of antiretroviral therapy, the women were observed to have lost the initial immunologic advantage they had. It was also observed that disease progression in HIV patients who were on antiretroviral therapy was impacted by socio-demographic variables [20].

Hawkins et al carried out a longitudinal study to assess sex differences in antiretroviral treatment outcomes among HIV-infected adults in an urban Tanzanian setting where 4,383 (34%) men and 8459 (66%) women participated, and the findings showed that at enrolment, 27% of men had stage IV disease against 23% of their female counterpart. Also, men had an average CD4 cell count, of 123 cells/ μ l, while the average CD4 cell count in women was 136 cells/ μ l. Multivariate analyses attributed higher mortality risk in men [hazard ratio 1.19, 95% confidence interval (CI) 1.05-1.30, $P < 0.001$]. Also attributed to men, were, higher immunologic failure with CD4 cell count less than 100 cells/ μ l after at least six months of initiating antiretroviral therapy (hazard ratio 1.74, 95% CI 1.44-2.11, $P < 0.001$) and higher tendency of loss to follow-up up (hazard ratio 1.19, 95% CI 1.10-1.30, $P < 0.001$). There were no significant changes when analyses were restricted to the period of good adherence for all patients. Overall, men were significantly more immunocompromised than women at enrollment in antiretroviral therapy [21].

In a systematic review and meta-analysis, Druyts et al conducted a study to assess male sex and the risk of mortality among

individuals enrolled in antiretroviral therapy programs in Africa. A total of twenty-three cohort studies, including 216,008 participants (79,892 men) were recruited. Findings from the analysis showed a pooled proportion of men receiving antiretroviral therapy as 35% [95% confidence interval (CI): 33-38%] with a pooled hazard ratio of 1.37 (95% CI: 1.28-1.47), indicating a significant increase in the risk of death for men when compared to women. The study concluded that the proportion of men enrolled in antiretroviral therapy programs in Africa is lower than women and there is an increased risk of death for men [22].

A retrospective study done at the Virologic Research Clinic of Obafemi Awolowo University Teaching Hospital, Ile-Ife, Osun State, Nigeria by Onayemi et al. reviewed 227 case notes of HIV-positive patients who were 18 years and above and found that women have better outcome compared to their male counterparts on ART [23].

A cross-sectional descriptive study by Isaac *et al*, to assess viral load suppression in adult Nigerians in a regional antiretroviral therapy programme in Northern Nigeria showed a slight difference in viral load suppression between males and females: viral load was >1000 c/ml in 22.8% (587/2577) males and 23.0% (1580/6873) females. The study however reported overall viral suppression of 77% but fell below the WHO threshold of 90% [24].

Methodology

Study design

A retrospective cross-sectional study was conducted on PLWHIV attending ART Clinic in FMC Abuja between January 2021 and December 2022.

Study location

The study was carried out in the ART Clinic of FMC Abuja where PLWHIV access to a wide range of services (including free

counselling and testing, diagnosis, treatment, and prevention of HIV) being offered by all the designated specialists in line with the current guidelines for the prevention and control of HIV/AIDS. The clinic was run twice weekly, Mondays and Thursdays, between the hours of 8 am and 4 pm. However, PLWHIV can be attended to any time they come to the clinic with complaints. The clinic is also open every day to counsel, test and register newly diagnosed HIV patients. The clinic has 1,150 patients and cares for about 20 of them per clinic day.

Study population

The study participants comprise of all registered PLWHIV attending the ART Clinic in FMC Abuja who were 18 years and above and have been on tenofovir/lamivudine/dolutegravir (TDF/3TC/DTG) for at least six months and had viral load between January 2021 and December 2022.

Inclusion Criteria

The study included the following:

1. all registered for PLWHIV receiving care at ART Clinic in FMC Abuja who were 18 years and above.
2. only those on TDF/3TC/DTG regimen for at least six months before viral load testing.

Exclusion Criteria

The study excluded the following:

1. children and adolescents less than 18 years.
2. those on a regimen other than TDF/3TC/DTG.
3. those who were less than six months on HAART.
4. those with incomplete data entry.
5. those who were ill and pregnant women.

Sample Size

The sample size was the total number of registered PLWHIV [27] who met the

inclusion criteria, derived from the database of ART Clinic in FMC Abuja (similar to the study by Isaac et al., to determine viral suppression in adult Nigerians in the Northern region of the country). Hence, a total of 595 record of PLWHIV were retrieved for the study.

Data Collection

Relevant data was retrieved from the database of ART Clinic in FMC Abuja. Baseline information was obtained. The viral load of patients who have been on TDF/3TC/DTG for at least six months were obtained, and where there was more than one viral load result, the most recent was used, provided it is not more than a year.

Quality Control of Data

During the data collection period, I ensured that no data was missed or wrongly inputted, and the data was entered by double entry. Also, the SPSS spreadsheet was verified by my supervisor to ensure the accuracy of the data. Only those on TDF/3TC/DTG were used for the study to ensure standardization.

Statistical Analysis

SPSS statistical software was used to compute and analyze data. Means, frequencies and percentages characterized the study

participants while tables and figures were used to summarize the data of the study participants.

Assumption

This study assumed that the clinical and immunologic parameters were essentially normal.

Limitation

Since viral load testing was not done at the same time for all the study participants, the results may not be a true reflection of their viral load status. Additional evaluation of the clinical and immunologic components would have given a balanced and objective conclusion about the effectiveness of ART response.

Result

This study retrieved data from the database of ART Clinic, FMC Abuja, where a total of 1,150 registered People Living with HIV Aids (PLWHA) received care between January 2021 and December 2022. Out of the 1,150 PLWHA, only 595 had viral load within the study period. Of the 595 study participants, there were 205 (34%) males and 390 (66%) females in a ratio of 1:1.9, see Figure 1 and Table 1

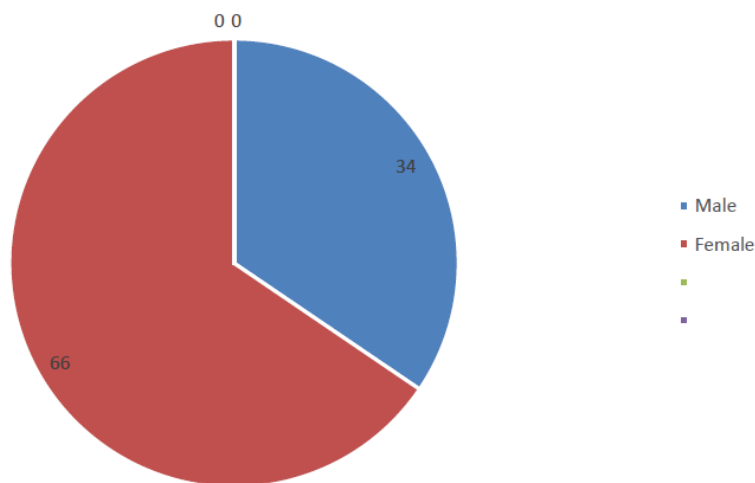


Figure 1. Pie chart showing males and female

The age of the study participants ranged from 18 to 78 years. The mean age was 44.6 years with a standard deviation of 9.2 years. The median age and mode of the study participants were 43.0 years and 44.0 years respectively. The difference in age between males and females was statistically not significant with a *p*-value of 0.057. The viral load of the study participants ranged from 0 to 3,970,000.00 copies/ml with a standard deviation of 310,099.63 copies/ml.

371 (62.3%) of the study participants fall within the age group 26 – 45yrs and the least age group was 18 – 25yrs. 553 (93%) of the respondents have attained a tertiary level of education while 30 (5%) have a secondary level of education and 3 (0.5%) have no formal education. 438 (73.6%) of the respondents were married, 149 (25%) were single and only 8 (1.4%) were divorced. See Table 1.

Table 1. Sociodemographic Characteristics

VARIABLE	FREQUENCY	PERCENTAGE (%)
SEX		
Male	205	34
Female	309	66
AGE (YEARS)		
18-25	14	2.4
26-45	371	62.3
46-55	143	24
56-65	51	8.6
66-100	16	2.7
LEVEL OF EDUCATION		
None	3	0.5
Primary	9	1.5
Secondary	30	5
Tertiary	553	93
Marital Status		
Divorced	8	1.4
Married	438	73.6
Single	149	25

561 (94.3%) of the total study participants had a viral load of less than 1,000 copies/ml, and 188 (31.6%) of them were males whereas 373 (62.7%) were females. The remaining 34 (5.7%) of the study participants who had a viral load greater than 1,000 copies/ml were

17 (2.8%) males and 17 (2.8%) females. The differences in the means of viral load between males and females were not statistically significant, with a *p*-value of 0.054. See Table 2 and Figure 2.

Table 2. Viral Load

VIRAL LOAD	MALE	FEMALE	TOTAL
Viral suppression	188 (31.6%)	373 (62.7%)	561 (94.3%)
Non-viral suppression	17 (2.8%)	17 (2.8%)	34 (5.7%)

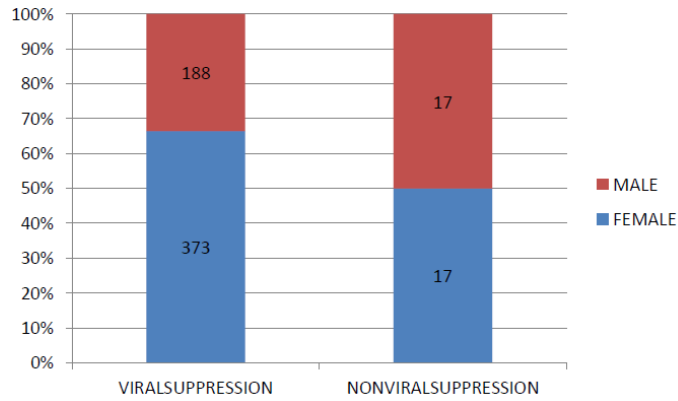


Figure 2. Relationship Between Viral Load Suppression And Sex

In terms of age group, viral suppression was achieved in the age group 26-45 years in 348(58.5%) of the respondents. 46-55yrs age group had achieved viral suppression in 133 (22.4%) of the respondents. Also, non-viral

suppression was 23 (3.9%) in the 26-45yrs age group, 10 (1.7%) in the 46-55yrs age group and zero in the 18-25yrs and 56-65yrs age groups respectively. See Table 3 and Figure 3.

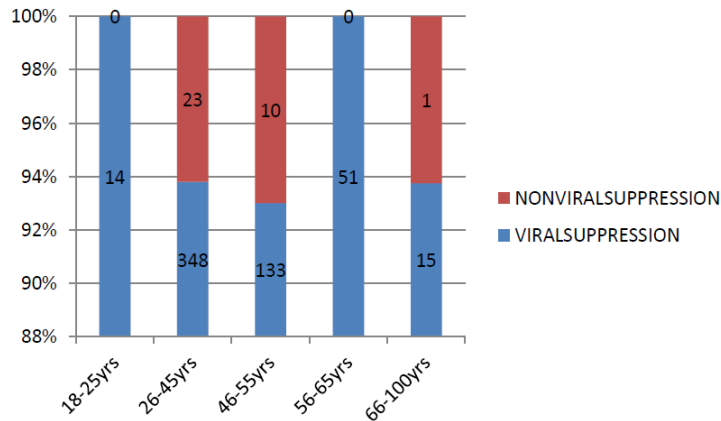


Figure 3. Relationship Between Viral Load Suppression And Age (Years)

Viral suppression was 413 (70.1%) among respondents who were married, 135 (22.7%) in those who were single and 8 (1.3%) among respondents who were divorced. However, there were 21 (3.5%) with non-viral

suppression even though married. The singles with non-viral suppression were 13 (2.2%) and there were none with non-viral suppression among the divorced. See Table 3 and Figure 4.

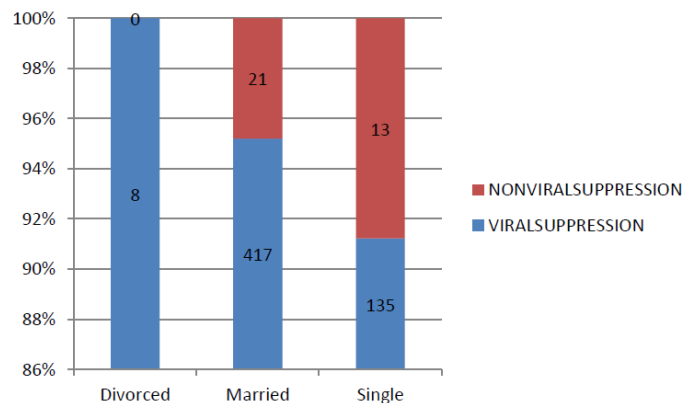


Figure 4. Relationship Between Viral Load Suppression And Marital Status

520 (87.4%) of the study participants had a tertiary level of education and were virally suppressed. 29 (4.9%) of the respondents had secondary education and were virally suppressed and there were 3(0.5%) of the respondents with no formal education and were virally suppressed. Conversely, 33

(5.5%) of the respondents with tertiary education were non-virally suppressed and 1(0.2%) with a secondary level of education were non-virally suppressed. Interestingly none was non-virally suppressed among those with a primary level of education or no formal education. See Table 3 and Figure 5.

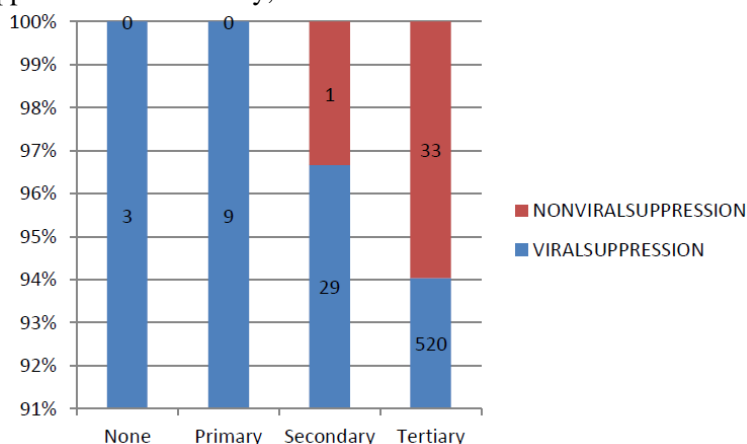


Figure 5. Relationship Between Viral Load Suppression And Educational Status

Table 3. Relationship Between Viral Load And Age, Marital Status And Educational Level

VARIABLE	VIRAL LOAD (<1000 copies/ml)	VIRAL LOAD (>1000 copies/ml)	P-VALUE
Age (years)			0.036
18-25	14 (2.4%)	0	
26-45	348 (58.5%)	23 (3.9%)	
46-55	133 (22.4%)	10 (1.7%)	
56-65	51 (8.6%)	0	
66-100	15 (2.5%)	1 (0.2%)	
Marital Status			0.082
Divorced	8 (1.3%)	0	
Married	413 (70.1%)	21 (3.5%)	
Single	135 (22.7%)	13 (2.2%)	
Level of Education			0.012
None	3 (0.5%)	0	
Primary	9 (1.5%)	0	
Secondary	29 (4.9%)	1 (0.2%)	
Tertiary	520 (87.4%)	33 (5.5%)	

Discussion

A total of 595 participants comprising 205 (34%) males and 390 (66%) females in a ratio

of 1:1.9 with a mean age (\pm standard deviation) of 45 ± 9.2 years were recruited for the study (Table 1). The higher prevalence of

HIV infections among females in developing countries may be accounted for by the preferential access to screening available to women through a specific range of services, and this study demonstrated a male-to-female ratio of 1:1.9. Generally, gender can influence causation and treatment outcome in PLWHIV. Some of the gender-related factors that affect treatment outcomes in PLWHIV include sociocultural, behavioural, body size and composition, genetic biochemical factors, and hormonal or reproductive influence. These factors can alter the pharmacologic properties of drugs and influence treatment outcomes in PLWHIV [25]. The results of viral load showed no statistically significant differences between males and females. Also, there was no statistically significant difference in terms of the age of male and female participants. Viral load has been recommended by the WHO as the gold standard to monitor response to ART [26]. Also, the UNAIDS proposed a strategy to achieve viral suppression in 90% of people on ART [26]. In this study viral suppression is considered as a viral load of less than 1,000 copies/ml. In contrast, some earlier studies in Nigeria define viral suppression as a viral load of less than 400 copies/ml [25].

In this study, viral suppression was found to be 96% which is higher than the 44.5% reported in Nigeria [43]. Viral suppression rates in some African countries like Kenya, Uganda, Congo, Ethiopia, Cameroon, South Africa and Ghana were reported as 62%, 32%, 86.4%, 73%, 79%, 56.2% and 69% respectively [27-32].

In this study, females were equally virally suppressed as the males. Similarly, some studies showed no gender differences in response to ART [33-34]. However, some studies showed that females were more virally suppressed than males [35].

This study did not show a significant association between age and sex differences in response to ART. However, some studies in

sub-Saharan Africa [27-28, 36] showed that viral suppression is more likely in younger adults than older adults.

The very high viral suppression reported in this study is in line with the United States Agency for International Development (USAID) target for 90% viral suppression among PLWHIV [31] and it is also higher compared with the national level of viral suppression (44.4%) as well as sub-national references in other regions of the country. Studies reported viral suppression of 84% in Borno State, Nigeria [37].

Conclusion

Viral suppression is very high among PLWHIV attending ART Clinic in FMC Abuja and quite satisfactory to the 90% viral suppression target by UNAIDS but there were no sex differences in response to HIV. Further research is recommended in determining the association between resistance testing and sex differences in response to ART.

Recommendation

Since this is the first study to investigate sex differences in response to ART in Abuja, the findings support the special need for further research of sex differences in response to ART to determine the clinical and immunologic status of PLWHIV. I also strongly recommend strengthening the current program as well as improving ART service provision to maintain high viral load suppression in PLWHIV in Abuja.

Conflict of Interest

I declare that there are no conflicts of interest.

Acknowledgement

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