ORIGINAL RESEARCH

Viral suppression among patients on antiretroviral therapy and the influence of demographic variables: Clinical evidence from a Nigerian tertiary hospital

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ABSTRACT

Background: Antiretroviral therapy is aimed at suppressing viral replication to undetectable level in the blood. This helps to slow down disease progression, reduce incidence of opportunistic infections, lower the risk of transmission and improve quality of life of patients. Viral suppression is increasingly becoming a clinical challenge as evidence of non-suppression is becoming more common among patients on HAART.
Objective: This study aims to determine the rate and factors associated with viral suppression among adult HIV/AIDS patients on highly active antiretroviral therapy
Methods: This was a retrospective study involving 405 patients on four different HAART regimens. The study was carried out between 2016 and 2018 in ARV clinic of a tertiary care hospital using data obtained from medical records of patients. The primary outcome measure of viral load suppression is defined as <1000 copies/ml. Analysis was carried out using descriptive and inferential statistics. P value < 0.05 was considered significant
Results: The proportion of patients who achieved viral suppression was 74.2% which is lower than 95% global target. The result showed no significant differences in the rate of viral suppression between the four HAART regimens in this study. There was also no significant association between demographic factors and viral suppression.
Conclusion: The rate of viral suppression in this study was lower than the UNAIDS target of 95%. This finding makes a case for greater improvement and strengthening of existing programme interventions aimed at promoting long term suppression of viral replication.

Keywords: HIV/AIDS, Viral load, Viral suppression, HAART, Adherence, Regimen

INTRODUCTION

The global HIV/AIDS pandemic continues to threaten the health and lives of millions around the world in spite of increasing availability and access to highly active antiretroviral therapy. Recent epidemiological data showed that 36.9 million people are living with HIV globally, of which 70% live in Africa. According to UNAIDS, sub Saharan Africa now accounts for 51% of new HIV infections and out of 650,000 AIDS related deaths globally an estimated 51,000 occurred in Nigeria[1-3]. While HIV infection in Nigeria is reported to be about 1.3% of the general population; current data from national agency for control of AIDS indicate that 1.8

million people are currently living with the virus[1].

The introduction of highly active antiretroviral therapy [HAART] and increasing access to free treatment has significantly reduced morbidity and mortality associated with the disease. Access to antiretroviral therapy varies widely between countries, and recent evidence showed that low and middle income countries are well behind in meeting global targets. An estimated 28.7 million patients out of the global population of infected persons have accessed to antiretroviral therapy as of the year 2021, which still leave millions out of therapy[1,4].

The primary goal of HAART is to achieve sustained suppression of viral replication[5,6] which can dramatically slow down disease progression. Viral suppression has demonstrated its positive impact not only in reducing the risk of perinatal and sexual transmission[1,7,8], promotion of immune reconstitution[9] but also significantly reduce morbidity and mortality associated with the infection[10,11]. The clinical benefits of therapy also extend to reduction in both rate and severity of opportunistic infections[12] as well as lowering the risk of drug resistance[13,14].

The current UNAIDS fast track action plan to end AIDS epidemic by 2030 based on 95 – 95 – 95 strategy set three key targets. These targets rely on projections that "95% of HIV infected people should know their status through testing of whom 95% of infected people shall be on medication and 95% should achieve sustained viral suppression by the year 2025[15]. The implementation of this strategy in most developing countries is well behind schedule, although some countries have made greater progress than others[1,4]. Literature evidence in Nigeria showed that viral suppression rates ranged between 44.4% and 84%[16-18], and comparable figures have also been reported in several sub–Saharan African countries[19-21]. In many developing countries, studies have reported viral load suppression levels of 59%[22], 77%[23] and 82%[24] all of which clearly indicated that many patients are not achieving viral suppression targets.

A number of predictors of viral non-suppression have been reported to include poor adherence[25,26], increasing age[27,28], delayed initiation of HAART[29] as well as behavioural and socio-demographic factors[30-32]. In other to achieve sustained virologic suppression, patients must have continuous access to antiretroviral drugs, regular testing of viral load and CD4 as well as other associated care services. The World Health Organization also recommended that viral load of patients on therapy should be measured every six months to detect early signs of treatment failure[33,34].

In low and middle income countries virologic non-suppression or rebound viral replication threshold was set at >1000 viral RNA copies in patients who have been on HAART for at least six months[34]. While transient increase in viral load has been reported among patients on long term therapy, the phenomenon was only noted among a subset of patients. Viral rebound has been reported to be frequent among patients with substance abuse, drug resistance and recent vaccination[5,36,37]. The influence of sociodemographic variables has produced contrasting results[18,19,21,24], which clearly indicate their highly variable influence on viral suppression rates among different sets of patients.

There is abundant clinical evidence that the current HAART regimens are potent enough to reduce viral load to undetectable levels in most drug – naïve patients within eight months, however the question of whether or not this suppression will be sustained over time is less clear. While immune reconstitution is influenced by CD4 cell count at the time of HAART initiation[38,39], viral rebound has been found to increase after three years of therapy[40]. The factors responsible for this observation is multidimensional, complex in nature and may often be associated with patient characteristics and study settings.

As access to antiretroviral therapy improve in the country, viral suppression monitoring will become increasingly critical not only to assess effectiveness of therapy, but also to achieve

target clinical outcomes[41]. Evidence of ineffective suppression obtained from review of patient's viral load may be used as an indicator of treatment failure or resistance that may necessitate switching of treatment regimen. The major objectives of this study are to determine the level of viral suppression and its association with demographic variables among patients on antiretroviral therapy.

METHODS

Setting
This study was carried out at the ARV clinic of University of Maiduguri Teaching Hospital, Borno State

Study design
This was a retrospective study using data obtained from the medical records of patients on four HAART regimen.

Inclusion criteria
- Patients must be at least 18 years of age and non-pregnant
- They must have been on HAART for at least two years with at least one year on the current regimen
- The viral load test records must be available for two years
- There should be no switch of regimen during the study period

Sample size/Sampling: The sample size was determined using Taro Yamane's formula for calculating sample size for finite populations. The sample size of 371 was determined at 95% confidence interval. A total 405 medical records of patients were eventually used for the study. A total of 135 medical records per year were selected for review using eligibility criteria [2016, 2017 and 2018]. The selection was carried out using simple random sample method.

Data collection
The medical records of selected patients were reviewed and details of their HAART regimen, comorbidities, viral load test results, opportunistic infections and demographic data were extracted.

HAART regimens
Regimen I: Tenofovir + Lamivudine + Efavirenz
Regimen II: Zidovudine + Lamivudine + Nevirapine
Regimen III: Tenofovir + Lamivudine + Dolutegravir
Regimen IV: Zidovudine + Lamivudine + Lopinavir + Ritonavir

Outcome measure
The primary outcome variable was viral suppression as defined by Nigeria's national guideline for treatment and control of HIV/AIDS 2018. It defined virologic suppression as viral load of 1000 copies of viral RNA/ml while patients with high than this value was considered to have achieved viral suppression.

Data analysis
The analysis was carried out using IBM SPSS [SPSS Inc., Chicago, USA] for windows version 21. The proportion of patients who achieved virologic suppression was expressed using descriptive statistics. The percentage of patients who achieved viral suppression was determined by dividing the number of patients who achieved viral load <1000 copies/ml to undetectable levels by the total number included in the study. The association between demographic factors [Gender, age, marital status, educational level and employment] and viral suppression was determined using Chi square and Fischer exact test as appropriate. The P value for statistical significance was set at <0.05.

Ethical issues
The study was carried out after ethical approval was obtained from health research ethics committee of the University of Maiduguri teaching hospital.

RESULTS

Demographic data showed that majority were females [64.7%] and were either self-employed or unemployed [78.8%]. Majority of selected patients had primary education [69.1%] and married [69.4%] [Table 1].

Table 1: Demographic data

Variable	Frequency [%]
Gender	
Male	143 [35.5]
Female	262 [64.7]
Marital status	
Single	54 [13.3]
Married	281 [69.4]
Divorced	70 [17.3]
Educational status	
Primary	280 [29.1]
Secondary	70 [17.5]
Tertiary	55 [13.4]
Occupation	
Civil service	69 [17]
Self employed	149 [36.8]
Unemployed	170 [42]
Student	17 [4.2]
Age [yrs.]	
18 – 30	114 [28.1]
31 – 49	160 [39.5]
≥ 50	131 [32.4]
Mean age: 41.9 ± 14.3	
Duration of HAART [yrs.]	
1 – 3	100 [24.6]
4 – 6	221 [54.6]
7 - 9	51 [12.6]
≥ 10	33 [8.2]
Mean duration: 5.1 ± 2.5	

The most frequently encountered opportunistic infections were upper respiratory infections and pulmonary tuberculosis accounting for 28.3% and 16.9% respectively. The major comorbidities were peptic ulcer disease [20.4%] and hypertension [8.8%]. [Figure 1].

The average percentage of patients who achieved viral suppression was 74.2% across the four HAART regimens included in this study. The suppression rate was highest for Regimen I [78.9%] and least for Regimen III [70.5%], while Regimen II [75.3%] and Regimen IV [72.2%] had rates that fell in between. The suppression rate included patients with undetectable viral load and those with viral load of < 1000 copies/ml. The results also showed that about a quarter of all patients did not achieve expected viral suppression [>1000 copies/ml]. There was no statistically significant association between HAART regimen, age, duration of therapy, presence of comorbidities and viral suppression [Table 2].

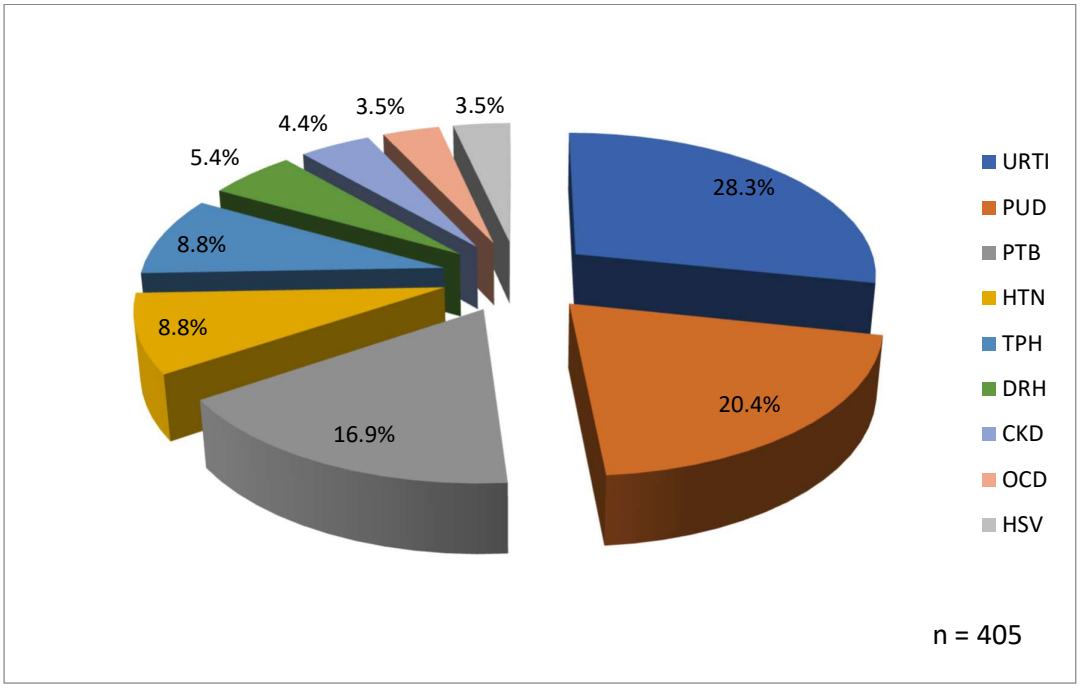

Figure 1: Comorbidity and opportunistic infections

Key: *URTI =upper respiratory tract infection, PUB =Peptic ulcer disease, PTB =Pulmonary tuberculosis, HTN =Hypertension, TPH =Typhoid, DRH = Diarrhoea, CKD = Chronic kidney disease, OCD = Oral candidiasis, HSV = Herpes simplex virus*

Table 2: Demographic variables and viral suppression

Variable	Suppressed [%]	Unsuppressed [%]	P value
HAART regimen			
I	210 [78.9]	56 [21.1]	0.4213
II	58 [75.3]	19 [24.7]	
III	31 [70.5]	13 [29.5]	
IV	12 [72.2]	6 [27.8]	
Average	**74.2**	**25.8**	
Age [yrs.]			
18 – 30	86 [75.4]	28 [24.6]	0.6273
31 – 49	122 [76.2]	38 [23.8]	
≥ 50	105 [80.1]	26 [19.9]	
Duration on HAART [yrs.]			
< 5	81 [81]	19 [19]	0.6563
5 – 9	169 [76.5]	52 [23.5]	
≥10	66 [78.6]	18 [21.4]	
Comorbidities			
Present	105 [77.2]	31 [22.8]	0.5290
Absent	200 [74.3]	69 [25.7]	
Year of study			
2016	92 [68.1]	43 [31.9]	0.2031
2017	99 [73.3]	36 [26.7]	
2018	105 [77.8]	30 [22.2]	
Total [n=405]	**309 [76.3]**	**96 [23.7]**	

The association between demographic factors [Gender, marital status, education and employment] and viral suppression was found to be statistically insignificant [Table 3].

Table 3: Demographic variables and viral suppression

Variable	Suppressed [%]	Unsuppressed [%]	P value
Gender			
Male	113 [79]	30 [21]	0.5808
Female	213 [81.3]	49 [18.7]	
Marital status			
Single	40 [74.1]	14 [25.9]	0.2327
Married	225 [80.1]	56 [19.9]	
Divorced	50 [71.4]	20 [28.6]	
Education			
Primary	219 [78.2]	61 [21.8]	0.6715
Secondary	55 [77.4]	16 [22.6]	
Tertiary	45 [83.3]	9 [16.7]	
Employment			
Civil service	54 [78.3]	15 [21.7]	0.4750
Self employed	123 [82.5]	26 [17.5]	
Unemployed	130 [76.5]	40 [23.5]	
Student	12 [70.6]	5 [29.4]	

DISCUSSION

Viral suppression is a major goal of antiretroviral therapy, so the monitoring of viral load is an essential component of effective therapy[42,43]. The results of this study showed that females constituted majority of patients on therapy similar to previous studies[44,45], though contrasting results have also been reported[46]. The most commonly encountered opportunistic infections were upper respiratory tract infections, pulmonary tuberculosis and typhoid which is consistent with previous studies[47-50], however similar studies reported variable incidence of infections[51]. The high incidence of opportunistic infections may be indicative of poor viral suppression and suboptimal immune recovery among patients[52-55].

The current HAART regimens are potent enough to achieve sustained viral suppression[17,21,57], however suppression rate was suboptimal for a quarter of patients in this study. Several studies have reported high variability of viral suppression rates between different HAART regimens [58-60], however there is no conclusive evidence of superiority of one regimen over another [61-63] similar to findings of this study. This study did not show significant association between viral suppression and demographic variables, which is in contrast to some previous studies[46,64]. A number of other studies reported significant association between viral suppression and demographic variables such as gender[65,66], duration of therapy[20,67], age[68-70], educational status[20], employment[42], marital status[18], adherence[72,73] and presence of comorbidities[71].

The influence of antiretroviral regimen type on viral suppression has been reported often with often contrasting conclusions[23]. While the results of this study did not show significant association with demographic variables[74,75], contrasting results has been reported in similar studies[23,46,76]. A review of viral suppression rates in sub Saharan countries reported values comparable to the results of this study[31,46,69], although a recent systematic review revealed higher suppression rates[77]. The differences in viral suppression rates may be related to a number of factors including study design, patient characteristics, type of antiretroviral regimen, duration of therapy and level of ART

programme performance within and between study settings[78,79].

In an effort to achieve viral suppression goal of 95% by 2030, there is need for concerted efforts by HIV/AIDS programme managers to upscale interventions along the whole spectrum of service delivery to patients. The proportion of patients with viral non-suppression may presence long term challenges in form of drug resistance, increased morbidity and mortality among patients on therapy.

CONCLUSION

The average viral suppression rate in this study was considerably well below UNAIDS target of 95%. There was no significant association between demographic variables and viral suppression in this study. There is the need to improve monitoring and early identification of suboptimal viral suppression which can help guide initiation of patient focused intervention(s) either by strengthening adherence support and/or switching to another regimen for better clinical outcomes.

LIMITATIONS

The study utilized retrospective viral load data which may not be incomplete. There was also the absence of data relating to adherence and viral resistance testing to make any inference on other possible contributory factors.

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