HIV/AIDS Patients' Adherence to Antiretroviral Therapy in Sobi Specialist Hospital, Ilorin, Nigeria

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ABSTRACT

Nigeria currently accounts for about 10 percent of the global HIV burden, therefore tackling this devastating pandemic is very imperative. This study was conducted to assess the level of patients' adherence to antiretroviral therapy and identify the factors responsible for non adherence in a major HIV/AIDS specialist hospital, Sobi, Ilorin, Nigeria. Adherence among 213 HIV infected patients on highly active antiretroviral therapy was assessed using self-reporting and pill counting methods for 20 months of therapy. Structured questionnaire, personal interview and patients' hospital records were used to evaluate access to medicines and patients' factors responsible for treatment adherence. Though, the level of patients' adherence to antiretroviral drugs was low (73.3%) compared with the standard (95%), there was significant improvement compared with the earlier reported in the sub-Saharan African countries including Nigeria. Low level of education of patients, adverse antiretroviral drug effects and stigmatization were the main factors given for non adherence. Thus, Nigeria government and non-governmental organizations should intensify efforts by improving the standard of education of the citizenry, increasing the level of awareness and encouragement on HIV/AIDS status as well as continuing funding to the rural communities to stem the tide of the menace.

Keywords: HIV/AIDS, antiretroviral drugs, adherence, counselling, patients, Nigeria

1. INTRODUCTION

According to UNAIDS, *human Immunodeficiency Virus* (HIV) affected 30.8 million adults and 2.5 million children worldwide as at the end of 2009. Sub-Saharan Africa with just over 10% of the world's population has the greatest burden of disease (68%). In the year 2009, about 1.8 million adults and children were infected, contributing to a total of 22.5 million people living with HIV in the region. Women are particularly affected with Southern Africa accounting for about 40% of the global women living with the disease. More than 90% of the children infected are babies born to women with HIV, who acquire the virus during pregnancy, labour or delivery, or through breast milk [1]. There is therefore the need for concerted efforts toward tackling this menace. The development and widespread use of antiretroviral therapy (ART) as the treatment of choice in HIV has improved significantly the health condition of HIV positive individuals who could have untimely death. The ART however, has transformed the perception of HIV/AIDS from a fatal incurable disease to a manageable chronic illness [2]. The treatment causes improvement in immunologic status and reduction in the viral load [3] which consequently reduces the incidence of hospitalization and mortality [4].

However, incomplete medication adherence is the most important factor in treatment failure and the development of resistance. Adherence is the term used to describe the patient's behavior of taking drugs correctly in the right dose, with the right frequency and at the right time. Antiretroviral treatment success depends on sustainable high rates of adherence to medication regimen of ART [5]. On the other hand, ART regimens are habitually complicated with variable dosage schedules, dietary requirements,

and adverse effects [6]. Treatment success can be precarious with missing of few doses of antiretroviral medication which leads to drug resistant strains of HIV [7]. An adherent patient is defined as one who takes 95% of the prescribed doses on time and in the correct way, either with or without food. Adherence is a major predictor of the survival of individuals living with HIV/AIDS [5] and poor adherence to treatment remains a major obstacle in the fight against HIV/AIDS worldwide. Low or incomplete medication adherence has been associated with detectable viral load (> 500 viral RNA copies/ ml of plasma) [8] with the development of cross resistance to other antiretrovirals of the same class [9]. Although, more potent antiretroviral regimens can allow for effective viral suppression at moderate levels of adherence [10], none or partial adherence can lead to the development of drug-resistant strains of the virus. Cross-resistance however can potentially interfere with future therapeutic regimens for HIV-infected patients undergoing treatment and for those who subsequently become infected with resistant strains of HIV [11]. The factors that influence adherence to antiretroviral therapy (ART) are in three categories viz., patient-related (psychosocial and educational) factors, patient-provider factors (interaction with physicians and other health workers and access to medications) and clinical factors (pill burden, dosing frequency and adverse effects of medications) [12].

Different levels of adherence have been reported in earlier studies in Nigeria. For instance, the levels reported for studies conducted in Kano (northern Nigeria), Sagamu, Niger Delta and Benin City (Southern Nigeria) are 49.2% [13], greater than 85% [14], 80% [15] and 58% [16] respectively. In several countries in sub-Saharan Africa and North America, varying levels have also been reported [5]. However, significant proportions of HIV-infected patients do not

reach high levels of adherence and this can lead to devastating public health problems. Getting patients to take drugs everyday without failure for the rest of their lives is one of the biggest challenges. Poor knowledge of HIV/AIDS and stigmatization are also prevalent among youths affecting adherence to medication. These challenges therefore justify the necessity of continuous assessment of adherence to ART in this area. This study was therefore conducted to assess the level of adherence to ART and identify the factors responsible for non adherence in a major HIV/AIDS specialist hospital, Sobi, Ilorin, Nigeria. This study offers essential information on factors associated with antiretroviral drug adherence among adult HIV/AIDS patients.

2. METHODS
2.1 Setting

This study was conducted at a designated HIV/AIDS treatment centre in the Sobi Specialist Hospital, Ilorin, Kwara State, located in the north central Nigeria. The hospital is a 264-bed secondary health facility with over 12 health departments offering health services to the residents of Kwara State and neighbouring States. The hospital was established by the Kwara State Government in April, 1985. The HIV/AIDS treatment centre took off in the hospital in May, 2009 with the provision of comprehensive HIV care services. As at December, 2010, 470 patients have been enrolled and 257 were receiving highly active antiretroviral therapy (HAART). The centre is currently receiving fund from a non-governmental organization (NGO), Friends for Global Health.

2.2 Population sample

The study sample was of 257 HIV-infected patients that enrolled and commenced HAART between May, 2009 and December, 2010. Two hundred and thirteen HIV/AIDS patients made up of 75 males and 138 females diagnosed to be living with HIV/AIDS (using both laboratory and clinical records) and on HAART treatment were selected for the study. Inclusion criteria were outpatients diagnosed and confirmed to be HIV positive, between ages of 16 and 60 years attending HIV/AIDS centre and refilling their prescription in the Pharmacy Department between May, 2009 and December, 2010. The patients were regular at the centre and using their HAART for a minimum of 6 months prior to the study. The patients also had received a fixed HAART of zidovudine(300mg), lamivudine (150mg) and nevirapine (200mg) twice daily, zidovudine(300mg), lamivudine(150mg) twice daily plus efavirenz (600mg) daily, tenofovir(300mg), emtricitabine(200mg) and efavirenz/nevirapine daily for a minimum of 6 months. The patients were consented to participate in the study. Patients excluded were children below age of 16 years and patients with history of serious cardiovascular illness, diabetes and/or cancer within the previous two years.

2.3 Study design

Ethical approval was sought from the management of the hospital and informed consent from all the patients participating in this study at the time of enrollment. Prior to the commencement of the study, a cross-sectional self-administered anonymous questionnaire survey was administered. Thirty patients were randomly selected and administered with a pre-tested structured questionnaire (with open-ended and/or closed questions) for the collection of socio-demographic characteristics, patients' and pharmacists' assessment of adherence and factors responsible for non-adherence among HIV/AIDS patients in the centre in order to look for flaws in the

questionnaire. The questionnaire was administered twice to the 30 selected patients to ensure reliability of the data collected. The data of the 30 patients were not included in the final computation of this study. All data collected were obtained from the medical records and personal interview of the patients. The interview was carried out in local language (Yoruba language) except for 22 participants who could not understand the language and had to be interviewed in respective English and Hausa languages. The importance of the study was duly highlighted to the patients by the researcher. Learned patients themselves completed a paper format questionnaire, which was explained in details prior to completion. The 36-point questionnaire was explained before completing the questionnaire to resolve any questions regarding the questionnaire. Each of the 36-point questions was tick box format with area for writing other relevant information. The researcher also inquired other drugs taken by the patients that were not in their medical records as well as their medication-related problems. Counselling of each HIV-infected patient was usually carried out monthly at the hospital using standard procedures whenever visit is made to refill their prescriptions.

2.4 Adherence assessment

Self-reporting and tablet counting methods were used to determine HAART treatment medication adherence at the end of each month consecutively for eighteen months. In tablet counting, patient's medical records were reconciled against the medicines yet to be used by the patients which were brought to the pharmacy as a routine for refill of prescriptions by patients. The numbers of drug doses that the patients should have been taken but missed were also recorded. In the self-reporting of patients' method, the patients were interviewed on adherence by asking them to recall how they administered drugs at home during refill of prescription. In both self-reporting and tablet counting methods, adherence was defined as taking 95% of prescribed doses over the previous month which corresponded to missing no more than one dose in a 10-day period (in a 2 times a day dosing regimen), one dose per week (in a 3 times a day regimen) or one dose per day (in a once daily dose regimen) in a 20-day period. Patients were classified as non-adherent if they missed more than 5% of their doses in at least one of the three categories or if they indicated missed doses in all three categories.

2.5 Statistical analysis

Data generated from the questionnaire were keyed into Genstat statistical package [17] and analysed for frequencies, mean, percentages and Chi-squared test. A p-value of < 0.05 was considered significant in all statistical analysis.

3. RESULTS
3.1 Socio-demographic characteristics

The Socio- demographic characteristics of the 213 patients are presented in Table 1. Out of the 257 recruited for the study, 213 met the inclusion criteria. Majority of the patients were females with 138 (64.8%), between 16 and 60 years old. The males were 75 (35.2%), some of the patients 168 (78.9%) were married, while as many as 72 (33.8%) had no formal education, but only 60 (28.1%) had primary education. The proportion of the patients with at least secondary education 81 (38.1%) is smaller compared with those without formal education. As many as 38 (36.6%) were traders and 48 (22.6%) were

unemployed. The rest were 33 (15.5%) civil servants, 45 (21.1%) self employed and 9 (4.2%) students.

Table 1 : Socio-demographic characteristics of HIV positive patients at specialist hospital, Sobi, Ilorin, Nigeria

Variable	Total % N= 213	Male (%) N= 75	Female (%) N= 138	P value
Age				
16-30	72(33.9)	24(11.3)	48(22.6)	
31 – 40	78(36.8)	27(12.6)	51(23.9)	0.012
41 – 50	51(24)	18(8.5)	33(15.5)	
›50	12(5.3)	6(2.8)	6(2.8)	
Marital status				
Single	21 (9.9)	6(2.8)	15(7.0)	
Married	168(78.9)	60(28.2)	108(50.7)	0.052
Widowed	15(7.0)	6(2.8)	9(4.3)	
Divorced	9(4.2)	3(1.4)	6(2.8)	
Level of education				
No formal education	72(33.7)	24(11.3)	48(22.5)	
Primary	60(28.2)	21(9.8)	39(18.3)	0.002
Secondary	51(24)	18(8.5)	33(15.5)	
Tertiary	30(14.1)	12(5.6)	18(8.5)	
Occupation				
Trader	78 (35.7)	27(12.7)	51(23.9)	
Civil servant	33(15.5)	12(5.6)	21(9.9)	
Self employed	45(21.1)	15(7.0)	30(14.1)	0.004
Student	9(4.2)	3(1.4)	6(2.8)	
Not employed	48(22.6)	18(8.5)	30(14.1)	

3.2 Treatment variables

In the ART clinic, the anti-retroviral drugs, opportunistic infection medicines and other palliative medications were provided free for all the HIV/AIDS patients in this setting. At the time of this study, 207 (97.2%) were on first line ART. The proportion of patients that used the different antiretroviral drug combinations were 40.9% (AZT + 3TC +NVP), 25.4% (AZT + 3TC +EFV), 2.8% (4DT + 3TC +NVP), 1.4% (4DT + 3TC + EFV), 19.7% (TDF + FTC+ EFV), 5.6% (TDF + FTC+NVP), 1.4% (ABC + 3TC + EFV) and 2.8% (AZD + 3TC + LPV/r). There were no switches from first line to second line regimen except 28% of the patients that were pregnant and were placed on second line regimen. All patients received cotrimoxazole, ferrous gluconate, folic acid, multivitamins, while some patients were on loratidine; 7.5%, amoxicillin ; 23.9%, acyclovir ; 2.3%, loperamide; 3.7%, metronidazole; 15.5%, paracetamol; 12.7%, nystatin; 3.5%; erythromycin; 7.5%, clotimazole; 2.8%, fluconazole; 6.5%, artemether-lumefantrine; 12.7% , bromazepam; 1.4%.

3.3 Side effects

The most experienced effect of ARV drugs in the patients were general body weakness 38% followed by dizziness 16.4%, severe headache 14.6%, sleep disturbances 12.7% , anaemia 3.3%, vomiting 3.3%, peripheral neuropathy 1.4%, chest pain 1.4% and night micturition 1.4% (Table 2).

Table 2: Treatment variables of HIV positive patients at the specialist hospital, Sobi, Ilorin, Nigeria

Antiretroviral drugs combination	N (%)
AZD + 3TC +NVP	87 (40.9)
AZD + 3TC +EFV	54 (25.4)
4DT + 3TC +NVP	6 (2.8)
4DT + 3TC + EFV	3 (1.4)
TDF + FTC+ EFV	42 (19.7)
TDF + FTC+NVP	12 (5.6)
ABC + 3TC + NVP	3 (1.4)
AZT + 3TC + LPV/r	6 (2.8)
Opportunistic infection Medicines	
Loratidine	16 (7.5)
Amoxicillin	51 (23.9)
Acyclovir	5 (2.3)
Loperamide	8 (3.7)
Metronidazole	33 (15.9)
Paracetamol	27 (12.7)
Nystatin	7 (3.5)
Erythromycin	16 (7.5)
Clotimazole	6 (2.8)
Fluconazole	14 (6.5)
Artemether-Lumefantrine	27 (12.3)
Bromazepam	3 (1.4)
Medication Side effects of antiretroviral drugs	
Rashes	16 (7.5)
Sleep abnormalities	27 (12.7)
Anaemia	7 (3.3)
Chest pain	3 (1.4)
Asthenia	81 (38.0)
Headache	31 (14.6)
Dizziness	35 (16.4)
Peripheral Neuropathy	3 (1.4)
Vomiting	7 (3.3)
Night micturition	3 (1.4)

3.4 Adherence

In the present study, based on pharmacists' adherence (Table 3), 70.8% of the patients adhered strictly to their medications while patients' self-report adherence was 73.3%. The factors that could be responsible for 29.2% adherence failure (Table 4) includes medication side effects 6.6%, away from home 5.2%, illiteracy 4.7%, high pill burden 3.7%, stigmatization 3.3%, herbal medicines 2.3%, too busy 1.9%, while forgetfulness is 1.4%.

Table 3: Patients' and pharmacists' assessment of adherence

Findings	Number of patients
Pharmacists assessment of adherence	
Adherent	151(70.9%)
Non-adherent	62(29.1%)
Self-report patient assessment of adherence	
Adherent	156(73.2%)
Non-adherent	57(26.8%)

Table 4: Factors responsible for non adherence among HIV/AIDS patients in Sobi specialist hospital

Adherence factors	Failed to take drugs as schedule		Total N =213 (%)	Males N=75 (%)	Females N=138 (%)	χ^2	P value
Away from home	Yes	No	11(5.2) 202(94.8)	7(3.3) 68(31.9)	4(1.9) 134(62.9)	1.646	0.199
Too busy	Yes	No	4(1.9) 209(98.1)	3(1.4) 72(33.8)	1(0.5) 137(64.3)	1.049	0.306
Forgetfulness	Yes	No	3(1.4) 210(98.6)	1(0.5) 74(34.7)	2(0.9) 136(63.9)	0.852	0.386
Herbal medicine	Yes	No	5(2.4) 207(97.2)	1(0.5) 74(34.7)	4(1.9) 133(62.4)	0.001	0.993
High pill burden	Yes	No	8(3.8) 205(96.2)	2(0.9) 73(34.3)	6(2.8) 132(62)	0.017	0.461
Medication side effects	Yes	No	14(6.6) 198(93)	5(2.3) 70(32.9)	9(4.2) 129(60.6)	0.461	0.038
Stigmatization	Yes	No	7(3.3) 206(96.7)	4(1.9) 71(33.3)	3(1.4) 135(63.4)	0.156	0.156
Illiteracy	Yes	No	10(4.7) 203(95.3)	3(1.4) 72(33.8)	7(33.3) 131(61.5)	0.052	0.303

4. DISCUSSIONS

In the management of HIV/AIDS worldwide, defaulting from treatment is one of the most important problems. Cross-resistance can potentially interfere with future therapeutic regimens for HIV-infected patients undergoing treatment and for those who subsequently become infected with resistant strains of HIV [13]. The present study showed that the youth between the ages of 16 and 40 years with mean age of 37.04 are those most vulnerable to HIV infection. This is in line with the findings of *Patrick and John* [18] that reported the majority are within the age range of 25-49 years and *Chjjioke et al.* [19] with mean age of 35.04 years in Port Harcourt. In this study, women are 2 to 4 times more vulnerable to HIV infection than men during unprotected sexual intercourse because of larger surface areas exposed to contact, the female is the recipient of semen and is prone to micro trauma during sexual activity and others include early exposure to sexual activity and poverty [20]. In this study, the proportion of female in the treatment group is almost two-fold than that of male counterpart. This corroborates with the study of *Kenneth et al.* [21] who reported that the proportion of females was more than two-fold greater than that of the males in Benin. Contrary to this was the work of *Fujie et al.* [22] in India whereby 51% of the study were male while with *Thejus* [23], 69% were males. The rationale behind the high percentage of females dominates that of males especially in Nigeria is due to the fact that in many cultural believes, men are expected to have many sexual relationships. Also, women suffer gender inequalities in nature and the culture creates barriers which prevent people from taken precaution especially the women [24]. In the present study, 78.9% of the population was married which is similar to the study of *Thejus*, [23] in India where 80% were married. This is expected since one of the route of HIV transmission is sexual intercourse which can easily spread among couples. This is inconsistence with work of *Chijioke et al.* [19] in Portharcourt where 43% of the patients were single and 40.1% were married.

In this present study, patients on zidovudine based regimen and nevirapine based regimen were more tolerable by the patients than stavudine based therapy due to its neuropathy effect. This is inconsistent with the study of *Bolton-Moore et al,* [25] that more of their patients were on stavudine based therapy compared to zidovudine regimen. In this clinical setting, the second line antiretroviral drugs were used mainly for pregnant women.The rational is to reduced as much as possible drug adverse effect on foetus,with Efavirenz being teratogenic in humans and nevirapine causes severe hepatotoxicity especially in women with CD4 count >250 cells/microliter.The adverse effects of antiretroviral drugs experienced by these patients do resolves after 2 to 8 weeks of therapy and tolerable by most of these patients [26]. Some patients may required other drugs to alleviate the symptoms of medication side effects. Loratidine is used for patients with skin rash induced by nevirapine and other skin disorders. Haematinics were prescribed for these patients to improved appetite for weight gain and to prevent anaemia initiated by zidovudine. Paracetamol, amoxicillin and artemether-lumefantrine were drugs of choice for HIV patients with malaria and persistent fever. Patients need to be adviced to take efavirenz an hour after an oily food to reduce nightmares and dizziness.Very few patients experienced night micturition which may be related to zidovudine. It is advice able to screen all patients on HAART for diabetes mellitus at baseline level.

It is difficult to measure adherence in the outpatient setting with absolute precision and accuracy [27]. Adherence may be measured in the clinical setting in a different ways such as patient self-reports(convenient and inexpensive), clinical assessments, pill counts(labour intensive), Directly Observed Therapy on AntiRetroviral Therapy (DOTART, theoretically associated with 100% adherence, labour intensive and impractical outside institutional setting),pharmacy records/ prescription refill monitoring, biological assays(plasma drug level) and medication event monitoring system(expensive) [28]. Adherence percentage is calculated as the observed number of doses divided by the number of expected tablets taken multiplied by hundred. In this research work, pharmacists' assessment of adherence of 70.8% was quite below 95% of adherence expected of these patients but higher in comparison with the studies of *Da Silvera et al.*[23] in Portharcourt with 49% and *Mary et al.* [29] in India of 60% adherence levels. The present study had a better adherence rate similar to the earlier findings of *Murri et al.*[30] of 74.3%. The reasons for improved adherence level in this hospital was that all the services rendered to these patients were at no cost which includes free, regular and uninterrupted supply of quality antiretroviral (ARV) drugs, medical laboratory tests and financial support. Also, drugs for opportunistic infections and palliative care were all made free for both in and out patients. Rapid improvement in symptoms and signs that brought the patients to the hospital encouraged adherence. No food restriction, proper follow up, monthly adherence counseling and high literacy level were contributing factors to adherence rate in this study. Less than one third of these patients failed to adhere to their medication schedule probably for the following reasons; medication side effects, away from home, high pill burden, illiteracy, herbal medicines, stigmatization and too busy at work/school. Medication adverse effects of antiretroviral drugs were a major barrier to drug adherence. Severe vomiting associated with zidovudine which did not resolve after 8 weeks of administration in very few patients could result to non adherence and therapeutic failure. Though in a very few patients, taking the drugs after food reduce this effect. Yellowish eyes, a pointer of liver injury may create fear for the patients to continue medication. Drug side effects as a non adherence factor is consistent with the works of *Attaran et al.* [31] and *Karl et al.* [11] in South Africa.

One quarter of the people living with HIV/AIDS demonstrated difficulty in comprehending simple medication instructions. Illiteracy has a disadvantage to drug adherence in this research work as supported by *Kalichman et al.*[32]. The higher the level of education, the better the understanding of the disease state and the comprehension of instructions given on drug usage. These could invariably enhance adherence. The minimum number of tablets to be swallowing daily by the patients throughout their lifetime is seven. The number is burdensome and disgusting for the patients to continue their medications. However, stigmatization of HIV/AIDS patients by the society contributes to non drug adherence. Some patients felt embarrassed while taking their medical folders to pharmacy for prescription refill, despite these folders were similar to other patients in the hospital. In agreement with present study, *Grierson et al.* [33], reported that HIV/AIDS patients have difficulties in taking drugs in public and carrying drugs around thereby adversely affecting adherence. The studies of *Talam et al.* [34] in Kenya *and Yao et al.* [35] in Togo also supported above listed factors associated with non adherence.

5. CONCLUSION

In Sobi specialist hospital, Ilorin, a resource poor area in Nigeria, the level of adherence to antiretroviral drugs is low compared with standard level of 95% drug adherence and this corroborates with earlier reports in Kano, Sagamu, Niger Delta, Portharcourt and Benin City in Nigeria, other African countries like Kenya, Togo and South Africa as well as India and North America. Level of education of the patients, adverse antiretroviral drug effects and stigmatization were the main factors for non adherence. Thus, Nigeria government and the NGOs should intensify their efforts by improving the standard of education of the people, increasing the level of awareness of HIV/AIDS; encourage the people to know their HIV status and continuing funding the projects to the rural communities.

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