British Journal of Medicine & Medical Research
4(31): 5003-5018, 2014

SCIENCEDOMAIN *international*
www.sciencedomain.org

Adherence to Antiretroviral Therapy: Prevalence, Determinants and Impact on Body Weight and Immunological Recovery among People Living with Human Immunodeficiency Virus in Osogbo, Nigeria

Adeolu Oladayo Akinboro[1*], Abdulkareem Afolabi Salawu[2] Roseline Opeyemi Awoyemi[3] and Olugbenga Edward Ayodele[4]

[1]Department of Internal Medicine, Ladoke Akintola University of Technology, and LAUTECH Teaching Hospital Ogbomoso, Oyo State, Nigeria.
[2]Department of Chemical Pathology, Ladoke Akintola University of Technology and LAUTECH Teaching Hospital Ogbomoso, Oyo State, Nigeria.
[3]People Living with Human Immunodeficiency Virus (PLWHIV) Clinic LAUTECH Teaching Hospital Osogbo, Osun State, Nigeria.
[4]Department of Internal Medicine, Ladoke Akintola University of Technology, and LAUTECH Teaching Hospital Ogbomoso, Oyo State, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author AOA designed the study, performed the statistical analysis, wrote the protocol and the first draft of the manuscript. Author AAS critically reviewed the manuscript and author ROA involved in the design of the manuscript and data collection. Author OEA critically reviewed the first draft manuscript. All authors read and approved the final manuscript.

Original Research Article

Received 1st May 2014
Accepted 23rd June 2014
Published 7th July 2014

ABSTRACT

Background: antiretroviral therapy has changed the outlook of AIDS. However, identifying factors that will strengthen its maintenance is vital to treatment success. Advocacy is growing on the need for close attention to immunological progress, prevention of excessive body weight gain and associated immunological and metabolic

**Corresponding author: Email: deolusteve111@yahoo.com;*

consequences for better long-term outcomes among PLWHIV in Africa.
Aims: To study prevalence, determinants of adherence, and the existing relationship between body weight and CD4 count among adherents and non-adherent patients on HAART.
Methodology: A cross-sectional design for sampling of 270 patients on HAARTS was made and pharmacy based adherence was calculated. Patients were categorized into weight groups according to WHO guideline and CD4 count was determined at baseline, third and sixth months.
Result: Calculated overall pharmacy adherence was 62.6% over six months. Disclosure to a close family member (p=0.013) and living outside the city of care (p=0.025) significantly predict adherence. Pretreatment overweight (BMI-25- 29.9) and obesity (BMI>30.0) were temporary beneficial to CD4 constitution at baseline (p=0.004), while overweight (p=0.041) and obesity (p=0.150) were associated with lower CD4count repopulation at six months post- HAART compared to normal body weight (BMI-18.5–24.9), p<0.001. Adherent PLWHIV participants had higher body weight increasing effect, but demonstrated lower CD4 lymphocyte count increasing effect compared to the non-adherent at six months post-HAART, (p<0.001).
Conclusion: Normal body weight and maintenance during HAART seems beneficial for immune reconstitution at six months post- HAART. While emphasizing good adherence to HAART, it becomes necessary for programme implementers to watch against excessive body weight gain and attendants adverse immunological consequences.

Keywords: Adherence; HAART; PLWHIV; overweight; obesity; Osogbo; Nigeria.

1. INTRODUCTION

The emergence of antiretroviral therapy (ART) approximately one and half decade ago has converted the dreaded human immunodeficiency virus infection (HIV) to a chronic disease [1]. The success recorded with treatment had significantly reduced the morbidity and mortality associated with acquired immunodeficiency deficiency syndrome (AIDS) [2] with consequent improvement in life expectancy [3,4]. This impact of the improved outcome associated with ART is not fully felt in sub-Saharan Africa due to limited accessibility to ART and challenges with adherence to medication. For example, of the 1.3 million Nigerians who required ART, only 600,000 are on medication as at 2012 [5]. Similarly, out of the 277,000 new infections, only 56,000 were commenced on treatment. To achieve the Millennium Development Goal 6 by 2015 [5], studies are needed to identify effective and sustainable evidence-based interventions in the course of standard care. New means of broadening access and maintaining PLWHIV in care are also needed.

Adherence is taking antiretroviral (ARVs) exactly as prescribed by the caregivers [6]. Optimal adherence is necessary for good clinical outcomes, reduction of morbidity and mortality [2,6,7]. The reported adherence rates to ART medication among people living with HIV (PLWHIV) in Nigeria vary from 44% to 98% [8-12] Factors shown to improve or associated with good adherence include text message as reminders, [8] patient selected treatment partners, [9] use of pill box, [10] age and gender [11]. On the other hand, psychiatric morbidity negatively had adverse impacts on adherence [12]. Current reports indicate increasing and growing concerns on HIV - associated multi-morbidity with a potential threat on healthy ageing HIV population with the capacity to overwhelm inadequate health care facilities in the era of ART [1]. Of these is the increasing problem of overweight and obesity, growing burden of risk factors for cardiovascular diseases, [13-16] chronic inflammation

induction [13,14] and cancer [14]. Although reports have been conflicting on the impact of body weight on immunological constitution of HIV patients [15-19]. Systemic hypertension, diabetes, dyslipidemia and cardiovascular diseases are common among obese and overweight PLWHIV [15,17]. Therefore, while optimal adherence has been widely emphasized in studies; concerns are also growing on the need for weight and CD4 count monitoring [15-18]. Studies have shown a high rate of adherence in the developing countries including Nigeria, but maintenance of adherence and retention in care has been a major concern [6,7,15-18].

In view of the foregoing, the present study examined factors associated with adherence, and investigated relationship between body weight and immune status of adherent and non-adherent PLWHIV at baseline and six months after HAART

2. PATIENTS AND METHODS

2.1 Study Location/Design

This cross-sectional study involved every alternate patients seen by caregivers at the dedicated clinic to PLWHIV of the Ladoke Akintola University of Technology Teaching Hospital, Osogbo, Osun State, Nigeria from February 2011 to January 2012. The HIV clinic is being supported through collaboration programme of Federal Government of Nigeria through the Institute of Human Virology Nigeria (IHV-N), President Emergency Fund for Aid Relief (PEPFAR) and other non - Governmental donors at the time of the study. Free drugs, laboratory support, technical assistance and social support were being offered to the clinic attendees by the collaborators.

2.2 Subject Selection

The study participants included 270 HIV- seropositive adults diagnosed by two antibody screening tests. The participants were adult (age ≥18years), non-pregnant and using highly active antiretroviral therapy (HAART) for not less than three months before the commencement of the study. The participants signed informed written consent. The study excluded PLWHIV, who were on ART less than three months, and those who refused to be part of the study. Research Ethical Committee of the LAUTECH Teaching Hospital approved this study.

2.3 Data Collection

2.3.1 General data

The attending physicians or the adherence counselors interviewed all consenting eligible participants using a semi-structured questionnaire. The questionnaire captured socio-demographic data such as the participant's age, the gender, ethnicity, the highest level of education attained, occupation, place of residence and approximate distance travelled before getting to the clinic, HAART, duration on HAART, and side effect profile of drugs. The side effects of drugs were grouped to gastrointestinal (GIT), skin, and central nervous system (CNS). Gastrointestinal symptom included nausea, vomiting and abdominal pain; skin side effects included presence of a new rash after commencement of HAART and pruritus; and central nervous system complications included headache, paraesthesia, dizziness and vivid dreaming. The clinical stages of the HIV infection at commencement of

HAART were noted. The participants' knowledge of the use of different evidence-based intervention or strategies to enhance adherence in the low- and middle- income countries was assessed irrespective of whether patient was using them presently. The study documented knowledge of interventions such as the pill box, drug partner, timed pill, and patient's education module by affirmative direct questioning (yes, or no).

2.3.2 Assessments of medication adherence

Medication refill takes place at the pharmacy attached to the clinic. In the early phase of treatment, the refill periods were typically short, initially every two weeks in the first month of therapy, subsequently monthly until the sixth month of therapy. The trained adherence counselors gave group and individual adherence counseling at every contact. The HAART was defined according to treatment guidelines of World Health Organization (WHO) for HIV treatment as applicable to adults and adolescents in the developing countries as adopted by the Federal Government of Nigeria [20]. Two nucleoside reverse transcriptase inhibitors (NRTIs) plus one NNRT were used as first-line therapy. The HAART combination were (Zidovudine (AZT)/Lamivudine, (3TC)/Efavirenz (EFV) and (AZT/3TC/Nevirapine(NVP) essentially. Very few participants were taking Tenofovir-based therapy [20]. Adherence to HAART was assessed over the last 3 to six months using the pharmacy-based adherence measure (PAM). Using the pill count category of PAM, the quantity of medication used was determined between two antiretroviral pickup date as a proportion of the number of pills dispensed expressed in percentage [21]. The PLWHIV with adherence rate equal or greater than 95% were categorized as been adherent while those with less than 95% calculated adherence categorized as non-adherent. All data related to medication intake were extracted from duplicate of pharmacy refill forms at the back of the patients' medical files.

2.3.4 Anthropometric assessments

Routinely in the clinic, the weight and height of participants were measured using a stadiometer to the nearest 0.1cm and 0.1kg respectively. Investigators extracted data of baseline height and weight, weight at the third and sixth months from the participants medical files. The body mass index (BMI) was calculated using the equation weight (kg)/ height^2 (m^2) and categorized according to WHO criteria as follows: underweight when BMI is <18.5kg/m^2, normal, BMI=18.5 -24.9kg/m^2, overweight, BMI=25 –29.9kg/m^2 and obese, BMI ≥30.0kg/m^2 [21].

2.3.5 CD4 count

All available CD4 count results done in the course of treatment: at baseline, at the third and sixth months of therapy were copied from participant's folders.

2.3.5 Statistical analysis

All the continuous and categorical variables of interest were documented as means ± SD and percentages respectively. Chi-square was employed to find the gender differences in the categorical variables of the participants. Differences between two means were assessed using Student's t test. Pharmacologic adherence was dichotomized to < or ≥95%, and the relationship with socio-demographic and clinical variables was estimated using chi-square, while strength of association for significant variables were tested using the odd ratio statistics. All significant factors associated with adherence in the bivariate analysis were entered into binary logistic regression model to identified factors that predict adherence. One

way analysis of variance (ANOVA) was used to determine significant difference in CD4 count across BMI categories at baseline, the pair means differences in CD4 count at three and six months were determined using student's t-tests. The pair changes in means of weight, BMI, and CD4 count for the adherent and non-adherent patients were tested using Wilcoxon signed rank test; effect size was calculated using Z/square root of N, where N is the number of paired data. P-values were two-tailed, values <0.05 were taken as significant. Statistical Programme for Social Sciences (SPSS) version 17 (SPSS Chicago Inc, IL.USA) was used for analysis.

3. RESULTS

The study participants consisted of 270 adults (202 females and 68 males) with a mean age of 38.0±8.8years, with the majority [208 (77%)] under 45 years of age. The men were significantly older and taller than the women. There was no gender difference in the educational status, mean weight and BMI of study participants at the baseline. Most participants had normal body weight 154 (59.0%), 16.1% were underweight, 17.2% were overweight, while 7.7% of participants were obese. The women had higher mean CD4 count than men at the baseline (255.17±168.60 vs. 181.71±168.60 cells/mm^3 (p=0.002), Table 1. Fifty-two percent of the participants were in the advanced (18.0%) and severe (34.0%) immunosuppression stages at the time of diagnosis, while 27.6% and 20.4% were in stages 1 and 2 respectively.

Majority of the study participants (85.6%) were placed on Nevirapine-based HAART, while 8.5% were on Tenofovir-based and 2.9% were on Efavirenz-based HAART. Two hundred and nineteen (82%) participants had been on HAART for at least six months before the commencement of the study while 48(18.0%) had been on the HAART for less than six months. The median duration of HAART use was 20months (Range: 3-84).

The calculated overall pharmacologic adherence over last six months was 62.6%. Table 2 shows the relationship between adherence and socio-demographic and clinical variables. There was no age, gender, ethnic, educational, and occupational difference between the adherent and non-adherent participants. However, the study members residing outside Osogbo (care center) metropolis were more adherent than those living within the city (p=0.01). Dichotomized travel distance (less or greater than 10kilometer) to the source of care did not influence the adherence pattern (p=0.266). No significant association was found between adherence, categorical CD4 count, extent of disease progression at the baseline, presence or absence of wasting and clinical staging, (Table 2).

Table 1. The participants' socio-demographic characteristics according to Gender

Characteristics	Total	Male	Female	p-value
Mean age±SD (years)	38.01±8.84	41.16±8.99	36.96 ±8. 55	0.001
Age groups (years)				
18–44	208 (77.0)	45 (21.6)	163 (78.4)	0.033
45–64	61 (22.6)	23 (37.7)	38 (62.3)	
≥65	1 (0.4)	0 (0.0)	1 (100.0)	
Education status				
None	37 (13.7)	6 (16.2)	31 (83.8)	0.119
Primary	80 (27.8)	26 (32.5)	54 (67.5)	
Secondary	74 (27.4)	21 (28.4)	53 (71.6)	
Tertiary	79 (29.3)	15 (19.0)	64 (81.0)	
Occupation status				
Government	48 (17.8)	15 (31.2)	33 (68.2)	<0.001
Non-Government	3 (11.5)	17 (54.8)	14 (45.2)	
Self employed	171 (63.3)	34 (19.9)	137 (80.1)	
Unemployed	20 (7.4)	2 (10.0)	18 (90.0)	
Mean height (m)±SD, N=269	1.62±12.01	1.68±15.01	1.60 ±10.0	<0.001
Mean Weight(kg)±SD,N=269	60.34±14.64	62.5±9.07	59.62±16.04	0.166
Mean BMI±SD, N=268	23.99±14.14	20.45±0.59	22.45±0. 86	0.078
Baseline BMI N=261				
<18.5	42 (16.09)	8 (19.0)	34 (81.0)	0.014
18.5–24.49	154 (59.00)	50 (32.5)	104 (67.5)	
25–29.99	45 (17.24)	8 (17.8)	7 (82.2)	
>30.0	20 (7.66)	1 (5.0)	19 (95.0)	
Mean CD4 count N=260	224.74±200.27	181.71±159.65	255.17±168.60	0.002
Baseline CD4 count				
<350	198 (76.2)	56 (28.3)	142 (71.7)	0.029
≥350	62 (23.8)	9 (14.5)	53 (85.5)	
HIV clinical staging N=250				
Stage 1	69 (27.6)	50 (72.5)	19 (27.5)	0.169
Stage 2	51 (20.4)	36 (70.6)	15 (29.4)	
Stage 3	45 (18.0)	24 (53.3)	21 (46.7)	
Stage 4	85 (34.0)	55 (64.7)	30 (35.3)	
HAART type				
Nevirapine based	231 (85.6)	156(67.5)	75 (32.5)	0.553
Efavirenz based	16 (2.9)	9 (56.2)	7 (43.8)	
Tenofovir based	23 (8.5)	14 (60.9)	9 (39.1)	
Duration on HAART				
<6 Months	48 (18.0)	15 (31.2)	33 (68.8)	0.310
≥6Months	219 (82.0)	53 (24.2)	166 (75.8)	

Key: SD-standard deviation

Table 3 shows the pattern of pharmacologic adherence in relation to the knowledge of adherence enhancers, medication side effects and serological status disclosure. The participants demonstrated good knowledge of the adherence enhancer instruments with an average of greater than 90% for all enhancers, except the pillbox that was 85.6%. However, there was no association between the knowledge of these instruments and adherence. Seventy-seven participants (59.7%) experienced one form of side effect or the other with gastrointestinal side effect being the commonest (61.5%). There was no relationship

between different side effects and adherence. In relation to disclosure, a greater percentage (92.2%) of participants had disclosed to at least one individual. Of all the forms of disclosure, disclosure to close family member was found to be significantly associated with pharmacologic adherence. Patients who disclosed to close family members were about 2.0 times more likely to be adherent than their counterparts who did not disclose. (OR: 2.0; CI=1.2 - 3.3, p=0.007), Table 3.

Table 2. Pattern of Pharmacologic adherence in relation to Demographic and Clinical Variables

Characteristics	Adherent	Not adherent	χ^2	p-value
Age				
≤ 40 years	108 (60.3)	71 (39.7)	1.156	0.282
> 40 years	61 (67.0)	30 (33.0)		
Gender				
Male	41 (60.3)	27 (39.7)	0.205	0.651
Female	128 (63.4)	74 (36.6)		
Education				
At least primary Education	76 (64.4)	42 (35.6)	0.295	0.587
At least Secondary Education	93 (61.2)	59 (38.8)		
Occupation				
Employed	156 (62.2)	95 (37.8)	0.146	0.702
Unemployed	12 (66.7)	6 (33.3)		
Place of Residence				
Within Osogbo	85 (55.9)	67 (44.1)	6.611	0.010
Outside Osogbo	84 (71.2)	34 (28.8)		
Travel distance to source of care, N=118				
<10km	16 (61.5)	10 (38.5)	1.238	0.266
>10km	67 (72.8)	25 (27.2)		
Baseline CD4 Count				
<350	126 (62.1)	77 (37.9)	0.096	0.757
≥350	43 (64.2)	24 (35.8)		
Extent of progression				
Asymptomatic Infection	51 (68.0)	24 (32.0)	1.297	0.255
Symptomatic Disease	118 (60.5)	77 (39.5)		
Presence or absence of wasting, N = 267				
Wasting present	31 (73.8)	11 (26.2)	2.870	0.090
No wasting	135 (60.0)	90 (40.0)		

Of these, the place of residence, and disclosure to close relative significantly predicted adherence to HAART on multivariate analysis having controlled for important factors such as age, education, BMI, CD4 Count and HIV clinical staging, Table 4.

At baseline, HIV patients experience a progressively increasing CD4 count across from the underweight to the overweight category, obese patients experienced reduce CD4 constitution compared to the overweight, p=0.004. At 3month post HAART, the underweight and obese categories gained higher mean CD4 count (+92.3, +102.10 respectively) compared to the overweight and normal body weight categories (+59.2, +68.8 respectively). The increase was only statistically significant for normal body weight (p<0.001) and the obese categories (BMI >30.0kg/m^2), p=0.015. At six months post HAART, normal body weight was associated with highest and significant CD4 count gain (+173.7, p<0.001),

overweight (+158.3,p=0.041) while the underweight (+110.1, p=0.115) and obese >30.0 kg/m^2 (+128.4, p=0.150) categories had lower mean CD4 count gain compare to normal weight category, Table 5.

Table 3. Pharmacologic adherence in relation to knowledge of Adherence Enhancers, medication side effects and HIV Serostatus Disclosure

Variables		Adherent (%)	Not adherent (%)	χ^2	p-value
Adherence enhancers					
Pill box	Yes	146 (63.2)	85 (36.8)	0.255	0.614
	No	23 (59.0)	16 (41.0)		
Education module	Yes	162 (63.8)	96 (36.2)	2.579	0.108
	No	7 (43.8)	9 (56.2)		
Treatment preparation	Yes	159 (62.4)	96 (37.6)	0.113	0.737
	No	1 0 (66.7)	5 (33.3)		
Time pill	Yes	159 (61.9)	98 (38.1)	1.198	0.274
	No	10 (76.9)	3 (23.1)		
Treatment partner	Yes	157 (63.1)	92 (36.9)	0.289	0.591
	No	12 (57.1)	9 (42.9)		
Medication side effects					
Side effect(s)	Yes	77 (59.7)	52 (40.3)	0.889	0.346
	No	92 (65.2)	49 (34.8)		
CNS	Yes	51(58.6)	36 (41.4)	0.865	0.352
	No	118 (64.5)	65 (35.5)		
GIT	Yes	72 (61.5)	45 (38.5)	0.098	0.754
	No	97 (63.4)	56 (36.6)		
Skin	Yes	55 (61.1)	35 (38.9)	0.127	0.722
	No	118 (64.5)	65 (35.5)		
Serostatus disclosure					
Spouse	Yes	101(60.5)	66 (39.5)	0.732	0.392
	No	67(65.7)	35 (34.3)		
Friend	Yes	13 (61.9)	8 (38.1)	0.003	0.957
	No	155 (62.5)	93 (37.5)		
Support group	Yes	49 (60.5)	32 (39.5)	0.190	0.663
	No	119 (63.3)	69 (36.7)		
Religious Clergy	Yes	14 (70.0)	6 (30.0)	0.525	0.469
	No	154 (61.8)	95 (38.2)		
Close family member	Yes	108 (69.2)	48 (30.8)	7.274	0.007
	No	60 (62.5)	53 (46.9)		

The pair means differences in CD4 count, weight, and BMI of adherent and non-adherent participants were examined from baseline to 6 months post-HAART period using the Wilcoxon signed rank test for two related data. The adherent participants had lower mean baseline weight, BMI, but higher CD4 cell count compared to the non-adherent participants at baseline. Both medication adherent and non-adherent participants had a significant increase in weight, BMI and CD4 count after six months of HAART, p<0.001. The adherent participants experienced a higher increasing effect size in weight (Z=-6.641, effect size=0.55, p<0.001 vs. Z=-4.216 effect size=0.46, p<0.001), and BMI (Z=-6.763, effect size=0.56, p<0.001vs. Z=-3.925, effect size=0.43, p<0.001), than the non-adherent. However, the adherent participants experienced a lower CD4 count increasing effect

compared to the non adherent participants (Z=-3.970, effect size =0.50, p<0.001 vs. Z=-3.778, effect size=0.58, p<0.001) Table 6.

Table 4. Pair Differences in CD4 Count after three and six months while on first line Highly Active Antiretroviral Therapy from baseline

Weight categories	Baseline		3 months post HAART			6 months post HAART		
	N	Mean CD4 Count (SE)	N	Pair Mean difference (SE)	p-value	N	Pair Mean difference (SE)	p-value
Underweight	41	166.24 (25.04)	12	- 92.33 (42.92)	0.055	4	- 110.07 (50.25)	0.115
Normal weight	147	230.97 (13.94)	92	- 68.82 (18.72)	<0.001	38	- 173.70 (34.65)	<0.001
Overweight	44	302.18 (27.69)	18	- 59.16 (66.42)	0.386	10	-158.30 (66.50)	0.041
Obese	20	252.60 (28.20)	14	- 102.10 (36.31)	0.015	7	-128.40 (77.75)	0.150

Key: N=Number; SE –Standard error, Weight in kg/m^2, CD4 count in cells/ mm^3,BMI - Body Mass Index < 18.5(underweight), 18.5 -24.9 (normal weights), 25 –29.9 (Over weight), ≥30.0 (Obese)

Table 5. Multiple Logistic Regressions of factors that predicts good pharmacologic adherence (≥95%) to highly active antiretroviral therapy

Variables	B	Odd Ratio	95%(CI) of odds Ratio	p-value
CD4 Count (cells/mm^3)	0.0	0.99	0.99 - 1.001	0.666
Place of Residence	-0.55	0.58	0.36 - 0.96	0.025
Disclosure to close family member	0.71	2.03	1.20 - 3.55	0.013

Key: HAART– highly active antiretroviral therapy, CI–confidence intervals, N=number

Table 6. Pair Differences in CD4 count, weight, and Body Mass Index of Adherent and Non-adherent Participants over six Months while on highly active antiretroviral therapy

Variables	Adherent or not	Baseline± SD	6 months post HAART±SD	Z-value	Effect Size	p-value
Mean CD4 count±SD	Adherent	246.54±191.59	412.63±223.86	-3.970	0.50	<0.001
	Not adherent	240.13±173.62	432.74±229.07	-3.778	0.58	<0.001
Mean weight±SD(Kg)	Adherent	59.4±14.2	62.48±13.1	-6.641	0.55	<0.001
	Not adherent	60.88±11.29	62.17±11.00	-4.216	0.46	<0.001
Mean BMI±SD (Kg/m^2)	Adherent	22.53±5,22	23.65±4.79	-6.763	0.56	<0.001
	Not adherent	23.11±4.07	23.72±4.29	-3.925	0.43	<0.001

Key: CD4 count in cells/ mm^3, SD-*standard deviation*

4. DISCUSSION

The present study shows adherence to HAART is significantly predicted by disclosure to close family member and residing outside the locality of the source of care. The pre-treatment overweight and obesity were beneficial and associated with initial higher CD4 count constitution. However, after six months of HAART, the benefit of high BMI appears eroded as normal body weight (BMI, 25 –29.9) category demonstrated highest CD4 count reconstitution effect compared to other weight categories. These tendencies to higher weight gain with concomitant reduce CD4 count reconstitution was found among HAART adherent

study members, thereby suggesting a negative impact of obesity on immune reconstitution in HAART era.

The overall pharmacy-based adherence rate of 62.6% documented in this study falls within quoted 45 – 100% range for most developing nations [6,10,11,12]. Sero-status disclosure to a close family member significantly predicts good adherence to HAART in the present study as documented by Stirratt et al. and other workers [22-24]. While some workers attributed adherence and tendencies of PLWHIV to disclose to their close family members and friends to help with medical care and counseling, [23] others did not find or assessed the types of practical support been rendered to PLWHIV by these acquaintances [21,24]. Family support could independently explain adherence while non-disclosure to a family member was associated with non-adherence in a Uganda study [25]. All initiatives that will encourage PLWHIV to disclose should be strengthened in the course of standard care in limited resource settings. Other studies are necessary to identify the content and extent of family support been rendered to PLWHIV in sub-Sahara Africa. Contrary to findings of other studies, characteristics like age, gender, education, occupation are not associated medication adherence in the present study [11].

Only 92.2% of participants in the present study have disclosed their HIV sero-status to at least one person, while 61.9% had disclosed to their spouses, a rate that falls within 41–89% found in other African studies [26-33] Threshold of disclosure has been noted to be lower in African settings compared to North Americans [6,7,21]. The low level of disclosure has been associated with fear of family violence, lack of economic power, fear of stigma, and discrimination, domestic violence, neglect or rejection by family members [23,26-33]. Residing outside the city where the source of care is located predicts good adherence as also shown by previous studies [34,35]. Carlucci et al. [35] found optimal adherence among HIV- positive participants that had to travel long to the source of care. In contrast to the present finding, long distance travelling has been associated with missed doses, poor adherence, and family financial constraints [34]. Long distance journey to the source of care was commoner among white males, elderly, those on multi-therapy and affluent rural dwellers in England [34]. We opined that having to traverse other nearby care centers to a distant location may be associated with stigma feeling and confidentiality protection. Further analysis of this cohort showed majority (78.0%) of this mobile participants were self-employed and were incurring extra travel expenses which their low socio - economic status may not be able to sustain for a long time. Sustainability due to financial constraint that may arise anytime in the course of treatment may reverse this primary trend. While current evidence-based decentralization of care to bring treatment close to PLWHIV is been pursued because of its documented advantages, more effort should be directed at means of reducing social stigma to prevent excessive mobility among PLWHIV [36].

Many of the participants showed good understanding of adherence enhancers such as the pill boxes, timed pill, treatment partners, and education module. Although none of the enhancers was predictive of adherence to HAART, participants with good knowledge of enhancer's demonstrated better adherence compared to those without knowledge. Opinions have been diverse in published studies on the impact of enhancers in Africa [37-40]. The use of patient's selected treatment partners [16] and "adherence club" were associated with superior adherence and better clinical outcomes respectively [37]. Kunutsor et al. [38] also found the combination of enhancers favored long term sustenance on ARVs better than systematic adherence monitoring.

The present study showed that highly active antiretroviral therapy induce weight gain among PLWHIV and body weight impacts CD4 lymphocyte count as previously shown in studies [15-19]. We found association between been underweight BMI <18.5 and lower pre HAART CD4 count, while overweight, and obesity were beneficial to CD4 count constitution at baseline and 3months post HAART only. Although the observation was not statistically significant, obesity seems less beneficial to the CD4 count reconstitution while normal weight category (BMI: 18.5-24.9) experienced significant, and highest CD4 count repopulation effect compared to the overweight and obesity at six months post HAART. Our finding is similar to the findings of other workers that showed lower gain in CD4 cell count among obese PLWHIV over a longer time frame, as CD4 was noticed to have progressively risen from baseline but to plateau in the overweight category [15,16,18,19]. This study is however different from other studies that showed obesity did not compromise immune cell response [17,41,43]. However, despite lower gain in CD4 count compared to normal weight category (BMI, 18–24.9), obese and overweight PLWHIV (BMI≥25) in contrast to a previous study [17], showed a higher likelihood to exceed CD4 count gain threshold of >100cells/mm^3 at six months post HAART. Much greater likelihood threshold (>350cells/μL) was observed by Womack et al. in their study among white women [44]. Womack et al. [44] suggested discrepancies observed in these studies may be attributed to analysis methods.

Low CD4 cell count as observed in pre HAART and post HAART underweight category in this study may be attributed to ongoing malnutrition among HIV patients [45]. Associated with malnutrition is apoptosis induced thymocyte depletion that has particular depleting effect on CD4 count and attenuation of cell proliferation. Studies have also confirmed protein-energy malnutrition (PEM) is associated with a reduction of fat cell mass and consequently decrease in circulating leptin, impaired production of pro-inflammatory cytokines (IFN γ, and TNF α) and low T cell activation as a possible link to decline of CD4 cell repopulation in this group [46-53]. Serum leptin levels showed a positive correlation with the extent of adiposity and higher in women than men [48]. The administration of leptin to congenitally deficient children led to the reversal of immunodeficient state: restoring IFN γ secretion, CD4 cells development and functions [47]. Although malnutrition is still a common problem in HAART era especially in Africa, certain conditions associated with reduced weight gains such as inadequate viral suppression and on-going intercurrent infections should be investigated as a possible cause of lower repopulation of CD4 count among underweight PLWHIV [43].

Researchers have also proposed the mechanism of lower CD4 count and increasing cardiovascular morbidity and mortality [1,13-16] among obese PLWHIV. Obesity has been associated with hyperlectinemia [47-49,53]. Studies have suggested tolerance or resistance to the effect of leptin as the cause of “leptin-deficient” state among obese individuals. High circulating leptin has been associated with alteration in expression of leptin signal molecules at the receptor level [48]. Deficient leptin signaling which is due to “leptin deficiency” state results in increasing obesity, lipid storage in muscle, liver and other human tissues, dysfunction of neuro-endocrine function, as well as immune function. High level of leptin has been linked with direct induction of an inflammatory state and is an underlying factor for insulin resistance and development of metabolic syndrome. Similarly, HAART-treated PLWHIV with HIV- associated lipodystrophy syndrome showed a significant reduction (40%) in leptin and reduced expression of transcription factors within their fat cells. They also had increased production of TNF-α, interleukin 6 (IL-6) and IL-8 expression [50-52]. The low adiponectin, shift in pro inflammation factors, profibrotic and dysregulated metabolic state are the factors that contributed to the reduction of cell differentiation including reduce CD4 cell activation, reduced fatty acid uptake and consequent dyslipidemia [1,50-53]. The elevation of many of the inflammatory markers has been attributed to increase disease and

all-cause mortality [1]. However, in this study, lower level of CD4 count in the obese category six months post HAART may be partly explained by a lower starting CD4 count at baseline compared to the overweight category. Other studies may be needed to examine the contributors to the chronic inflammation induction and reduce immune activation among obese PLWHIV.

The prevalence of pre HAART overweight and obesity (24.9%) found in the present study falls within 8.1 – 35.1% and 20 -30% documented among Nigerian and American general population respectively, but lower than 63% documented at last visit in a study among HIV-positive military men in United States [15,19,54]. However, the multiplication effect of high national HIV prevalence in most African countries portends grave consequences for already burdened health care system. The cardiovascular and metabolic consequences among PLWHIV are a time bomb that may shape the future needs of HIV as a chronic disease [1,13-16,41].

From this study, excessive weight gain and the consequent complications are more likely to occur among the ARV-adherent populations. PLWHIV and programme implementers must pay close attention to clients that are “doing well” as evidence by increasing weight and other physical parameters. Close attention to immunological progress, weight monitoring, and frequent assessment for cardiovascular risk factors are important implementable programme needed now in Africa. Studies are needed to examine allowable limits of weight necessary for optimal immunological outcomes for PLWHIV on HAART. Similarly, a change that physical therapy would make on weight reduction, weight maintenance and immunological recovery should be examined in a longitudinal study among PLWHIV.

This study was fraught with some limitations. Viral load (VL) assessment is not routinely done in our centre and due to constraint of funds VL assessments were not done. Similarly, attrition during treatment, morbidity and mortality were not examined as end point since our focus is on adherence as related to weight and immune constitution. The assessment of BMI in these patients only suggests weight gain but not a good estimate of body fat composition.

5. CONCLUSION

In Conclusion, disclosure to close relative and residing outside the source of care predict adherence to HAART. Stigma and confidentiality protection are still influencing the decision of PLWHIV to travel far to source for care. The HAART adherent PLWHIV demonstrated higher increasing weight effect but lower CD4 reconstitution effect. Normal body weight and its maintenance during HAART seems beneficial for immune reconstitution at six months post- HAART. While emphasizing adherence, careful emphasis should be placed on weight and immunological monitoring.

ACKNOWLEDGEMENT

We thank all the PLWHIV receiving treatment at the LAUTECH Teaching Hospital, Osogbo, the Doctors, Nurses, Pharmacist, and adherence counselors working at the clinic for their cooperation during the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. Lancet. 2013;382:1525–533.
2. Reid SD, Fidler SJ, Cooke GS. Tracking the progress of HIV: the impact of point-of-care tests on antiretroviral therapy. Clin Epidemiol. 2013;5:387–96.
3. Van Sighem AI, Gras LA, Reiss P, Brinkman K, de Wolf F. ATHENA national observational cohort study Life expectancy of recently diagnosed asymptomatic HIV-infected patients approaches that of uninfected individuals. AIDS. 2010;24(10):1527-535.
4. Hontelez JA, Lurie MN, Bärnighausen T, Bakker R, Baltussen R, Tanser F, et al. Elimination of HIV in South Africa through Expanded Access to Antiretroviral Therapy: A Model Comparison Study. PLoS Med. 2013;10(10):e1001534. Epub 2013 Oct 22.
5. Abah Roland Clement. Nigeria Deliberates on Quantification Assumptions of HIV Treatment Commodities.
   Available: http://naca.gov.ng/content/view/457/lang,en/. Accessed November 6th, 2013
6. Scanlon ML, Vreeman RC. Current strategies for improving access and adherence to antiretroviral therapies in resource-limited settings. HIV/AIDS - Research and Palliative Care. 2013;5:1–17
7. Redal AA, Biadgilign S. Determinants of Adherence to Antiretroviral Therapy among HIV-Infected Patients in Africa. AIDS Research and Treatment. 2012;574656. Epub 2012 Feb 22.
8. Maduka O, Tobin-West CI. Adherence counselling and reminder text messages improve uptake of antiretroviral therapy in a tertiary hospital in Nigeria. Niger J Clin Pract. 2013;16(3):302-28.
9. Taiwo BO, Idoko JA, Welty LJ, Otoh I, Job G, Iyaji PG, et al. Assessing the Viorologic and Adherence Benefits of Patient-Selected HIV Treatment Partners in a Resource-limited Setting. Acquir Immune Defic Syndr. 2009;00:000–000
10. Ukwe CV, Ekwunife OI, Udeogaranya OP, Iwuamadi UI. Self-reported adherence to HAART in South-Eastern Nigeria is related to patients' use of pill box. SAHARA J 2010;7(1):10-15.
11. Olisah VO, Baiyewu O, Sheikh TL. Adherence to highly active antiretroviral therapy in depressed patients with HIV/AIDS attending a Nigerian university teaching hospital clinic. Afr J Psychiatry (Johannesbg). 2010;13(4):275-79.
12. Salami KA, Fadeyi A, Ogunmodede JA, Desalu O. Factors influencing adherence to antiretroviral medication in Ilorin, Nigeria. J Int Assoc Physicians AIDS Care (Chic). 2010;9(3):191-95.
13. Lake JE, Currier JS. Metabolic disease in HIV infection. Lancet Infect Dis. 2013;13(11):964-75.
14. Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. The Lancet. 2007;370:59-67.
15. Crum-Cianflone N, Tejidor R, Medina S, Barahona I, Ganesan A. Obesity among patients with HIV: the latest epidemic. AIDS Patient Care STDS. 2008;22(12):925-30.
16. Crum-Cianflone N, Roediger MP, Eberly L, Headd M, Marconi V, Ganesan A. Increasing rates of obesity among HIV-infected persons during the HIV epidemic. PLoS One. 2010;5(4):e10106
17. Tedaldi EM, Brooks JT, Weidle PJ, Richardson JT, Baker RK, Buchacz K, et al. Increased body mass index does not alter response to initial highly active antiretroviral therapy in HIV-1-infected patients. J Acquir Immune Defic Syndr. 2006;43(1):35-41.

18. Akinboro AO, Onayemi O, Ayodele OE, Mejiuni AD, Atiba AS. The impacts of first line highly active antiretroviral therapy on serum selenium, CD4 count and body mass index: a cross sectional and short prospective study. Pan Afr Med J. 2013;15:97.
19. Crum-Cianflone NF, Roediger M, Eberly LE, et al. Obesity among HIV-infected persons: impact of weight on CD4 cell count. AIDS. 2010;24:1069– 072.
20. National guidelines for HIV/ AIDS treatment and care in adolescents and adults. Federal Ministry of Health, Abuja Nigeria.
Available: www.who.int/hiv/pub/guidelines/nigeria_art.pdf. Accessed August, 2010.
21. McMahon JH, Jordan MR, Kelley K, Bertagnolio S, Hong SY, Wanke CA, et al. Pharmacy Adherence Measures to Assess Adherence to Antiretroviral Therapy: Review of the Literature and Implications for Treatment Monitoring. Clin Infect Dis 2011;52(4):493–06
22. Stirratt MJ, Remien RH, Smith A, Copeland OQ, Dolezal C, Krieger D, et al. The role of HIV serostatus disclosure in antiretroviral medication adherence. AIDS Behav. 2006;10(5):483-93
23. Li L, Wu S, Wu Z, Sun S, Cui H, Jia M. Understanding family support for people living with HIV/AIDS in Yunnan, China. AIDS Behav. 2006;10(5):509-17.
24. Ncama BP, McInerney PA, Bhengu BR. Social support and medication adherence in HIV disease in KwaZulu-Natal, South Africa. Int J Nurs Stud. 2008;45(12):1757-763.
25. Bajunirwe, Arts FE, Tisch DJ, King CH, Debanne SM, Sethi AK. Adherence and treatment response among HIV-1-infected adults receiving antiretroviral therapy in a rural government hospital in Southwestern Uganda, JIAPAC. 2009;8(2):139–47.
26. Nachega JB, Morroni C, Zuniga JM, Sherer R, Beyrer C, Solomon S, et al. HIV-Related Stigma, Isolation, Discrimination, and Serostatus Disclosure: A Global Survey of 2035 HIV-Infected Adults. JIAPAC. 2012;11:172.
27. Patel SV, Patel SN,Baxi RK, Golin CE, Mehta M, Shringarpure K, et al. HIV serostatus disclosure: Experiences and perceptions of people living with HIV/AIDS and their service providers in Gujarat, India. Ind Psychiatry J. 2012;21(2):130-36.
28. Kiula ES, Damian DJ, Msuya SE. Predictors of HIV serostatus disclosure to partners among HIV-positive pregnant women in Morogoro, Tanzania. BMC Public Health. 2013;13:433.
29. Amoran OE. Predictors of disclosure of sero-status to sexual partners among people living with HIV/AIDS in Ogun State, Nigeria. Niger J Clin Pract. 2012;15(4):385-90.
30. Sagay AS, Musa J, Ekwempu CC, Imade GE, Babalola A, Daniyan G, et al. Partner disclosure of HIV status among HIV positive mothers in Northern Nigeria. Afr J Med Med Sci. 2006;35:119-23.
31. Johnson OE. Social impact of HIV/AIDS on clients attending a teaching hospital in Southern Nigeria. SAHARA J. 2012;9(2):47-53.
32. Tadese Asfaw Erku, Berihun Megabiaw, Mamo Wubshet. Predictors of HIV status disclosure to sexual partners among People living with HIV/AIDS in Ethiopia. Pan Afr Med J. 2012;13:87. Epub 2012 Dec 28.
33. Vu L, Andrinopoulos K, Mathews C, Chopra M, Kendall C, Eisele TP. Disclosure of HIV status to sex partners among HIV-infected men and women in Cape Town, South Africa. AIDS Behav. 2012;16(1):132-38.
34. Cook PA, Downing J, Wheater CP, Bellis MA, Tocque K, Syed Q et al. Influence of socio-demographic factors on distances travelled to access HIV services: enhanced surveillance of HIV patients in north west England. BMC Public Health. 2009; 9:78.
35. Carlucci JG, Kamanga A, Sheneberger R, Shepherd BE, Jenkins CA, Spurrier J, et al. Predictors of adherence to antiretroviral therapy in rural Zambia. J Acquir Immune Defic Syndr. 2008;47(5):615-622.

36. Chan AK, Mateyu G, Jahn A, Schouten E, Arora P, Mlotha W, et al. Outcome assessment of decentralization of antiretroviral therapy provision in a rural district of Malawi using an integrated primary care model. Trop Med Int Health. 2010;15(Suppl 1):90-97.
37. Luque-Fernandez MA, Van Cutsem G, Goemaere E, Hilderbrand K, Schomaker M, Mantangana N, et al. Effectiveness of patient adherence groups as a model of care for stable patients on antiretroviral therapy in Khayelitsha, Cape Town, South Africa. PLoS one. 2013;8(2):Epub 2013 Feb 13.
38. Kunutsor S, Walley J, Muchuro S, Katabira E, Balidawa H, Namagala E, et al. Improving adherence to antiretroviral therapy in sub-Saharan African HIV-positive populations: an enhanced adherence package .AIDS Care. 2012;24(10):1308-315
39. Kunutsor S, Walley J, Katabira E, Muchuro S, Balidawa H, Namagala E, et al. Improving clinic attendance and adherence to antiretroviral therapy through a treatment supporter intervention in Uganda: a randomized controlled trial. AIDS Behav. 2011;15(8):1795–802.
40. Mugusi F, Mugusi S, Bakari M, Hejdemann B, Josiah R, Janabi M, et al. Enhancing adherence to antiretroviral therapy at the HIV clinic in resource constrained countries; the Tanzanian experience. Trop Med Int Health 2009;14(10):1226–232.
41. Shor-Posner G, Campa A, Zhang G, Persaud N, Miguez-Burbano MJ, Quesada J,et al. When obesity is desirable: A longitudinal study of the Miami HIV-1-infected drug abusers (MIDAS) cohort. J Acquir Immune Defic Syndr. 2000;23:81-88.
42. Keithley JK, Duloy AM, Swanson B, Zeller JM.. HIV Infection and Obesity: A Review of the Evidence. J Assoc Nurses AIDS Care. 2009;20(4):260-74.
43. Koethe JR, Jenkins CA, Shepherd BE, Stinnette SE, Sterling TR. An optimal body mass index range associated with improved immune reconstitution among HIV-infected adults initiating antiretroviral therapy. Clin Infect Dis. 2011;53(9):952-60.
44. Julie Womack, Phyllis C. Tien, Joseph Feldman, Ja Hyun Shin, Kristopher Fennie, Kathryn Anastos, et al Obesity and immune cell count in women. Metabolism. 2007;56(7):998–1004.
45. John Chan, Yu Tian, Kathryn E, Tanaka Ming S. Tsang, Keming Yu, et al. Effects of protein-calorie malnutrition on tuberculosis in mice. Proc. Natl. Acad. Sci. U. S. A. 1996;(93):14857–14861
46. Chan JL, Moschos SJ, Bullen J, Heist K, Li X, Kim YB, Kahn BB, Mantzoros CS. Recombinant methionyl human leptin administration activates signal transducer and activator of transcription 3 signaling in peripheral blood mononuclear cells in vivo and regulates soluble tumor necrosis factor-alpha receptor levels in humans with relative leptin deficiency. J Clin Endocrinol Metab. 2005;90(3):1625-31.
47. Farooqi IS, Matarese G, Lord GM, Keogh JM, Lawrence E, Agwu C, Sanna V, Jebb SA, Perna F, Fontana S, Lechler RI, DePaoli AM, O'Rahilly S. Beneficial effects of leptin on obesity, T cell hyporesponsiveness, and neuroendocrine/metabolic dysfunction of human congenital leptin deficiency. J Clin Invest. 2002;110(8):1093-103.
48. Jéquier E. Leptin signaling, adiposity, and energy balance. Ann N Y Acad Sci. 2002;967:379-88.
49. Martín-Romero C, Santos-Alvarez J, Goberna R, Sánchez-Margalet V. Human leptin enhances activation and proliferation of human circulating T lymphocytes. Cell Immunol. 2000;199(1):15-24.
50. John R Koethel, Todd Hulgan, Kevin Niswender. Adipose Tissue and Immune Function: A Review of Evidence Relevant to HIV Infection. J Infect Dis. 2013;208(8):1194-201.

51. Lihn AS, Richelsen B, Pedersen SB, Haugaard SB, Rathje GS, Madsbad S, et al. Increased expression of TNF-alpha, IL-6, and IL-8 in HALS: implications for reduced adiponectin expression and plasma levels. Am J Physiol Endocrinol Metab. 2003;285:E1072–80.
52. Bastard JP, Caron M, Vidal H, Jan V, Auclair M, Vigouroux C, et al. Association between altered expression of adipogenic factor SREBP1 in lipoatrophic adipose tissue from HIV-1-infected patients and abnormal adipocyte differentiation and insulin resistance. Lancet. 2002;359:1026–10.
53. Susann Blüher, Christos S Mantzoros. Leptin in humans: lessons from translational research. Am J Clin Nutr. 2009;89(3):991S–997S.
54. Adeyemo WL, Bamgbose BO, Ogunlewe MO, Ladeinde AL, Taiwo OA. Overweight and obesity among patients attending a Nigerian oral surgery clinic: implications for oral surgical practice in Nigeria. Afr Health Sci. 2010;10(1):40–45.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=590&id=12&aid=5230