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Full Length Research Paper

Highly active antiretroviral therapy (HAART) and body mass index (BMI) relationship in people living with HIV/AIDS (PLWHA) in the Federal Capital Territory, Nigeria and the neighbouring states

K. B. Mustapha[1]*, T. S. Ehianeta[2], R. A. Kirim[1], F. T. Osungwu[3] and D. K. Oladepo[4]

[1]Department of Medicinal Chemistry and Quality Control, National Institute for Pharmaceutical Research and Development, Abuja, Nigeria.
[2]Department of Pharmaceutical Technology and Raw Materials Development, National Institute for Pharmaceutical Research and Development, Abuja, Nigeria.
[3]National Institute for Pharmaceutical Research and Development Clinic, Abuja, Nigeria.
[4]Department of Microbiology and Biotechnology, National Institute for Pharmaceutical Research and Development, Abuja, Nigeria.

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This study was set to establish the relationship between highly active antiretroviral therapy (HAART) and body mass index (BMI) in people living with HIV/AIDS (PLWHA) in the Federal Capital Territory (FCT) and the neighbouring states within Nigeria- a representative data for sub-Sahara Africa. The study made use of 3 groupings: 44 healthy individuals, 79 HAART-treated HIV (human immuno deficiency syndrome) infected individuals and 21 non-HAART treated HIV-infected individuals from a pool of 402 subjects and age, weight and height were documented and statistically analyzed (Graph Pad, Prism 3). The result showed that significant weight loss was typified by low BMI values (<20) presented in non-HAART HIV-infected subjects. The trend of BMI cum weight loss in HIV infected subjects follows the order: non-HAART PLWHA > HAART treated PLWHA > healthy subjects. It was found that weight loss and consequently low BMI is not gender-dependent in HAART and non-HAART subjects.

Key words: Body mass index (BMI), highly active antiretroviral therapy (HAART), people living with HIV/AIDS (PLWHA).

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS), a disease of the human immune system and caused by the human immunodeficiency virus (HIV), is now a pandemic (Kallings, 2008). In 2009, an estimate of 33.3 million people worldwide were living with HIV. That same year, some 2 million people died of AIDS-related illnesses, 2.6 million people were newly infected and 2.5 million children were living with HIV worldwide. Globally, less than one person in five at risk of HIV has access to basic HIV prevention services. Only 36% of people who needed HIV treatment had access to it by the end of 2009, using the WHO 2010 criterion for treatment initiation of a CD4 count of 350 cells/mm^3 (WHO, UNAIDS, 2010). Sub-Saharan Africa remains the region that is most heavily affected by HIV, with Southern Africa remaining the area most affected by the epidemic. In 2009, sub-Saharan Africa accounted for approximately 70% of people living with HIV worldwide and new infections among adults and children. The region also accounted for 72% of the world's AIDS-related deaths in 2009 (UNAIDS, 2010).

About 25% of people living with HIV and AIDS (PLWHA) was reported to have stopped therapy within

*Corresponding author. E-mail: bolakud@yahoo.com. Tel: 08033076199.

the first year on highly active antiretroviral therapy (HAART) because of side effect like diarrhoea as a result of gastrointestinal intolerance, abdominal cramps and lactic acidosis which are contributing indices to weight loss (d'Arminio, 2000). Almost the same number of patients do not take the recommended dosages of their medication due to concerns regarding the side effects (Chesney, 2000). Patients, who reported significant side effects, are more often non-adherent to therapy (Ammassari, 2001). Reconstitution of the immune system, a major goal of HAART treatment, may even carry risks in some patients. A debilitating inflammatory syndrome has recently been linked to HAART treatment (Stoll and Reinhold, 2004).

The trend of progressive and selective wasting of subcutaneous fat from the face and limbs of HIV infected patients being treated with antiretroviral therapy emerged in 1997 and was widely reported in diverse populations throughout 1998 and 1999 (Viraben and Aquilina, 1998; Gervasoni et al., 1999). The lipodystrophy syndrome was ascribed to a unique cumulative toxicity of HIV protease inhibitor (PI) therapy (Carr et al., 1998) having been noted only 2 years after the introduction of PI into routine clinical practice. The development of subcutaneous fat wasting, intra-abdominal obesity and buffalo humps in PI-naive patients has now been documented within several cohorts (Saint-Marc et al., 1999; Madge et al., 1999). As NRTIs have been used sequentially and fat wasting is a progressive and cumulative phenomenon, there are potential bias against agents used more recently, such as stavudine and PI.

All drug dosages must account for the weight of the patient, because weight plays a role in the distribution of the drug in the body's tissues. There are two concerns with drug doses. The first is that in an unusually lean patient, a normal dosage might be too much, thus increasing the side effects to the patient and in effect potentially contributing to patient discomfort which may result to overdose in some cases. In fat patients, if given the same dose the drug may become too diluted, necessitating a higher dosage which is somewhat larger than that calculated to suit patients in the normal range (Smith, 2010).

HIV and the medications used to treat the virus affect the body in many ways. As people live longer, we are beginning to see some of the effects of long-term HIV medication use. The problem of lipodystrophy, the loss of fat from the arms and legs and subsequent weight gain in the abdomen and back of the neck has significantly impacted the body image of many HIV-infected people. Wasting syndrome, the excessive weight loss seen in advanced cases of HIV, is not only a threat to physical health but to body image and emotional health as well (Van der Sande et al., 2004). In order to manage these two problems, their progress must be closely monitored. This can be done using body composition testing. Body mass index (BMI) is an indirect measurement of body composition. Specifically, BMI is a measure of comparison between your body's fat composition and that of established standards seen in the average healthy person. By knowing how your amount of body fat compares to the average healthy person, doctors can assess your risk for diabetes, heart disease, or hypertension. In the case of wasting syndrome, BMI allows your doctor to monitor body fat composition, providing additional information valuable in the assessment of excessive weight loss. If the BMI indicates that body fat is below the established standards, the doctor can intervene in an effort to slow or reverse the loss. Calculating BMI is one of the best methods for population assessment of overweight and obesity. The correlation between the BMI number and body fatness is fairly strong; however, the correlation varies by sex, race and age. Because calculation requires only height and weight, it is inexpensive and easy to use for clinicians and the general public (Prentice and Jebb, 2001).

In this study, following the intensity, variation and reproducibility of complaints, we have made use of body mass index as a screening tool to identify possible weight problems for people on antiretroviral therapy, specifically HAART. Beyond relating BMI to HAART, the study also aimed to compare weights of healthy subjects to those living with HIV/AIDS (PLWHA).

METHODOLOGY

This was a cross-sectional study carried out among 144 subjects registered in our research clinic which is an accredited United States Presidential Emergency Plan for AIDS Relief (PEPFAR) center in the Federal capital territory, Abuja, Nigeria. They were sub-selected from a pool of 402 CD4-documented infected individuals from a total of 2491 infected persons who registered for anti retroviral therapy at the clinic, following a carefully designed inclusion and exclusion criteria. The resident locations of the subjects spans from the neighboring states around the FCT, which are Nasarawa, Benue, Plateau, Niger and Kogi states. The study method includes pre-test counseling, informed consent and clinical evaluation.

Subjects with HIV infection on stable HAART were enrolled in the study from January 2003 to January 2010. Subjects attended routine medical follow-up and periodic CD4 cell counts from the clinic facility. Subjects were also recruited from HIV/AIDS clinics in the neighbouring States on referrals. Information regarding the type and duration of HAART was obtained from subjects' dispensing cards. Details of the study procedures were given on volunteers' information sheet. The benefits, confidentiality and voluntary participation features of the study were explained and written informed consent were obtained from the subjects. Healthy volunteers were recruited randomly as subjects from the out-patient department as registered patients of the clinic, most of whom are staff of the institute, following the stated inclusion-exclusion exercise, so as to gain constant access to the required parameters needed for the study. They were afterwards grouped into HAART-treated groups, HAART-untreated group and healthy volunteers.

The HAART considered in the study includes the use of two nucleoside reverse transcriptase inhibitors (NRTI) + one non-nucleoside reverse transcriptase inhibitor (NNRTI)/protease inhibitor (PI). (a)Truvada™ + Nevirapine; (b) Truvada™ + Efavirenz;
(c) Combivir™ + Nevirapine; (d) fixed dose combinations of Stavudine/Lamivudine/NevirapineorLamivudine/Tenofovir/

Nevirapine.

Inclusion criteria for eligibility were that the subjects have documented HIV infection details, and are between the age range of 18 to 50 years. The stable WHO-recommended HAART greater or equal 6 months was considered and study subjects were graded according to the WHO clinical staging and a maximum CD4+ count of 350 cells/µl. All subjects had no active opportunistic infections or significant symptoms of HIV disease which could adversely influence their expectations of quality of life and decrease performance status. Also, included in the study were subjects who were initially considered HAART-untreated PLWHA and during the course of study, marked as HAART-treated individuals at the time of commencement of ARVs. Pregnant women and directly observed short-course therapy (DOT) patients were excluded from the study.

Subjects' demographic characteristics including age, gender, occupation, education, data about HIV infection, type and duration of HAART, frequency of administration and compliance rate, were all obtained at the time of administration of the questionnaires. Body weights and heights were measured by an experienced investigator using a WEYLUX scale and a Stadiometer while observing standard precautions (RNIS, 2000). For consistency of data on weights and heights, one experienced investigator took the first body weight and height and this was then confirmed by another investigator for each subject in each group. The height (in meters), weight (kg), body mass index (BMI) [calculated by the quetlet index, that is, weight (kg)/height squared (m) ^{2}], were measured while the subject was standing, wearing light clothing and no shoes. Weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. Two measurements were taken per subject in each group, and when there was a more than 2 cm difference between the two, a third measurement was taken. The mean of the closest two measurements was used to calculate BMI. This procedure was repeated at 3 months interval for each subject on appointed visit to the clinic. HAART–treated and non-HAART-treated subjects were clinically evaluated on each visit to the clinic. However, the healthy volunteers were certified HIV-free pre- and post-window period during the last 12 months of the study and thus subjected to similar data determination like test subjects.

The data were analyzed using Fisher's exact test to determine the differences between groups, such as statistical significance. Continuous variables were analysed by paired t-test. Mean values of the age, weight, height and BMI were calculated and tabulated. All p values were 2-tailed, and statistical significance was set at 99.9% confidence level ($p > 0.01$). All data analysis was performed with statistical package (Graph Pad, Prism 3) and presented as mean ± SEM, range, median (interquartile range) and normality test P value.

RESULTS AND DISCUSSION

The results in Figure 1 shows that subjects who are HIV infected but not placed on HAART (non-HAART treated subjects) at the time of the study presented signs of weight loss typified by a low BMI, followed by HAART treated HIV subjects (HAART). The frequency of subjects who are underweight supports the postulation that the disease course is a contributing factor to weight loss and wasting syndrome as seen in some subjects, irrespective of HAART regimen. HIV free individuals (healthy) who were underweight obviously were not on HAART and the low BMI could be attributed to nutritional deficiencies. There was no statistical significant difference among the 3 groups in the normal weight status. More HIV infected subjects placed on HAART regimen of Zidovudine + Lamivudine + Nevirapine or Combivir + Nevirapine showed signs of a normal weight status than those on Stavudine + Lamivudine + Nevirapine. A larger percentage of the healthy subjects fell outside the normal weight status and thus were grossly overweight and clinically obese. Relatively, HAART treated individuals on HAART combinations of Truvada™ + Nevirapine, were not as obese and overweight as healthy individuals. Highly active antiretroviral therapy, consequently did not contribute to weight-related health threatening conditions of overweight and clinically obese when compared with healthy individuals. This, however, is not conclusive when compared with HAART untreated subjects Table 1.

Figure 2 shows the frequency distribution of the BMI of male subjects and a similar trend as that of the whole population in Figure 1 was observed, except that none of the male non-HAART subjects was overweight and clinically obese. Again as seen in the Figure 2, healthy subjects were prone to overweight and clinically obese while more male HAART subjects were normal than underweight. A number of HAART subjects who took part in the study did not progress into full-blown AIDS, that is, PLWAIDS, owing to adherence to the prescribed HAART regimen. Male subjects not on HAART did not seem to show a significant deviation from their usual body weights (UBW) prior to HAART regimens of (a) Truvada™ + Nevirapine; (b) Truvada™ + Efavirenz; (c) Combivir™ + Nevirapine; (d) fixed dose combinations (FDCs) of Stavudine/Lamivudine/Nevirapine or Lamivudine/Tenofovir/Nevirapine and compositionally, Truvada (Emtricitabine + Tenofovir), Combivir (Zidovudine + Lamivudine),

Weight loss as seen in Figure 3 followed the trend: non-HAART > HAART > healthy subjects. Within the normal range of BMI, the least frequency was seen in non-HAART subjects. More healthy female subjects depicted overweight and clinical obese when compared to the male subjects. There was no statistical significant difference ($p < 0.1$) between HAART-treated and healthy female subjects in the normal BMI range. Female HIV study subjects not on HAART showed signs of underweight prior to HAART regimen. However, as the female subjects were started on HAART, the BMIs increased and thus it was comparable to that of healthy female subjects. Comparing Figures 2 and 3, the study shows that there is a time-dependent increase in weight in female HAART subjects than in male HAART subjects, indicating that females on HAART are more prone to weight gain and lipid dystrophy than males on HAART.

Tables 2 to 4 illustrates the statistically significant difference ($p < 0.10$) in height and body mass index in the HAART treated subjects relative to same parameters in the non-HAART treated and healthy Subjects. Thus, height and BMI parameters failed the p normality test in the HAART treated subjects. A p value ≥ 0.10 seen in the age of the healthy subjects suggests no significant

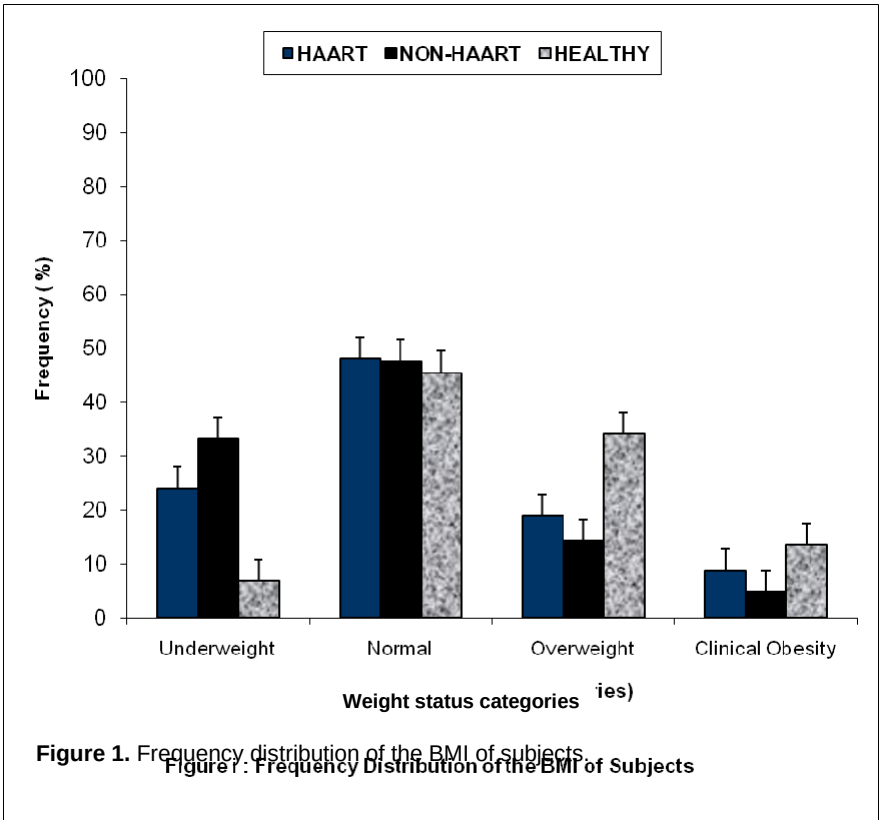

Figure 1. Frequency distribution of the BMI of subjects.

Table 1. Percentage frequency of weight status categories of the grouped subjects.

	HAART-treated subjects (%): 79	Non-HAART-treated subjects (%): 21	Healthy subjects (%): 44
Underweight	24.05	33.30	6.80
Normal	48.10	47.60	45.50
Overweight	18.99	14.30	34.10
Clinical obesity	8.86	4.80	13.60

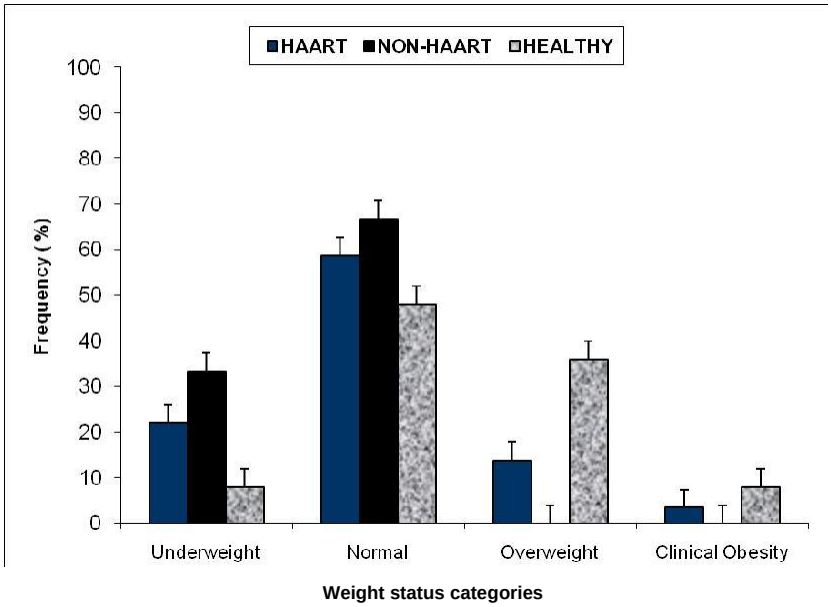

Figure 2. Frequency distribution of the BMI of male subjects.

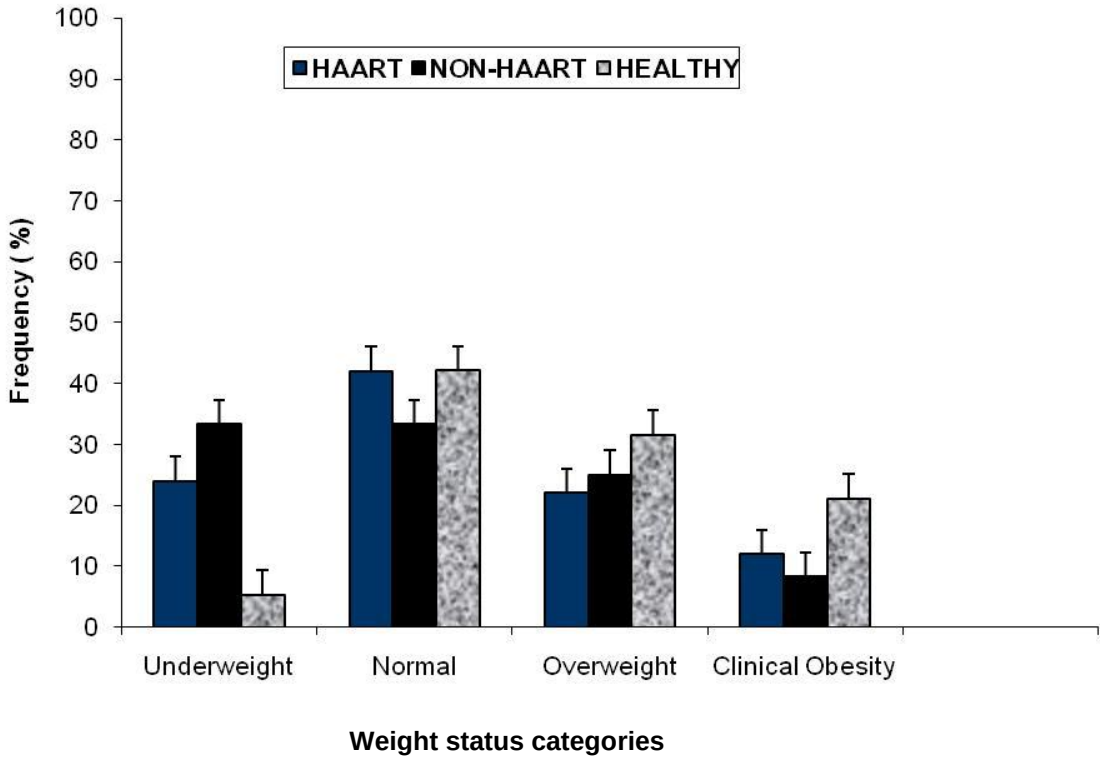

Figure 3. Frequency distribution of the BMI of female subjects.

Table 2. Statistical parameters for HAART-treated subjects.

	Age (years)	Weight (kg)	Height (m)	Body mass index (kg/m^2)
Mean ± SEM	34.86 ± 0.84	61.59 ± 1.35	1.64 ± 0.01	23.20 ± 0.50
Range	20-58	33.4 - 90.3	1.41 - 1.91	14.84 - 38.71
Median	35	59.65	1.62	22.33
Normality test p value	>0.10	>0.10	0.0002	0.0021

Table 3. Statistical parameters for non- HAART treated subjects.

	Age (years)	Weight (kg)	Height (m)	Body mass index (kg/m^2)
Mean ± SEM	30.95 ± 1.65	59.39 ± 2.17	1.64 ± 0.02	22.25 ± 0.97
Range	18-46	35 - 72.7	1.41 - 1.85	15.86 - 32.87
Median	30	60.5	1.66	21.60
Normality test p value	>0.10	>0.10	>0.10	>0.10

Table 4. Statistical parameters for healthy subjects.

	Age (years)	Weight (kg)	Height (m)	Body mass index (kg/m^2)
Mean ± SEM	33.88 ± 2.29	68.69 ± 1.91	1.65 ± 0.02	25.24 ± 0.84
Range	18-56	42-90	1.50 - 1.83	17.70 - 32.50
Median	33.50	69.50	1.65	25.45
Normality test p value	0.08	> 0.10	> 0.10	> 0.10

statistical difference when compared to the ages of the HAART treated and non-HAART treated study subjects.

Conclusion

The main advantage of the study is that the BMI can be used as an overtly index in the monitoring and evaluation of people living with HIV/AIDS, amongst other diagnostic indices, most especially in developing countries. Within and across the 3 groups, a higher frequency of subjects fell within the normal BMI bracket than those that were underweight, overweight and clinically obese. Subjects not placed on HAART regimen showed signs of underweight and clinical muscle wasting than HAART treated subjects. Healthy subjects, who showed signs of underweight during the study, may be attributed to nutritional deficiencies. Healthy subjects, HAART treated and non-HAART treated subjects, in that order, showed similar trend for overweight and clinical obesity. Since the goal of ARV therapy is to reduce morbidity rate and consequently mortality rate, it therefore follows that ensuring a BMI normal weight status per patient in clinical settings is pertinent. The study shows that PLWHA on HAART regimen within the FCT, Abuja and her neighbouring states were 'healthier' than HAART untreated and even some healthy subjects, amazingly based on BMI. Within the premise of a normal BMI, the HAART regimens implicated were in the order: Truvada + Nevirapine, Truvada + Efavirenz, Zidovudine + Lamivudine + Nevirapine and Stavudine + Lamivudine + Nevirapine.

Certain limitations were experienced during the course of the study such as subjects not reporting to clinic on appointed days, abrupt switch in HAART regimen owing to adverse drug reactions or idiosyncratic reactions, reduced number of study subjects due to death during the seven years study period, stringent follow-ups to ensure subjects do not combine their HAART regimen with herbal medicines reputed to reduce viral load. We advise the development of further studies to assess the BMI-HAART relationships in people living with HIV/AIDS using anthropometric measurements as well as computed tomography to detect fat redistribution, bearing these limitations in mind.

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