

# Effect of aerobic exercise training on cardiovascular parameters and CD4 cell count of people living with human immunodeficiency virus/acquired immune deficiency syndrome: A randomized controlled trial

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## Abstract

**Objective:** Despite the significant positive effect of Highly Active Antiretroviral Therapy on physical and psychosocial well-being of people living with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) (PLWHA); decreased physical activity and its associated cardiovascular risk still pose some consequences for health and general well-being. This study investigated the effect of an 8 week aerobic exercise training on cardiovascular parameters and CD4 cell (T-cells) count of PLWHA.

**Materials and Methods:** This randomized controlled trial recruited 30 age matched PLWHA who were randomly assigned into exercise group (EG) ( $n = 15$ ) and control group (CG) ( $n = 15$ ) respectively. The PLWHA were patients receiving treatment in President's Emergency Plan for AIDS relief at the HIV clinic of the University of Nigeria Teaching Hospital, Nigeria. The EG in addition to conventional therapy received moderate intensity continuous exercise training (60-79% of the maximum heart rate [max]) of between 45 and 60 min, 3 times/week for 8 weeks, while the CG received conventional therapy involving antiretroviral therapy and counseling only. Systolic blood pressure (SBP), diastolic blood pressure (DBP), maximum oxygen uptake ( $VO_2$  max) and CD4 cell count were assessed at baseline (week 1) and week 8 respectively. Analysis of co-variance and Pearson correlation tests were used in data analysis.

**Results:** Findings of the study revealed a significant effect (ANCOVA test) of moderate intensity continuous exercise training program on, SBP, DBP,  $VO_2$  max and CD4 cell count at  $P < 0.05$ . Changes in  $VO_2$  max significantly correlated (Pearson correlation test) with changes in CD4 cell count ( $r = 0.528$ ) at  $P < 0.05$ .

**Conclusion:** Moderate intensity aerobic exercise is an effective complementary therapy in lowering blood pressure and increasing CD4 cell count in PLWHA.

**Key words:** Aerobic exercise, cardiovascular parameters, CD4 count, human immunodeficiency virus/acquired immune deficiency syndrome, Nigeria

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## Introduction

Acquired immune deficiency syndrome (AIDS) is a disease caused by the retrovirus human immunodeficiency virus (HIV) and characterized by profound immunosuppression that

leads to opportunistic infections, secondary neoplasm and neurological manifestations.<sup>[1]</sup> HIV/AIDS represent an

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urgent world-wide problem with an impact on the social, cultural, economic, political and ethical dimensions.<sup>[1]</sup> The profile of HIV infection has changed over time, as it was once viewed as an illness progressing steadily toward death, but HIV infection can now present as a chronic and episodic disease for people who are able to access and tolerate highly active antiretroviral therapy (HAART). These developments to chronic and episodic disease have been mirrored by the increasing prevalence of impairments, activity limitations and participation restrictions for many people living with HIV.<sup>[2,3]</sup>

The use of exercise in the management of chronic illnesses has substantial support in literature<sup>[4-7]</sup> Exercise has been shown to improve strength, cardiovascular function and psychosocial status in general populations.<sup>[8]</sup> Consequently, the use of exercise as an adjunct therapy in the management of impairments resulting from HIV/AIDS is becoming increasingly common among physical therapists. Furthermore, effective and safe exercise may enhance the effectiveness of HIV management, thus improving overall health outcomes for adults living with HIV.<sup>[6,9]</sup>

Although, HAART has improved physical and psychosocial well-being of people living with HIV/AIDS (PLWHA); however, known associated decreased physical activity may have consequences for cardiovascular disease risk.<sup>[6]</sup> The differences in exercise uptake and accommodation in health and disease as affected by heredity, genetics, ethnicity and interracial differences.<sup>[10-14]</sup> Studies are scanty on the effect of exercise among PLWHA who are on conventional antiretroviral treatment in sub-Saharan Africa. The purpose of this study was to investigate the effect of an 8 week aerobic exercise training on cardiovascular parameters and CD4 cell (T-cells) count of PLWHA.

## Materials and Methods

### Subjects

This study recruited PLWHA who were receiving treatment under the President's Emergency Plan for AIDS Relief at the HIV clinic of the University of Nigeria Teaching Hospital, Ituku Ozalla (UNTH), Enugu. A total of 33 PLWHA were enrolled in the study. All participants gave informed consent to participate in the study following full explanation of the protocol. The study's protocol was based on the American College of Sports Medicine guidelines,<sup>[15]</sup> Ethical approval was granted by the Research and Ethics Committee of the UNTH, Enugu.

### Study design

This study employed randomized controlled trial design. Eligible participants were randomized using simple random assignment into the exercise group (EG) and the control group (CG) respectively. The participants in the two

groups were age-matched. All procedures were conducted at the Physiotherapy Department of the UNTH. The EG participated in a continuous training program for the duration of 8 weeks and the CG received conventional therapy involving antiretroviral therapy and counseling only, at the end of the exercise training and conventional therapy period a post-test procedure was administered to all subjects.

### Inclusion criteria

Subjects who had been screened for HIV with results indicating positive (+ve); and who volunteered to participate in the study were recruited. Only sedentary male and female adult subjects living with HIV/AIDS participated in the study.

### Exclusion criteria

Subjects with acute infections/critically ill, severe muscle wastage, smokers, alcoholic, diabetics and other cardiac, renal, respiratory disease subjects were excluded. Those involved in vigorous physical activity and above averagely physically fit ( $VO_2$  max > 27 and > 33 ml/kg min for over 60 and 50 years old respectively) were also excluded.

A total of 33 subjects with HIV/AIDS satisfied the study (EG [ $n = 17$ ] and CG [ $n = 16$ ] (17) and control (16) groups. About 30 subjects (15 from exercise and 15 from CG) completed the 8 weeks training program. Three subjects (2 from exercise and 1 from CG) dropped out because of non-compliance and incomplete data; therefore, the data of 30 subjects (exercise [15] and control [15]) were used in the statistical analysis' [Figure 1].

### Outcome variables

The study outcome measures included the systolic blood pressure (SBP), diastolic blood pressure (DBP),  $VO_2$  max and CD4 count

### Pre-test procedure

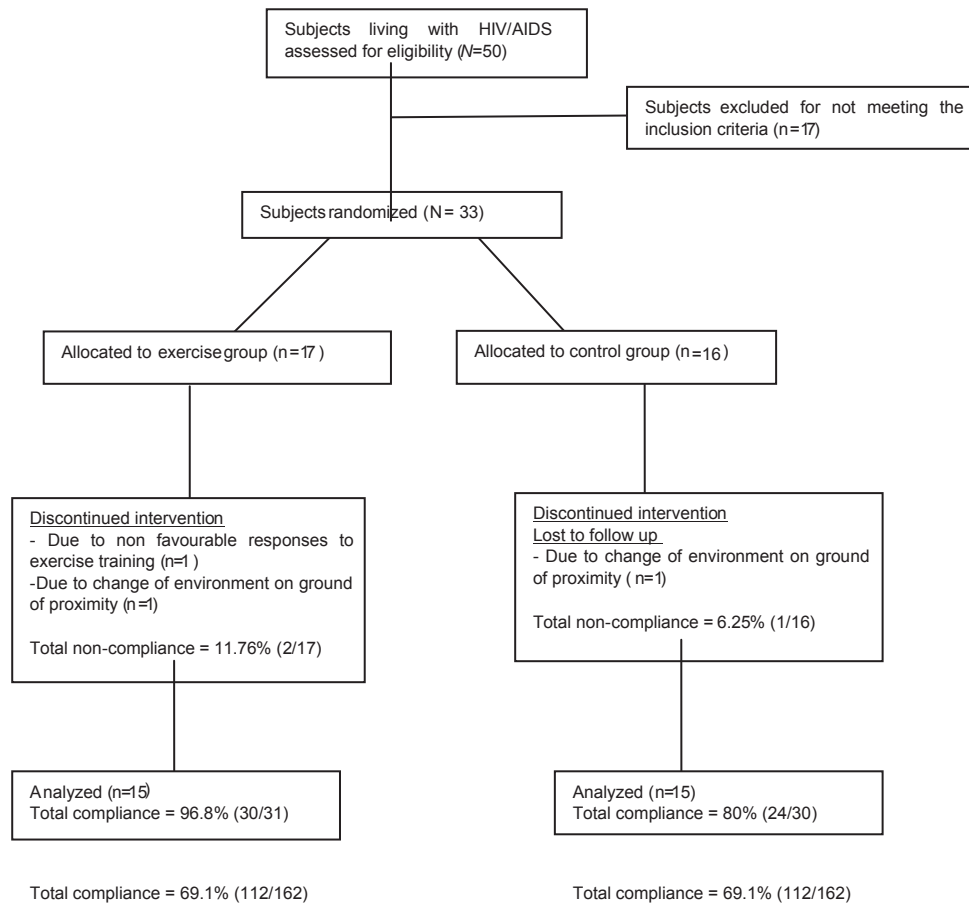
Subjects' resting SBP and DBP were monitored from the right arm as described by Musa *et al.*<sup>[16]</sup> using an automated digital electronic blood pressure (BP) monitor (Omron digital BP monitor, Model 11 EM 403c; Tokyo Japan).

### Anthropometric measurement

Subjects' physical characteristics (weight [kg] and height [m]) and body composition (body mass index [ $kg/m^2$ ]) assessment was carried out in accordance with standardized anthropometric protocol.<sup>[17]</sup>

### Blood sample collection (venipuncture method)

Pre-treatment venous blood samples were obtained from the antecubital vein. A volume of 5 ml syringe was used for whole blood sample collection, using the procedure described by Bachorik.<sup>[18]</sup> About 2 ml of blood were drawn into vial containing ethylenediaminetetraacetic



**Figure 1:** Consolidated standard for reporting trials (consort) chart

acid (EDTA) under sterile conditions; the blood samples were shaken gently to mix with the EDTA and immediately taken to the laboratory for analysis.

#### Assessment of CD4 count

CD4 count was determined using pan-leucogating protocol as described by Glencross *et al.*<sup>[19]</sup>

#### Pretest stress test

The modified Bruce protocol was used to assess the subject's aerobic power ( $VO_2$  max) as described by Guimarães *et al.*<sup>[20]</sup> Subjects were asked to refrain from both strenuous physical activities and the consumption of any stimulants such as coffee etc., for 24 h before the exercise test and not to eat at least 2 h before the start of the test. The modified Bruce protocol is a multistage, well-standardized test; subject jogged time (T) to exhaustion on the treadmill was then extrapolated into Bruce protocol formula for estimating  $VO_2$  max as stated by Wilmore and Costill<sup>[21]</sup> as follows:

$$\text{For men } VO_2 \text{ max (ml/kg/min)} = 14.8 - (1.379 \times T) + (0.451 \times T^2) - (0.012 \times T^3)$$

$$\text{For women } VO_2 \text{ max (ml/kg/min)} = 4.38 \times T - 3.9$$

T = Total time on the treadmill measured as a fraction of a minute.

The stress test was conducted under the supervision of experts in basic life support care and the emergency unit of the hospital was made ready to accommodate any incident that might occur during the stress test.

#### Test (training) procedure

##### Training program

Following stress test and prior to the exercise training, all subjects in both control and continuous exercise groups were re-assessed by the physician.

#### Intervention

##### The EG

In addition to conventional therapy, participants in the EG received exercised of moderate intensity of between 60% and 79% of their heart rate (HR) reserve as recommended by ACSM quantified by jogging on a treadmill.<sup>[15]</sup> The starting workload was Bruce stage 1 (1.7 mph) at 0% grade for 3 min; the jogging workload was later increased to obtain a HR reserve of 60%. This was increased in the first 2 weeks to and leveled up at 79% HR reserve throughout the remaining part of the training period. The exercise session

was increased from 45 min in the first 2 weeks of training to and leveled up at 60 min throughout the remaining part of the training. Exercise session of 3 times/week for 8 weeks.

The CG received conventional therapy only. Post-test procedure post-test SBP, DBP, VO<sub>2</sub> max, CD4 count and post-test stress test were conducted as earlier described in the pretest procedures using standardized protocols, techniques and methods. All post-test procedures were conducted on following training session.

### Statistical analysis

Data were analyzed using descriptive of means and standard deviations (SD) and inferential statistics of independent *t*-test, ANCOVA test and Pearson product moment correlation test respectively. All statistical analyses were performed on a Toshiba compatible microcomputer using the statistical package for the social science (SPSS), (version 16.0 Chicago IL, USA). Alpha level was set at  $P < 0.05$ .

## Results

The participants' ages ranged between 22 and 63 years mean (SD) age of participants in EG and CG was 38.77 (9.98) and 40.07 (9.72) years respectively. Physical characteristics of participants is presented in Table 1. Independent *t*-test comparison of physical characteristics and baseline measures of CD<sub>4</sub> and VO<sub>2</sub> max between EG and CG indicated that both groups were comparable except DBP. The baseline mean  $\pm$  SD CD4 cell count ( $492.27 \pm 229.86 \text{ mm}^3$ ) of the subjects in both groups indicated that the subjects were primarily in about the symptomatic stage of HIV disease at the time of the data collection.

ANCOVA tests and groups' pre- and post-treatment mean BP (SD) mmHg; fasting blood sugar (mg/dl) and VO<sub>2</sub> max (ml/kg/min) are depicted in ANCOVA summary Table 2. ANCOVA analysis indicated a significant difference in groups' pre- and post-treatment SBP ( $F = 31.377, P = 0.000$ ) DBP ( $F = 9.004, P = 0.000$ ) CD4 count ( $F = 26.597, P = 0.000$ ) and VO<sub>2</sub> max ( $F = 6.643, P = 0.013$ ).

Results indicated 27.18% (140.27/516) and 30.43% (7/23) increased in CD4 cell count and VO<sub>2</sub> max to baseline values respectively in the EG; while the CG showed

3.60% (17.73/492.27) increased in CD4 cell count and  $-1.38\%$  ( $-0.33/24$ ) decreased in VO<sub>2</sub> max. Detailed CD4 cell count and aerobic capacity (VO<sub>2</sub> max) changed score values are display in Figure 2. There was a significant positive correlation between changes between VO<sub>2</sub> max and changes in CD4 count ( $r = 0.528$ ) following continuous aerobic exercise training at  $P < 0.05$  [Figure 3].

## Discussion

Findings from the present study revealed a significant decrease in SBP, DBP and increase in CD4 count and VO<sub>2</sub> max in the EG compared with CG. Furthermore, results of the present study indicated a significant positive correlation between changes in VO<sub>2</sub> max and changes in CD4 count. The favorable changes resulting from aerobic training in SBP, DBP and VO<sub>2</sub> max demonstrated in the present study is consistent with several other studies on healthy subjects,<sup>[22-24]</sup> mild to moderate hypertension<sup>[25-27]</sup> and HIV/AIDS.<sup>[7,28]</sup>

The effect of aerobic exercise training on the CD4 cell count level in HIV patients has been a battle for researchers over the years. The results of the present study concur with the study of LaPerriere *et al.*<sup>[29]</sup> in their study; they investigated the effect of moderate intensity 12-week interval training on CD4 count of 28 subjects living with HIV. They reported a significant increase in CD4 cell counts as a result of aerobic interval training. Perna *et al.*<sup>[30]</sup> conducted a similar study to assess the effects of a 12 week laboratory based aerobic

**Table 1: Independent *t* test comparison of physical characteristics and baseline measures of CD4 and VO<sub>2</sub> max between exercise and control group**

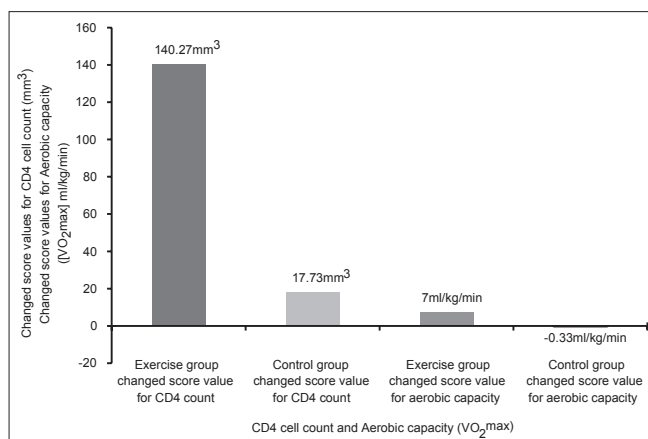
Variables	Group X $\pm$ SD n=15		P values	t values
	Exercise	Control		
Age (years)	40.07 $\pm$ 9.72	32.47 $\pm$ 10.41	0.707	0.485
BMI (kg/m <sup>2</sup> )	28.65 $\pm$ 7.11	29.01 $\pm$ 4.42	-0.164	0.871
SBP (mmHg)	149.20 $\pm$ 5.33	138.93 $\pm$ 4.20	1.492	0.147
DBP (mmHg)	91.60 $\pm$ 3.14	75.20 $\pm$ 6.58	8.713	0.000*
CD4 count (cells/mm <sup>3</sup> )	516.00 $\pm$ 265.49	492.27 $\pm$ 229.86	0.267	0.792
VO <sub>2</sub> max (ml/kg/min)	23.00 $\pm$ 2.54	24.00 $\pm$ 2.54	0.878	0.878

SD=Standard deviation, BMI=Body mass index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; VO<sub>2</sub> max=Maximum oxygen uptake. \*Significant at 0.05

**Table 2: ANCOVA test and groups mean  $\pm$  SD for pre-test and post-test values (N=30)**

Variables	X $\pm$ SD				P values
	Exercise pretest	Exercise posttest	Control pretest	Control posttest	
SBP (mmHg)	149.20 $\pm$ 5.33	123.13 $\pm$ 7.56	138.93 $\pm$ 4.20	139.33 $\pm$ 4.64	0.000*
DBP (mmHg)	91.60 $\pm$ 3.06	80.33 $\pm$ 3.06	75.20 $\pm$ 6.58	75.87 $\pm$ 6.30	0.000*
VO <sub>2</sub> max (ml/kg/min)	23.00 $\pm$ 2.54	30.87 $\pm$ 4.37	24.00 $\pm$ 2.54	23.87 $\pm$ 2.65	0.000*
CD4 count (cells/mm <sup>3</sup> )	516.00 $\pm$ 256.49	656.27 $\pm$ 189.17	492.27 $\pm$ 229.86	510.93 $\pm$ 226.14	0.000*

\*Significant at 0.05. SD=Standard deviation; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; VO<sub>2</sub> max=Maximum oxygen uptake



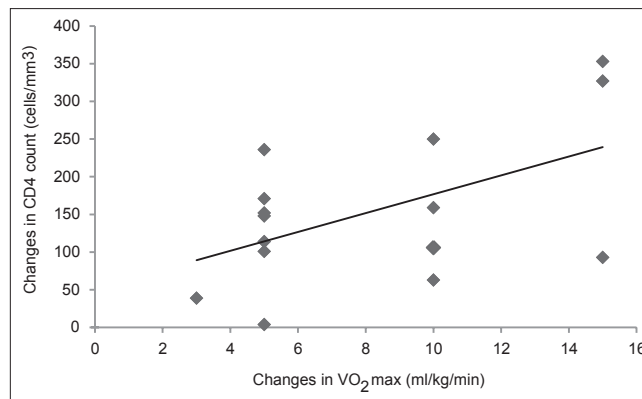
**Figure 2:** CD4 cell count and VO<sub>2</sub> max changed score values for exercise and control groups (N = 30)

exercise program on CD4 cell count among symptomatic AIDS/HIV infected individuals. In their study, 28 subjects were randomly assigned to exercise or control conditions. They reported significant effect of aerobic training over control in CD4 cell count. Bopp *et al.*<sup>[31]</sup> conducted a study on physical activity level and immunity in subjects living with HIV. They investigated a sample of 66 males and females between the ages of 18 and 64 years from a hospital based HIV/AIDS clinic. They reported a significant inverse relationship between mean physical activity level and viral load. They suggested that increasing levels of physical activity might have beneficial effects on viral load in individuals living with HIV/AIDS.

The result from this study disagrees with the finding of O'Brien *et al.*<sup>[7]</sup> the investigators conducted a meta-analysis on the effect of aerobic exercise training on CD4 cell count of adults living with HIV. They reported a small non-significant change in CD4 cell count, viral load and VO<sub>2</sub> max. MacArthur *et al.*<sup>[28]</sup> investigated the effects of aerobic exercise CD4 cell count and in a sample of 25 HIV-infected men. At the end of their 24-week intervention, it was observed that there was no significant changes in CD4 count in both higher and moderate intensity groups. Baigis *et al.*<sup>[32]</sup> conducted a study on the effectiveness of a home-based exercise intervention on 99 subjects living with HIV/AIDS in a randomized trial. They reported no significant changes in CD4 (T lymphocyte) count. Several other studies<sup>[31-34]</sup> have reported similar non beneficial effect of exercise on CD4 count and viral load.

Smith *et al.*<sup>[35]</sup> conducted a study on physical activity level and immunity in subjects living with HIV. They reported a significant inverse relationship between mean physical activity level and viral load. They suggested that increasing levels of physical activity might have beneficial effects on viral load in individuals living with HIV/AIDS.

In apparently healthy individuals free of HIV infection, acute, moderate-intensity exercise will cause neutrophil proliferation,



**Figure 3:** Correlation between training changes in VO<sub>2</sub> max and CD4 count (N = 15),  $r = 0.528$ , \*significant at 0.05

epinephrine and cortisol secretion, a temporary decline in lymphocyte levels and an elevated number of natural killer cells and increased cytokine levels (interleukin [IL-1], tumor necrosis factor- $\alpha$ , IL-6). Regular participation in aerobic exercise could lead to more permanent benefits. This response is also applicable to in HIV-infected individuals following a single exercise session but blunted.<sup>[36]</sup> Moderate-intensity exercise has been most often recommended for HIV-infected individuals. Several immunological variables are of significance to HIV-infected individuals, including HIV-1 ribonucleic acid viral load and CD4 cell count. Unfortunately, the data available in the literature describing the relationship of these markers and exercise are ambiguous. Exercisers also displayed slower disease progression to AIDS, less symptomology and decreased rates of mortality compared to sedentary life style. However, lower CD4 cell count levels have been linked with noncompliance to prescribed exercise in HIV/AIDS individuals.<sup>[28]</sup>

## Conclusion

This study demonstrated that moderate intensity aerobic exercise is an effective complementary therapy in lowering BP and increasing CD4 cell count in PLWHA.

## Clinical implications

The present study supports the use of moderate intensity therapeutic aerobic exercise training as an adjunct therapy in the treatment of symptoms of HIV/AIDS infection. In symptomatic PLWHA, aerobic exercise should begin as soon as possible after the diagnosis of HIV infection in an attempt to delay the down slope of CD4 cell count and finally delaying decrease the severity of those symptoms already present, potentially delaying the disease progression and decreased rates of mortality compared to sedentary individuals.

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