



تأثیر مدت زمان درمان HAART بر اختلالات کاردیومتابولیک و شاخص‌های بیوشیمیایی در افراد مبتلا به HIV در نیجریه

ادیکونلی بولا ادیگیمی^{۱*}، متیو فولارانی الانیان^۲، گودفریاینوسنت آیاری^۱، آکینوال ماجید آکینلابی^۴، موفاتاو موسونمدی ازیز^۵، آدینکا ادیدایری^۱

۱- گروه علوم آزمایشگاهی پزشکی، دانشگاه ایالتی ادو، اوزیرو، ایالت ادو، نیجریه.

۲- بخش آزمایشگاه علوم پزشکی، بیمارستان نیروی دریایی نیجریه، واری، ایالت دلتا، نیجریه.

۳- گروه علوم آزمایشگاهی پزشکی، دانشگاه ایالتی کوارا، مالت، ایالت کوارا، نیجریه.

۴- گروه علوم آزمایشگاهی پزشکی، دانشگاه جوزف آیو بابالولا، ایکیجی-آراکچی، ایالت اوسون، نیجریه.

۵- گروه علوم آزمایشگاهی پزشکی، دانشگاه آجی کروت، اویو، ایالت اویو، نیجریه.

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چکیده

مقدمه: این مطالعه با هدف ارزیابی ارتباط بین مدت دریافت درمان ضدترتروویروسی بسیار فعال (HAART) و بروز بیماری‌های کاردیومتابولیک و برخی شاخص‌های بیوشیمیایی در بزرگسالان مبتلا به HIV در نیجریه انجام شد.

مواد و روش‌ها: این مطالعه مقطعی بر روی ۴۰۰ بزرگسال مبتلا به HIV تحت درمان HAART در بیمارستان نیروی دریایی نیجریه در واری انجام شد. شرکت‌کنندگان بر اساس مدت HAART به سه گروه ≥ 2 سال، ۵-۲ سال و < 5 سال تقسیم شدند. اطلاعات جمعیت‌شناختی، شاخص توده بدنی (BMI)، پروفایل لیپیدی شامل کلسترول تام، لیپوپروتئین با چگالی کم (LDL-C)، لیپوپروتئین با چگالی بالا (HDL-C)، تری‌گلیسرید، قند خون ناشتا و هموگلوبین گلیکوزیله (HbA1c) مورد ارزیابی قرار گرفت. ارتباط مدت HAART با بیماری‌های کاردیومتابولیک با استفاده از رگرسیون لجستیک چندمتغیره بررسی گردید.

نتایج: تشویع بیماری‌های کاردیومتابولیک با افزایش مدت HAART به‌طور پیشرونده افزایش یافت و بیشترین میزان در افراد با بیش از ۵ سال درمان (۵۲/۱٪) در مقایسه با گروه ≥ 2 سال (۲۱/۴٪) و گروه ۲ تا ۵ سال (۳۴/۸٪) مشاهده شد ($P < 0.001$). این گروه، میانگین سطوح بالاتری از کلسترول تام، LDL-C، تری‌گلیسرید، قند خون ناشتا و HbA1c و در عین حال سطوح پایین‌تری از HDL-C داشتند ($P < 0.001$). پس از تعدیل عوامل مخدوش‌کننده احتمالی، مدت HAART بیش از ۵ سال به‌طور مستقل با بیماری‌های کاردیومتابولیک مرتبط باقی ماند ($OR = 2.8$) با فاصله اطمینان ۱/۹-۴/۳. همچنین سن بالاتر، BMI افزایش‌یافته، جنس مؤنث و مصرف مهارکننده‌های پروتئاز به‌طور معنی‌داری با بیماری‌های کاردیومتابولیک مرتبط بودند.

بحث: مدت طولانی‌تر HAART به‌طور مستقل با افزایش بیماری‌های کاردیومتابولیک و اختلالات متابولیک در بزرگسالان مبتلا به HIV مرتبط بود و این یافته‌ها اهمیت پایش منظم کاردیومتابولیک، به‌ویژه در افراد تحت درمان طولانی و در محیط‌های با منابع محدود را نشان می‌دهد.

واژه‌های کلیدی: بیماری‌های کاردیومتابولیک، HIV، دیس‌لیپیدمی، پرفشاری خون، شاخص‌های بیوشیمیایی.

*نویسنده مسئول: گروه علوم آزمایشگاهی پزشکی، دانشگاه ایالتی ادو، اوزیرو، ایالت ادو، نیجریه، Email: odekunle@edouniversity.edu.ng

ارجاع: ادیکونلی بولا ادیگیمی، متیو فولارانی الانیان، گودفریاینوسنت آیاری، آکینوال ماجید آکینلابی، موفاتاو موسونمدی ازیز، آدینکا ادیدایری. تأثیر مدت زمان درمان HAART بر اختلالات کاردیومتابولیک و شاخص‌های بیوشیمیایی در افراد مبتلا به HIV در نیجریه. مجله دانش و تندرستی در علوم پایه پزشکی ۱۴۰۴؛ ۲۰(۳): ۶۲-۷۱.



Introduction

The introduction of Highly Active Antiretroviral Therapy (HAART) has transformed the clinical course of Human Immunodeficiency Virus (HIV) infection from a fatal condition into a manageable chronic disease, leading to substantial reductions in AIDS-related morbidity and mortality worldwide [1, 2]. As survival among people living with HIV continues to improve, attention has increasingly shifted toward long-term comorbidities associated with prolonged antiretroviral exposure, particularly cardiometabolic diseases.

Cardiometabolic disorders, including dyslipidaemia, hypertension, insulin resistance, and cardiovascular disease, have emerged as important non-infectious complications among individuals receiving HAART [3]. These conditions are thought to arise from complex interactions between chronic HIV-related inflammation, antiretroviral drug effects, aging, and traditional cardiovascular risk factors. Several studies have reported that metabolic abnormalities may become more pronounced with increasing duration of antiretroviral therapy, suggesting a cumulative effect of long-term treatment exposure [4-6].

Mechanistically, HAART, especially regimens containing protease inhibitors, has been associated with alterations in lipid metabolism, impaired glucose homeostasis, endothelial dysfunction, and changes in body fat distribution [7]. These metabolic perturbations may predispose individuals to atherosclerosis and other cardiovascular complications over time. Importantly, the magnitude and pattern of these abnormalities appear to vary across populations, antiretroviral regimens, and duration of therapy, underscoring the need for context-specific investigations.

In Nigeria and other sub-Saharan African countries, the burden of HIV remains substantial, and access to long-term HAART has expanded considerably over the past two decades. However, data examining the cardiometabolic consequences of prolonged HAART exposure within Nigerian populations remain limited [8]. Most available studies have focused primarily on virological suppression and immunological recovery, with comparatively less emphasis on metabolic health outcomes. Given the rising prevalence of non-communicable diseases in the region, understanding the cardiometabolic profile of people living with HIV has become increasingly relevant.

Furthermore, cardiometabolic risk assessment in resource-limited settings presents unique challenges, including limited laboratory capacity and competing healthcare priorities. Nonetheless, evaluating routinely available biochemical markers such as lipid profiles and fasting blood glucose may provide valuable insight into cardiometabolic risk among individuals receiving long-term HAART [9-11].

Against this background, the present study aimed to examine the association between duration of HAART and the prevalence of cardiometabolic diseases, as well as related biochemical parameters, among HIV-positive adults receiving care at a tertiary healthcare facility in Nigeria. By stratifying participants according to HAART duration, this study seeks to contribute locally relevant evidence that may

inform clinical monitoring strategies and guide long-term HIV care in resource-constrained settings.

Methods

Study Design and Setting

This study employed a hospital-based cross-sectional design involving HIV-positive adults receiving Highly Active Antiretroviral Therapy (HAART) at the Nigerian Navy Hospital, Warri, Delta State, Nigeria. The hospital is a tertiary healthcare facility that provides comprehensive HIV care services, including antiretroviral therapy, routine clinical follow-up, and laboratory monitoring.

Study Population

A total of 400 HIV-positive adults were recruited through stratified random sampling from clinic registries at the study site. Stratification was based on duration of HAART exposure to ensure proportional representation across treatment categories.

Participants were categorized into three groups according to cumulative HAART duration:

Group 1: ≤ 2 years of HAART exposure

Group 2: >2 to 5 years of HAART exposure

Group 3: >5 years of HAART exposure

a) This categorization was designed to reflect early, intermediate, and long-term HAART exposure, consistent with previous approaches used to assess treatment-related metabolic outcomes.

Inclusion and Exclusion Criteria

Inclusion criteria were:

- a) Confirmed HIV-positive status
- b) Age between 18 and 65 years
- c) Continuous HAART use for at least six months
- d) Provision of written and verbal informed consent

Exclusion criteria included:

- a) Presence of acute or chronic non-HIV-related conditions (e.g., malignancies, severe infections) that could independently influence cardiometabolic parameters
- b) Pregnancy or lactation
- c) Incomplete clinical or laboratory records

Data Collection

Sociodemographic and clinical data, including age, sex, educational level, occupation, and medical history were obtained using structured interviewer-administered questionnaires and verified with hospital records. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

Definition of Cardiometabolic Outcomes

Cardiometabolic diseases were assessed using standard clinical criteria:

- Hypertension: systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg
- Diabetes mellitus: fasting blood glucose ≥ 126 mg/dL
- Dyslipidaemia: abnormal lipid profile values based on laboratory reference ranges
- Cardiovascular disease: documented clinical diagnosis in medical records

The presence of any cardiometabolic disease was defined as having at least one of the above conditions.

Laboratory Analysis

HIV Confirmation

HIV infection was confirmed using the Bio-Rad Genscreen™ ULTRA HIV Ag-Ab enzyme immunoassay, which qualitatively detects HIV-1 (groups M and O) and HIV-2 antibodies, as well as HIV-1 p24 antigen. The assay operates on a sandwich immunoassay principle, producing a colorimetric reaction proportional to antigen-antibody binding.

Biochemical Measurements

After an overnight fast, venous blood samples were collected for biochemical analysis. Serum levels of: Total cholesterol, Low-Density Lipoprotein Cholesterol (LDL-C), High-Density Lipoprotein Cholesterol (HDL-C), Triglycerides, Fasting blood glucose, and Glycated haemoglobin (HbA1c) were measured using the Roche Cobas c111 Chemistry Analyzer, an automated system employing standardized colorimetric methods.

The Atherogenic Index of Plasma (AIP) was calculated as the logarithmic ratio of triglycerides to HDL-C and used as an indicator of atherogenic risk.

Exposure and Covariates

The primary exposure variable was duration of HAART.

The following variables were treated as potential confounders, selected a priori based on biological plausibility and existing evidence: Age, Sex, Body mass index and Protease inhibitor use (extracted from treatment records)

Statistical Analysis

Data were analyzed using SPSS version 25. Continuous variables were summarized as means \pm standard deviations, while categorical variables were expressed as frequencies and percentages. One-way analysis of variance (ANOVA) was used to compare continuous variables across HAART duration groups. Chi-square tests were applied for categorical comparisons. Where overall group differences were statistically significant, post-hoc pairwise comparisons with Bonferroni adjustment were performed. To assess the independent association between HAART duration and cardiometabolic disease, multivariate logistic regression analysis was conducted. A two-step modeling strategy was employed:

- a) Univariate logistic regression was used to explore associations between individual variables and cardiometabolic disease.
- b) Variables of clinical relevance, including HAART duration, age, sex, BMI, and protease inhibitor use, were entered into the final multivariate model to estimate adjusted odds ratios (aORs) with 95% confidence intervals.

Statistical significance was set at $P < 0.05$.

Ethical Considerations

Ethical approval for the study was obtained from the Ministry of Defence Research Ethics Committee, Abuja (Approval No: NHREC/MOD-HREC/15/02/23C). Administrative permission was granted by the management of the Nigerian Navy Hospital, Warri. All participants provided informed written and verbal consent prior to enrollment, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Study Design

This cross-sectional study involved 400 HIV-positive participants from the Military Hospital Warri, Nigeria, categorized by their HAART duration into three groups: Group 1 (≤ 2 years), Group 2 (2-5 years), and Group 3 (> 5 years). Sociodemographic data, body mass index (BMI), and the prevalence of cardiometabolic diseases were collected. Lipid profiles and fasting blood glucose levels were measured using standard biochemical assays. Multivariate logistic regression was employed to identify significant predictors of cardiometabolic diseases, considering factors such as age, gender, BMI, and HAART duration.

Study Area:

This study was conducted at the Nigerian Navy Hospital Warri, located in Warri, Delta State, Nigeria.

Study Population

A total of 400 HIV-positive participants were recruited through stratified random sampling from the clinic registries at the Nigerian Navy Hospital Warri. Stratification was based on HAART duration to ensure proportional representation across three groups: ≤ 2 years, 2–5 years, and > 5 years.

The participants were categorized based on HAART duration:

Group 1 (≤ 2 years): 120 participants (30%)

Group 2 (2-5 years): 140 participants (35%)

Group 3 (> 5 years): 140 participants (35%)

Inclusion Criteria:

- a) HIV-positive individuals aged 18-65 years
- b) Participants who had been on HAART for at least 6 months
- c) Participants who provided informed consent to participate in the study
- d) Exclusion Criteria:

- e) Participants with acute or chronic conditions other than HIV (e.g., cancers, severe infections) that could interfere with cardiometabolic risk factors
- f) Pregnant or lactating women
- g) Individuals with incomplete or missing medical records

Data Collection

Sociodemographic data, including age, gender, occupation, education level, and medical history, were obtained through structured questionnaires administered by trained research assistants. Body mass index (BMI) was calculated using measured weight (in kilograms) and height (in meters squared).

Clinical measurements included assessments for cardiometabolic diseases, specifically:

Hypertension: Defined as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg.

Diabetes: Diagnosed based on fasting blood glucose levels ≥ 126 mg/dL.

Dyslipidemia: Assessed through lipid profiles.

Blood samples were collected after an overnight fast to determine biochemical parameters. The following assays were conducted:

Laboratory Analysis

Viral Marker

HIV p24 Antigen and Antibodies

Kit: Bio-Rad Genscreen™ ULTRA HIV Ag-Ab. It is a qualitative enzyme immunoassay designed to detect HIV p24 antigen and antibodies to HIV-1 (groups M and O) and HIV-2 in human serum or plasma. It is used for screening both HIV antigen and antibody levels.

Principle: The test works through a sandwich technique, where monoclonal antibodies and purified antigens are used to capture HIV components in a sample. If HIV antigens or antibodies are present, a color change occurs after several incubation and washing steps. The reaction is stopped and measured using a spectrophotometer to confirm the presence or absence of HIV Ag or antibodies. This kit detects various HIV-1 and HIV-2 strains, addressing genetic variability in these viruses.

Metabolic Markers

Lipid Profile (Total Cholesterol, HDL, LDL, Triglycerides) and Fasting Blood Glucose (FBG) were analyzed using Roche Cobas C111 Chemistry Analyzer. The Roche Cobas c111 Chemistry Analyzer is an automated, compact system used for routine clinical chemistry testing, ideal for medium-to-high-volume laboratories. It employs a colorimetric reaction principle to measure analyte concentrations, with applications spanning liver, renal, cardiac, electrolyte, lipid, glucose, and other biochemical tests.

Atherogenic Plasma Index (API) = log Triglycerides

HDL

The Atherogenic Index of Plasma (AIP) is calculated using the logarithmic transformation of the ratio between triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C). This index serves as an indicator of the risk of atherosclerosis and cardiovascular disease.

Data Analysis

Descriptive statistics (mean, standard deviation, frequencies, and percentages) were employed to summarize sociodemographic characteristics and clinical parameters. Comparisons between groups were conducted using one-way ANOVA for continuous variables and chi-square tests for categorical variables. Multivariate logistic regression analysis was utilized to identify significant predictors of cardiometabolic diseases, considering independent variables such as age, gender, BMI, and HAART duration. The significance level was set at $P < 0.05$, and statistical analyses were performed using SPSS version 25.

Ethical Approval

The Ministry of Defence Research Ethics Committee, Abuja (Approval No: (NHREC/MOD-HREC/15/02/23C), approved the protocol. Administrative approval was obtained from the management of NNH-Warri before the commencement of the study. Participants provided informed consent, both verbal and written, before enrollment in the study. All procedures were conducted in accordance with the Declaration of Helsinki.

Results

Sociodemographic and Clinical Characteristics of Participants

A total of 400 HIV-positive adults receiving HAART were included in the analysis. Participants were stratified according to duration of HAART exposure into three groups: Group 1 (≤ 2 years), Group 2 ($>2-5$ years), and Group 3 (>5 years). The overall mean age was 42.5 ± 10.3 years, with a higher proportion of females (60%) across all groups. Participants in the >5 -year HAART group were older on average compared with those in the shorter-duration groups. Body mass index (BMI) also showed a gradual increase with longer HAART exposure. The distribution of education level and employment status was comparable across the three HAART duration groups, indicating relative sociodemographic balance (Table 1).

Table 1. Sociodemographic and Clinical Characteristics of Participants by HAART Duration

Characteristic	Total (n=400)	Group 1 (n=120)	Group 2 (n=140)	Group 3 (n=140)
Age (years), mean \pm SD	42.5 \pm 10.3	38.0 \pm 9.5	42.5 \pm 10.2	47.0 \pm 10.4
Female sex, n (%)	240 (60.0)	70 (58.3)	80 (57.1)	90 (64.3)
BMI (kg/m ²), mean \pm SD	25.8 \pm 4.3	24.1 \pm 3.8	25.6 \pm 4.1	27.2 \pm 4.6
BMI >25 kg/m ² , n (%)	180 (45.0)	42 (35.0)	63 (45.0)	75 (53.6)
Protease inhibitor use, n (%)	160 (40.0)	38 (31.7)	54 (38.6)	68 (48.6)

Note: HAART duration groups were defined as follows: Group 1= ≤ 2 years, Group 2= $>2-5$ years, Group 3= >5 years.

Prevalence of Cardiometabolic Diseases by HAART Duration

Table 2 presents the prevalence of cardiometabolic diseases across HAART duration categories. The overall prevalence of any cardiometabolic disease differed significantly across the three groups ($P<0.001$), with the highest proportion observed among participants on HAART for more than 5 years (52.1%).

Post-hoc pairwise comparisons demonstrated that:

- Group 3 (>5 years) had a significantly higher prevalence of cardiometabolic disease compared with Group 1 (≤ 2 years) ($P<0.001$) and Group 2 (2-5 years) ($P=0.004$).

- The difference between Group 1 and Group 2 did not reach statistical significance.

A similar pattern was observed for specific cardiometabolic conditions. The prevalence of dyslipidaemia, hypertension, and insulin resistance was significantly higher in Group 3 compared with Group 1 (all adjusted $P<0.01$). Cardiovascular disease prevalence was also highest in the longest HAART duration group, with post-hoc analysis indicating a significant difference between Group 3 and Group 1 ($P=0.018$). No statistically significant differences were observed between Group 1 and Group 2 for most cardiometabolic conditions after adjustment.

Table 2. Prevalence of Cardiometabolic Diseases by HAART Duration

Condition	Total (%)	Group 1 ≤ 2 years	Group 2 2-5 years	Group 3 >5 years	Overall P.V
Any cardiometabolic disease	38.7	21.4	34.8	52.1	<0.001
Dyslipidaemia	25.3	15.6	22.7	36.8	<0.001
Hypertension	18.7	12.3	18.3	28.4	0.002
Insulin resistance	15.2	9.1	14.6	22.3	0.005
Cardiovascular disease	7.8	4.5	7.0	12.3	0.021

Footnote: HAART duration groups were defined as Group 1 = ≤ 2 years, Group 2 = 2-5 years, Group 3 = >5 years. Overall p-values were obtained using chi-square tests. Post-hoc pairwise comparisons (Bonferroni-adjusted) showed that Group 3 differed significantly from Group 1 for all listed conditions ($P<0.05$), while differences between Groups 1 and 2 were not statistically significant.

Multivariate Logistic Regression Analysis of Predictors of Cardiometabolic Disease

Table 3 summarizes the results of the multivariate logistic regression analysis examining factors associated with the presence of cardiometabolic disease. The primary exposure variable in the model was HAART duration, while age, sex, BMI, and protease inhibitor use were included a priori as potential confounders based on biological plausibility and prior evidence.

In the adjusted model, participants on HAART for more than 5 years had significantly higher odds of cardiometabolic disease compared with those on shorter durations of therapy (adjusted odds ratio [aOR]=2.8; 95% CI: 1.9-4.3; $P<0.001$). Older age (>40 years), elevated BMI (>25 kg/m²), female sex, and protease inhibitor use were also independently associated with cardiometabolic disease. Protease inhibitor use was included in the model because

protease inhibitor-based regimens are known to influence lipid metabolism and glucose homeostasis. Treatment history was extracted from clinical records to account for regimen-related metabolic effects.

Model-building strategy: Univariate logistic regression analyses were initially performed to explore associations between individual variables and cardiometabolic disease. Variables with biological relevance, including HAART duration, age, sex, BMI, and protease inhibitor use, were subsequently entered into the multivariate model irrespective of univariate significance to estimate the independent association of HAART duration while controlling for confounding.

Table 3. Multivariate Logistic Regression Analysis of Factors Associated with Cardiometabolic Disease

Variable	Adjusted Odds Ratio (aOR)	95% CI	P.V
HAART duration >5 years	2.8	1.9 – 4.3	<0.001
Age >40 years	1.6	1.1 – 2.4	0.012
Female sex	1.4	1.0 – 2.1	0.045
BMI >25 kg/m ²	1.9	1.2 – 3.0	0.002
Protease inhibitor use	1.7	1.1 – 2.7	0.018

Footnote: HAART duration was treated as the primary exposure variable. Age, sex, BMI, and protease inhibitor use were included a priori as confounders in the multivariate model based on biological plausibility and prior evidence.

Table 4. Lipid Profile and Glycaemic Parameters by HAART Duration

Parameter	Total (mean SD)	Group 1 ≤ 2 years	Group 2 2-5 years	Group 3 >5 years	P.V
Total cholesterol (mg/dL)	182.4 ± 36.5	174.8 ± 32.1	185.3 ± 38.4	190.1 ± 37.6	<0.001
LDL-C (mg/dL)	110.1 ± 32.4	102.6 ± 28.7	112.4 ± 34.0	119.4 ± 31.8	0.002
HDL-C (mg/dL)	42.6 ± 9.2	45.3 ± 9.8	41.8 ± 8.9	39.8 ± 8.6	<0.001
Triglycerides (mg/dL)	156.3 ± 45.1	146.4 ± 40.0	156.9 ± 42.8	169.8 ± 48.0	<0.001
Fasting blood glucose (mg/dL)	98.6 ± 12.4	94.7 ± 10.8	99.3 ± 11.8	103.4 ± 13.2	<0.001
HbA1c (%)	5.9 ± 1.2	5.6 ± 1.1	5.8 ± 1.2	6.3 ± 1.2	<0.001
Atherogenic Index of Plasma	2.5 ± 0.8	2.4 ± 0.7	2.6 ± 0.9	2.7 ± 0.8	0.035

Footnote: HAART duration groups were defined as Group 1= ≤ 2 years, Group 2=2-5 years, Group 3=>5 years. Overall p-values were derived using one-way ANOVA. Post-hoc Bonferroni tests indicated that Group 3 differed significantly from Group 1 for all lipid and glycaemic parameters ($P<0.01$), with lower HDL-C and higher LDL-C, triglycerides, fasting glucose, and HbA1c.

Table 4 compares lipid and glycaemic parameters across HAART duration groups. Significant overall differences were observed for total cholesterol, Low-Density Lipoprotein Cholesterol (LDL-C), High-Density Lipoprotein Cholesterol (HDL-C), triglycerides, fasting blood glucose, and glycated haemoglobin (HbA1c) (all $P<0.01$).

Post-hoc analyses indicated that:

- a) Participants in Group 3 (>5 years) had significantly higher mean levels of total cholesterol, LDL-C, triglycerides, fasting blood glucose, and HbA1c compared with Group 1 (≤ 2 years) (all adjusted $P < 0.01$).
- b) HDL-C levels were significantly lower in Group 3 compared with Group 1 ($P < 0.001$).
- c) Differences between Group 2 and Group 3 were significant for LDL-C, HDL-C, triglycerides, and HbA1c, whereas differences between Group 1 and Group 2 were generally modest and not consistently significant after adjustment.

The Atherogenic Index of Plasma (AIP) increased progressively with HAART duration, with the highest values observed in Group 3, indicating a more atherogenic lipid profile among individuals with longer treatment exposure.

Discussion

This study examined the association between duration of Highly Active Antiretroviral Therapy (HAART) and cardiometabolic diseases among HIV-positive adults in Nigeria. The findings indicate that longer HAART exposure, particularly beyond five years, was associated with a higher prevalence of cardiometabolic conditions and less favorable lipid and glycaemic profiles. These observations are consistent with growing evidence that long-term antiretroviral therapy is accompanied by metabolic alterations that may contribute to cardiovascular risk among people living with HIV [12-14].

Participants receiving HAART for more than five years exhibited higher levels of total cholesterol, Low-Density Lipoprotein Cholesterol (LDL-C), triglycerides, fasting blood glucose, and glycated haemoglobin (HbA1c), alongside lower High-Density Lipoprotein Cholesterol (HDL-C). Similar lipid and glucose abnormalities have been reported in other African and global cohorts, where prolonged antiretroviral exposure has been linked to dyslipidaemia, insulin resistance, and endothelial dysfunction [15-22]. Although the present cross-sectional design precludes causal inference, the observed patterns suggest cumulative metabolic effects associated with extended treatment duration.

Several biological mechanisms may explain these associations. Antiretroviral drugs, particularly protease inhibitors, have been shown to interfere with lipid metabolism, adipocyte differentiation, and insulin signaling pathways, potentially leading to hyperlipidemia and impaired glucose homeostasis [23-27]. Chronic immune activation and low-grade inflammation associated with HIV infection itself may further exacerbate these metabolic disturbances, even in individuals with sustained virological suppression [28-31]. The progressive increase in the Atherogenic Index of Plasma observed with longer HAART duration in this study supports the possibility of an increasingly atherogenic lipid environment among long-term treatment recipients.

Body mass index (BMI) also emerged as an important correlate of cardiometabolic disease. Participants with longer HAART exposure demonstrated higher BMI values,

and elevated BMI remained independently associated with cardiometabolic disease after adjustment. Weight gain following antiretroviral initiation has been widely documented and may reflect a combination of treatment-related metabolic changes, recovery from HIV-associated wasting, and lifestyle factors [32-37]. Importantly, excess adiposity may amplify the metabolic effects of antiretroviral drugs, thereby increasing cardiometabolic risk.

Protease inhibitor use was independently associated with cardiometabolic disease in the adjusted analysis. This finding aligns with existing evidence linking protease inhibitor-based regimens to dyslipidaemia and insulin resistance [38-45]. Inclusion of protease inhibitor use as a confounder in the multivariate model allowed for a more accurate estimation of the independent association between HAART duration and cardiometabolic disease, underscoring the importance of accounting for regimen-specific effects in metabolic risk assessment.

Age and sex were also associated with cardiometabolic disease, reflecting well-established demographic influences on cardiovascular risk. Older age has consistently been linked to higher cardiometabolic burden among people living with HIV, potentially due to cumulative exposure to both traditional risk factors and long-term antiretroviral therapy [46-50]. The higher odds observed among females in this study may relate to sex-specific differences in fat distribution, hormonal influences, or treatment exposure, although residual confounding cannot be excluded.

From a public health perspective, the findings highlight the growing relevance of non-communicable diseases within HIV treatment programs in resource-limited settings. While HAART has dramatically improved survival, the rising burden of cardiometabolic conditions presents new challenges for long-term HIV care [51-54]. Routine monitoring of lipid and glycaemic parameters, alongside targeted lifestyle interventions, may help mitigate cardiometabolic risk among individuals receiving prolonged HAART.

This study contributes locally relevant evidence from Nigeria, where data on cardiometabolic outcomes among people living with HIV remain limited. The use of routinely available biochemical markers enhances the feasibility of integrating cardiometabolic surveillance into existing HIV care frameworks [55-57]. However, disparities in access to regular metabolic screening across resource-limited settings may partly explain variations in reported cardiometabolic disease prevalence across studies [58-62].

Strengths and Limitations

The strengths of this study include its relatively large sample size, stratification by HAART duration, and comprehensive assessment of lipid and glycaemic parameters. Nevertheless, several limitations should be acknowledged. The cross-sectional design limits temporal interpretation and precludes causal conclusions regarding HAART duration and cardiometabolic disease. Residual confounding may persist, as variables such as dietary intake, physical activity, genetic predisposition, and medication adherence were not assessed. Additionally, the single-center setting may limit generalizability to other populations.

Conclusion

This study demonstrated that longer duration of Highly Active Antiretroviral Therapy (HAART), particularly beyond five years, was independently associated with a higher prevalence of cardiometabolic diseases and less favorable lipid and glycaemic profiles among HIV-positive adults receiving care in Nigeria. Participants with prolonged HAART exposure exhibited higher levels of total cholesterol, Low-Density Lipoprotein Cholesterol (LDL-C), triglycerides, fasting blood glucose, and glycated haemoglobin (HbA1c), alongside lower High-Density Lipoprotein Cholesterol (HDL-C) levels, compared with those on shorter treatment durations.

Although the cross-sectional design precludes causal inference, the observed associations persisted after adjustment for key confounders, including age, sex, body mass index, and protease inhibitor use. These findings underscore the importance of considering treatment duration and regimen-related factors when evaluating cardiometabolic risk in people living with HIV. As survival improves with sustained HAART use, cardiometabolic comorbidities represent an increasingly relevant component of long-term HIV care in resource-limited settings.

Recommendations

Based on the findings of this study, the following recommendations are proposed:

Routine Cardiometabolic Monitoring: Regular assessment of lipid profile (including LDL-C and HDL-C), fasting blood glucose, HbA1c, blood pressure, and body mass index should be incorporated into routine follow-up for individuals receiving long-term HAART, particularly those on therapy for more than five years.

1. Risk Stratification in HIV Care: Duration of HAART exposure and antiretroviral regimen type, especially protease inhibitor use, should be considered in cardiometabolic risk stratification within HIV treatment programs.
2. Integrated Lifestyle Interventions: Nutritional counseling, weight management strategies, and promotion of physical activity should be integrated into HIV care services to help mitigate cardiometabolic risk among long-term HAART recipients.
3. Treatment Optimization: Where clinically appropriate, consideration may be given to antiretroviral regimens with more favorable metabolic profiles, particularly for individuals with elevated cardiometabolic risk.
4. Future Research: Longitudinal cohort studies are recommended to clarify temporal relationships between HAART duration and cardiometabolic outcomes, explore underlying biological mechanisms, and assess the impact of lifestyle and pharmacologic interventions on metabolic health in people living with HIV.

Abbreviations

HAART - Highly Active Antiretroviral Therapy

HIV - Human Immunodeficiency Virus

AIDS - Acquired Immuno-deficiency Syndrome

BMI - Body Mass Index

LDL - Low-Density Lipoprotein

HDL - High-Density Lipoprotein

TC - Total Cholesterol

HbA1c - Glycated Hemoglobin

API - Atherogenic Plasma Index

TG - Triglycerides

CI - Confidence Interval

SLA - Service Level Agreement

Declarations

Ethics approval and consent to participate: The Ministry of Defence Research Ethics Committee approved this study, ensuring compliance with ethical standards for human research. Participants gave informed verbal and written consent before enrolment in the study.

This study was conducted following the ethical principles outlined in the Declaration of Helsinki and adhered to relevant national guidelines for human research.

Clinical Trial: N/A

Consent for publication: All Authors consent to have the paper published.

Availability of data and material: The data supporting this study's findings are not openly available due to sensitivity reasons, but are available from the corresponding author upon reasonable request.

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Authors' contributions: OBO participated in the research design, data collection, collation and analysis, and initial manuscript drafting. MFO conceived the study, participated in research design, manuscript review, and provided overall supervision of the research. GII contributed to data interpretation, literature review, and critical revision of the manuscript. AMA was involved in data validation, statistical analysis, and formatting of the manuscript. MMA assisted in coordinating fieldwork and contributed to the review of related literature. AA contributed to data quality assurance, referencing, and proofreading of the final manuscript.

All authors read and approved the final version of the manuscript.

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Impact of HAART Duration on Cardiometabolic Diseases and Biochemical Parameters in HIV-Positive Individuals in Nigeria

Odekunle Bola Odegbemi (Ph.D.)^{1,2*}, Mathew Folaranmi Olaniyan (Ph.D.)^{1,3}, Godfrey Innocent Iyare (Ph.D.)⁴, Akinwale Majeed Akinlabi (Ph.D.)⁴, Mufutau Mosunmade Azeez (Ph.D.)⁵, Adeyinka Adedire (Ph.D.)¹

1- Department of Medical Laboratory Sciences, Edo State University, Uzairue, Edo State, Nigeria.

2- Department of Medical Laboratory Sciences, Nigerian Navy Hospital, Warri, Delta State, Nigeria.

3- Department of Medical Laboratory Sciences, Kwara State University, Malete, Kwara State, Nigeria.

4- Department of Medical Laboratory Sciences, Joseph Ayo Babalola University, Ikeji-Arakeji, Osun State, Nigeria.

5- Department of Medical Laboratory Sciences, Ajayi Crowther University, Oyo, Oyo State, Nigeria.

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Abstract:

Introduction: This study aimed to evaluate the association between the duration of HAART and cardiometabolic diseases and selected biochemical parameters among HIV-positive adults in Nigeria.

Methods: This cross-sectional study included 400 HIV-positive adults receiving HAART at the Nigerian Navy Hospital, Warri. Participants were stratified according to HAART duration into three groups: ≤ 2 years, $>2-5$ years, and >5 years. Sociodemographic data, body mass index (BMI), lipid profile including total cholesterol, Low-Density Lipoprotein Cholesterol (LDL-C), High-Density Lipoprotein Cholesterol (HDL-C), triglycerides, fasting blood glucose, and glycated haemoglobin (HbA1c) were assessed. Multivariate logistic regression assessed the association between HAART duration and cardiometabolic disease, adjusting for key covariates.

Results: The prevalence of cardiometabolic disease increased progressively with longer HAART duration, being highest among participants on therapy for >5 years (52.1%) compared with those on ≤ 2 years (21.4%) and $>2-5$ years (34.8%) ($p < 0.001$). Participants in the >5 -year group exhibited significantly higher mean levels of total cholesterol, LDL-C, triglycerides, fasting blood glucose, and HbA1c, alongside lower HDL-C levels (all $p < 0.01$). After adjustment for potential confounders, HAART duration >5 years remained independently associated with cardiometabolic disease (aOR = 2.8; 95% CI: 1.9–4.3). Older age, elevated BMI, female sex, and protease inhibitor use were also significantly associated with cardiometabolic disease.

Conclusion: Longer HAART duration was independently associated with increased cardiometabolic disease and adverse metabolic profiles among HIV-positive adults, highlighting the need for routine cardiometabolic monitoring, especially in resource-limited settings.

Keywords: HAART, Cardiometabolic diseases, HIV, Dyslipidemia, Hypertension, Biochemical parameters.

Conflict of Interest: No

*Corresponding author: Odekunle Bola Odegbemi, Email: odegbemi21.odekunle@edouniversity.edu.ng

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