

Original Research

Prevalence and Determinants of Subclinical Atherosclerosis in People Living with HIV on Antiretroviral Treatment in Hospitals in Kinshasa

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ABSTRACT

Introduction: The objective of this work was to identify the traditional, emerging, and therapeutic cardiometabolic risk factors for subclinical atherosclerosis in human immunodeficiency virus (HIV)-infected patients under antiretroviral treatment in the era of dolutegravir (DTG) in hospitals in the Kinshasa, Democratic Republic of the Congo (DRC).

Methods: This was a descriptive and analytical cross-sectional study held between January 2017 and December 2021 among people living with HIV (PLWHIV) on antiretroviral treatment (ART) for at least 6-months, supported in the structures of the Network Catholic of the Diocesan Office of Medical Works (BDOM) and at the University Clinics of Kinshasa (UCK). Sub-clinical atherosclerosis was defined by: pulse pressure (PP) \geq 60 mm Hg; a carotid intima-media thickness (CIMT) $>$ 0.8 mm and a systolic pressure index (SPI) $<$ 0.9. Logistic regression was used in the statistical study of associations.

Results: A total of 321 PLWHIV on ART were recruited. The average age of PLWHIV was 51 ± 11 -years with a female predominance of 72% ($n=231$); the independent determinants of subclinical atherosclerosis were married (aOR: 4, 95% CI 1.5-10.5; $p<0.006$), low socio-economic status (aOR: 10.7, 95% CI 2.3-48, $p<0.002$), duration of HIV infection (ORa: 6.6, 95% CI 2.8-16; $p<0.0001$), duration of antiretroviral treatment \geq 9-years (ORa: 0, 3, 95% CI 0.2-0.7; $p<0.005$) and the total cholesterol/high-density lipoprotein-cholesterol ratio (CT/HDL-C) (ORa: 2, 95% CI 1.1-3.6; $p=0.034$). Dyslipidaemia (hyper low-density lipoprotein-cholesterol (LDL-C), hyper HDL-c and hypertriglyceridemia) has been identified in PLWHIV on DTG. The prevalence of subclinical atherosclerosis in PLWHIV on ART was 31.1% ($n=116/321$).

Conclusion: Married people, low socioeconomic level, duration of HIV infection, duration of antiretroviral treatment beyond 9-years, and the CT/HDL-C ratio are identified as independent determinants of subclinical atherosclerosis in PLWHIV on ART in Kinshasa hospitals. Dyslipidemia is found in PLWHIV on DTG and the prevalence of subclinical atherosclerosis among PLWHIV on ART is low compared to that of Côte d'Ivoire.

Keywords

Subclinical atherosclerosis; HIV/AIDS; Antiretroviral therapy; Kinshasa/DRC.

INTRODUCTION

The introduction of highly active antiretroviral treatments (HA-ART) in April 1996 enabled, on the one hand, a substantial reduction in HIV-related morbidity and mortality and, on the other hand, increased the life expectancy of patients infected with HIV (people living with HIV (PLWHIV)).¹⁻⁵

As a result, opportunistic infections have given way to chronic complications such as cancers, and metabolic (lipid carbohydrate) abnormalities known as major risk factors for cardiovascular disease (CVD), and chronic kidney disease (CKD).¹⁻⁵ After 2016, the World Health Organization (WHO) proposed dolutegravir (DTG) as a therapeutic alternative for first-line treatment in adults. The National Program for the Fight against human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) (PNLS) in the Democratic Republic of the Congo (DRC) has adopted DTG-based antiretroviral treatment (ART) as first-line treatment. The combination Tenofovir (TDF), Lamivudine (3TC), DTG (TLD) or fixed-dose TLD should be introduced gradually with newly eligible patients.⁶

Thus, the objective of the present study was to identify the traditional, emerging, and therapeutic risk factors for subclinical atherosclerosis in patients living with HIV infection on antiretroviral therapy in the era of DGT in hospital settings, Kinshasa, DRC.

METHODS

Design and Framework of the Study

This is a descriptive and analytical cross-sectional study carried out in the structures of the Catholic network of the Diocesan Office of Medical Works (BDOM) and at the University Clinics of Kinshasa (UCK) between January 2017 and December 2021. The BDOM is a network that contains a larger sample of PLWHIV in the city of Kinshasa. On the other hand, the University Clinics of Kinshasa which constitute a tertiary level of care, a level of high technicality was retained as a frame of reference.

Study Population

It concerned PLWHIV aged at least 18-years on ART for at least 6-months and have freely given their consent; were excluded PLWHIV with pregnancy, nephrotic syndrome, hepatic cirrhosis, those using lipid-lowering drugs or insulin, and those who refused to sign informed consent. The sample size was calculated from the Schwartz formula: $n = z^2 p (1-p) / e^2$. The true prevalence of subclinical atherosclerosis among PLWHIV in the DRC is unknown, the prevalence of atherosclerosis of 64.7% in PLWHIV, reported by Djallo et al⁷ at the Center Hospitalier Universitaire de Treichville in Côte d'Ivoire served as a baseline. Hence the present study has retained a frequency of 65% for the calculation of the minimum sample size $n = (1.96)^2 \times 0.65(1-0.65) / (0.05)^2 = 349.58$. The calculated sample size was 350 HIV+ subjects.

Collection of Data

It was based on an ad hoc data collection sheet containing socio-

demographic characteristics (age, sex, marital status, and socio-economic level), clinical data (clinical stages of infection by HIV, duration of infection, duration of HIV treatment and treatment regimen), anthropometry recorded weight, height, waist circumference (WC), hip circumference (HC), body mass index (BMI=weight, kg/height in m²) using standard methods in participants with light clothing and without shoes, using an OMRON BF214 type BODY Composition Monitor impedance scale and tape measure and a measuring board. Blood pressure (BP), including systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse pressure (PP) (SBP-DBP) after the participant rested for 10-minutes seated in a quiet room, was measured in the left arm with the elbow flexed at the level of the heart at the using an Omron HEM 705 electronic manometer (Omron Life Science Co. Ltd, Tokyo, Japan).

Laboratory tests included: C-reactive protein (CRP), glucose, total cholesterol (TC), triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), serological tests for HIV, uric acid, and serum creatinine. Viral load values dating back no more than 3-months were collected from participants' medical records. All the analyzes (hematology and biochemistry) were carried out in the Laboratory of Biochemistry and Hematology of the University Clinics of Kinshasa. The HIV serological test was carried out on each blood sample (according to the algorithm of the National Program for the Fight against HIV/AIDS (PNLS)/DRC in force to confirm the seropositivity of the HIV cases included. The medical imaging data were including the systolic pressure index (SPI) or ankle brachial index (ABI) determined using an 8 MHz continuous wave Doppler device probe, brand HUNTLEIGH, held in the hand as described by Kwiatkowska et al⁶ and Olalla et al⁷ and measurement of the carotid intima-media thickness (CIMT) performed using a Doppler ultrasound device equipped with a 7.5 MHZ linear probe from PHILIPS brand. Scanning was done first at the level of the right common carotid then the left. The areas of interest were defined as a distance of 0.5 cm, 1 cm and 2 cm from the bifurcation.

On each area of interest, the near and far wall thicknesses were measured; the maximum values of the intima-media thickness (IMT) measurements were used if there was an atherosclerotic plaque. The ABI (IPS) value was determined by dividing the higher pressure of the two arteries at the ankles by the higher brachial systolic blood pressure. Using the formula below, SPI was calculated as follows: SPI = Ankle peripheral arterial stiffness (PAS) / Arm PAS. With PAS ankle (the systolic pressure of the posterior tibial artery or the dorsum of the foot artery).

Working Definitions

Arterial hypertension was defined by SBP ≥ 140 mmHg and DBP ≥ 90 mm Hg or current intake of antihypertensives.^{8,9} Body mass index (BMI) was defined by the ratio of weight expressed in kg to height in m², with total obesity being defined by a value > 30 kg/m².¹⁰ Diabetes mellitus was defined by fasting blood glucose ≥ 126 mg/dL or taking antidiabetics.¹⁰ An increase in HDL-C ≥ 75 mg/dL was considered a cardiovascular risk factor.^{10,11} Subclinical (preclinical) atherosclerosis was defined by: PP ≥ 60 mmHg; an

carotid IMT (cIMT)>0.8 mm and an ABI<0.9.¹²⁻¹⁴ A suppressed viral load was defined by a plasma HIV-ribonucleic acid (RNA) level≤1000 copies/mL and an undetectable viral load was <50 copies/mL.¹⁵ CRP>3 mg/L was considered a cardiovascular risk factor.¹⁶ Chronic kidney disease was defined by a ClCr<60 ml/min with reference to the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (K/DOQI) classification.^{17,18} Hyperuricemia was defined as uricemia≥7 mg/dL.¹⁹ The TG/Glucose (TyG) ratio was calculated by $\ln(\text{TG} \text{ (mg/dL)} \times \text{FG} \text{ (mg/dL)})/2$, which allows to determine insulin resistance, it is a more effective biomarker than its separate components to identify abnormalities glucose metabolism.²⁰ Its normal value is set at 4.49. Non-HDL-C was calculated by the differential between TC and HDL-C.²¹ In patients considered at high cardiovascular risk, the non-HDL cholesterol level is <130 mg/dL. In patients considered to be at very high cardiovascular risk, this rate is <100 mg/dL. The CT/HDL-C ratio is used to measure cardiovascular risk.^{21,22} Its normal value must be <5. Low-density lipoprotein (LDL)/HDL atherogenic coefficient was considered to predict cardiovascular risk if the ratio was >3.3²³. The TG/HDL-C ratio ≥3 was considered to be a marker of insulin resistance.²⁴ Uric acid/HDL-C ratio ≥10.9% was considered a predictor of metabolic syndrome.²⁵

Statistical Analysis

Data were entered using Excel 2013 software, exported, and analyzed using IBM® statistical package for the social sciences (SPSS®) 26 software. Statistical analyses considered a descriptive (mean±standard deviation, frequency, proportion), univariate comparative approach for associated factors and multivariate analysis of the binary logistic regression type to identify the independent determinants predisposing to subclinical atherosclerosis (dependent variable) after adjustment for confounding variables (Adjusted odds ratio (ORa); 95% confidence interval (95% CI)). A value of $p<0.05$ was considered statistically significant.

Ethical Considerations

All participants provided written informed consent before participating in the study. However, patient records/information were anonymized and anonymized before analysis. The protocol for this study was submitted and approved by the ethics committee of the School of Public Health of the University of Kinshasa under the Helsinki recommendations (App No: ESP/CE/101/2020).

RESULTS

Sociodemographic, Clinical and Therapeutic Characteristics of the Study Population

A total of 321 HIV-infected patients on ART were enrolled in this study.

Women were in the majority at 72% (n=231); the mean age of the patients was 51±11-years; the age group of 43-59-years was the most encountered in 49.2% (158); 243 (75.7%) were married; 269 (83.8%) had a low socio-economic level; 101 (31.5%) patients were at WHO stage 3; 224 (69.8%) of the patients were on the TDF+3TC+Efavirenz (EFV) combination; 110 (34.3%) had a

duration of HIV infection of fewer than 8-years; 137 (42.7%) of the patients had a duration of antiretroviral treatment of fewer than 5-years (Table 1).

Table 1. Sociodemographic, Clinical and Therapeutic Characteristics of the Study Population

| Variables | N=321(100%) |
|---|-------------|
| Sociodemographic Data | |
| Sex | 90(28%) |
| • Male | 231(72%) |
| • Feminine | 51±11 |
| Average Age (years) | |
| Age range (years) | |
| ≥60 | 92(28.7) |
| 43-59 | 158(49.2) |
| <43 | 71(22.1) |
| Marital Status | |
| • Married | 243(75.7%) |
| • Single | 78(24.3) |
| Socio-Economic Level | |
| • Down | 269(83.8%) |
| • Pupil | 52(16.2) |
| Clinical and Therapeutic Data | |
| WHO clinical stages | |
| • 1 | 90(28) |
| • 2 | 77(24) |
| • 3 | 101(31.5) |
| • 4 | 53(16.5) |
| Therapeutic Diet | |
| • TDF+3TC+EFV | 224(69.8) |
| • TDF+3TC+DTG | 76(23.6) |
| • TDF+3TC+LPV/r | 14(4.4) |
| • AZT+3TC+NVP | 7(2.2) |
| Duration of Infection (years) | |
| • ≥14 | 103(32.1) |
| • 8-13 | 108(33.6) |
| • <8 | 110(34.3) |
| Duration of Antiretroviral Treatment (years) | |
| • ≥9 | 107(33.3) |
| • 5-8 | 77(24) |
| • <5 | 137(42.7%) |
| TDF(Tenofovir); 3TC (lamivudine); EFV(Efavirenz); DTG(Dolutegravir); LPV/r(lopinavir/ritonavir); AZT(Zidovudine); NVP(Nevirapine) | |

Comparisons across Antiretroviral Therapy Regimens

According to traditional variables: Except for diastolic BP ($p>0.05$), there was an unequal and highly significant variation ($p=0.000$) in mean values for age, SBP, PP, WC, HC, WC/HC, BMI, blood sugar, LDL-cholesterol (LDL-C), HDL-C, TG and TC from DTG to LPV/r (Table 2).

According to emerging variables: Except for LDL-C/HDL-C ($p>0.05$), there was an unequal and very significant variation ($p=0.000$) in the mean values of creatinine, uric acid, CRP, SPI, cIMT, TyG ratio, non-HDL-C, TG/HDL-C ratio and TC/HDL-C ratio from DTG to LPV/r (Tables 3 and 4).

Extent of Subclinical Atherosclerosis

The overall extent of subclinical atherosclerosis was estimated at

Table 2. Comparisons of Mean Values of Traditional Subclinical Atherosclerosis Variables across ART Groups

| Statistical Characteristics/ Independent Variables | DTG+other ARTs | EFV+other ART | NVP+other ARTs | LPV/r+other ART | p-value |
|---|----------------|---------------|----------------|-----------------|---------|
| Age (years) | 46±10.3 | 52.9±10.6 | 68±9.4 | 75.3±0.8 | <0.0001 |
| SBP (mm Hg) | 124.3±19.3 | 131±19.9 | 131.3±14.1 | 177.9±13.1 | <0.0001 |
| DBP (mm Hg) | 78.5±12.2 | 79.6±12.1 | 73.7±6.5 | 78.2±17.5 | 0.565 |
| PP (mm Hg) | 45.4±13.6 | 51±16.2 | 57.5±15.8 | 99.7±15.8 | <0.0001 |
| Waist circumference (cm) | 86.2±13.6 | 89.2±12.2 | 115.7±10.7 | 130.2±4.9 | <0.0001 |
| Hip circumference (cm) | 97.5±14.1 | 101.5±11 | 114.8±11.5 | 128.3±10.2 | <0.0001 |
| Waist/Hip Circumference | 0.9±0.7 | 0.9±0.7 | 1.01±0.12 | 1.02±0.11 | <0.0001 |
| BMI (Kg/m^2) | 24.3±4.9 | 25.5±5.1 | 34.4±2.6 | 34.4±2.8 | <0.0001 |
| Blood glucose (m/dL) | 94.3±26.3 | 91.6±20.6 | 115.6±7.7 | 177.7±78.6 | <0.0001 |
| LDL-C (mg/dL) | 107.2±37 | 92.7±33.5 | 58.4±13.5 | 36±14.4(SE) | <0.0001 |
| HDL-C (mg/dL) | 47.3±6.3 | 34.5±16.2 | 15.5±6 | 8.1±1.7 | <0.0001 |
| TG (mg/dL) | 92.8±34.5 | 84±33.8 | 69.7±25.4 | 19.4±4.8 | <0.0001 |
| Total cholesterol (mg/dL) | 155.6±15.6 | 200.3±58.4 | 243.4±67 | 279.5±70.2 | <0.0001 |

DTG: Dolutegravir, Efv: Efavirenz, Nvp: Nevirapine, Lpv/r: Lopinavir/ritonavir, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PP: Pulse pressure, BMI: Body mass index, LDL-C: Low-density lipoprotein-cholesterol, HDL-C: High-density lipoprotein-cholesterol, TG: Triglycerides, Analysis of variance (ANOVA).

Table 3. Comparisons of Mean Values of Subclinical Atherosclerosis Emergent Variables across ART Groups

| Statistical Characteristics/ Independent Variables | DTG+other ARTs | EFV+other ART | NVP+other ARTs | LPV/r+other ART | p-value |
|---|----------------|---------------|----------------|-----------------|---------|
| Creatinine (md/dL) | 0.94±0.21 | 1.02±0.26 | 1.37±0.77 | 3.12±1.44 | <0.0001 |
| Uric acid (mg/dL) | 5.6±1.7 | 6.4±2.2 | 5.9±2.2 | 9±3.5 | <0.0001 |
| CRP (mg/L) | 2.2±0.4 | 8.3±7.6 | 65.8±12.2 | 72.1±1.5 | 0.565 |
| SPI | 0.99±0.1 | 1.01±0.2 | 1.23±0.3 | 1.49±0.1 | <0.0001 |
| Mean cIMT (mm) | 1.14±0.24 | 2.2±1.2 | 3.07±1.2 | 3.91±0.72 | <0.0001 |
| TyG after | 4.5±0.27 | 4.5±0.26 | 4.54±0.20 | 4.9±0.45 | <0.0001 |
| Front TyG | 9.29±0.27 | 9.9±0.26 | 10.24±0.20 | 10.8±0.45 | <0.0001 |
| No HDL-C (mg/dL) | 110.6±17.7 | 143±51.7 | 145.6±38 | 284.9±79.7 | <0.0001 |
| TG/HDL-C | 1.95±0.79 | 2.30±1.06 | 3.11±1.20 | 2.31±0.31 | 0.007 |
| LDL-c/HDL-C | 2.25±0.79 | 2.43±0.81 | 2.58±0.58 | 2.65±12.7 | 0.179 |
| CT/HDL-C | 3.32±0.56 | 5.24±2.75 | 7.47±1.79 | 36.58±12.7 | <0.0001 |
| Uric acid/HDL-C (%) | 11.6±0.04 | 36.4±32.1 | 76.7±24.9 | 154.2±53.8 | <0.0001 |

DTG: Dolutegravir, Efv: Efavirenz, Nvp: Nevirapine, Lpv/r: Lopinavir/ritonavir, CRP: C-reactive protein, SPI: Systolic Pressure Index, cIMT: Carotid Intima-media Thickness, TyG: Triglyceride/glucose, No HDL-C: No High-density lipoprotein-cholesterol, LDL-C/HDL-C: low-density lipoprotein cholesterol/High-density lipoprotein-cholesterol, CT/HDL-C: Total cholesterol/High density lipoprotein-cholesterol

Table 4. Comparison of Mean Values of Traditional and Emerging Cardiometabolic Risk Markers in Women

| Variables | HIV+ | Naive HIV+ | HIV+/DTG | HIV+EFV | HIV+/NVP | VIH+/LPV/r |
|----------------------|------------|------------|-----------|------------|------------|------------|
| Creatinine (md/dL) | 1.2±0.8 | 2.2±1.1 | 1±0.7 | 1.1±0.7 | 1.6±1.9 | 3.8±1 |
| Glycemia (mg/dL) | 80.3±4.4 | 104.3±47.6 | 95.8±26 | 90.2±21 | 82.3±23 | 157.2±72 |
| LDL-c (mg/dL) | 115.8±28 | 149±10.5 | 112±41.3 | 112.2±38 | 106.3±36 | 172±20 |
| HDL-c (mg/dL) | 49±15 | 59.6±34.7 | 44.9±14.4 | 45±13 | 58.5±19 | 9±2 |
| Triglyceride (mg/dL) | 114±43 | 276.2±66 | 96±34 | 90.6±34 | 87.5±35 | 139.4±65.3 |
| TC (mg/dL) | 161.9±21.8 | 68.2±9.2 | 159±19.3 | 196.5±77.4 | 176.7±32.2 | 291±89 |
| Non HDL (mg/dL) | 112.9±21.7 | 8.6±38.6 | 115.2±22 | 146.3±73.5 | 118.2±43.1 | 282±89 |
| TG/HDL | 2.7±1.5 | 8±5.9 | 2.5±1.4 | 2.5±2.1 | 1.8±1.2 | 16.6±9.9 |
| LDL/HDL | 2.6±1 | 3.8±2.9 | 2.8±1.4 | 2.8±1.4 | 2.1±1.3 | 20±5.2 |
| CT/HDL | 3.6±1.3 | 1.9±1.6 | 4±1.4 | 4.9±3.8 | 3.4±1.5 | 33.8±14.5 |
| ABI | 1.2±0.1 | 2.1±0.2 | 1.3±0.2 | 2.4±0.2 | 2.4±0.1 | 2.6±0.2 |
| cIMT (mm) | 0.7±0.4 | 0.5±0.1 | 1.2±0.1 | 2.3±1.1 | 3±1.3 | 4±0.9 |

LDL: Low-density lipoprotein; HDL: High-density lipoprotein; TC: Total cholesterol; CIIMT: Carotid intima-media thickness test; ABI: ankle-brachial index; Non-HDL: CT-HDL

over 1/3 (36.14%) of patients (n=116/321).

Independent Determinants of Traditional, Emerging and Therapeutic Cardiometabolic Risk of Subclinical Atherosclerosis in PLWHIV on ART

Considering all the traditional and emerging biomarkers of significant cardiovascular risk in univariate analysis, only married people (ORa: 4, 95% CI 1.5-10.5; $p<0.006$), the low socioeconomic level (ORa: 10.7, 95% CI 2.3-48.7 $p<0.002$), duration of HIV infection (ORa: 6.6, 95% CI 2.8-16; $p<0.0001$), duration of antiretroviral treatment ≥ 9 -years (ORa: 0.3, 95% CI: 0.2-0.7; $p<0.005$) and CT/HDL-C ratio (ORa: 2, IC 95% 1.1-3.6; $p=0.034$) were retained as independent determining biomarkers in the multivariate analysis of the binary logistic regression type (Table 5).

DISCUSSION AND CONCLUSION

The present study identified the traditional, emerging, and therapeutic risk factors for subclinical atherosclerosis in PLWHIV infection on antiretroviral treatment in the era of DGT in a hospital setting in Kinshasa.

The population of this study was characterized by an advanced age. The mean age was 51 ± 11 -years. We observe senility in PLWHIV (oxidative stress) linked to contamination beyond the age of 50, but also to antiretroviral treatment, which keeps patients alive and healthy for a long time.^{26,27} The female gender was twice as common in the study population. That is 28% (n=90) men against 72% (n=231) women. This feminization of HIV infection is observed in all countries and more markedly in those where heterosexual transmission is very predominant, particularly in Sub-Saharan Africa.²⁸ Sixty-nine point eight percent (69.8%) (n=224) of PLWHIV were on EFV. The initial therapeutic choice is an essential decision for the therapeutic future of the patient.

Except for peripheral artery disease (PAD) and LDL-C/HDL-C, all traditional and emerging markers in this study were elevated in the LPV/r group, except LDL-C, HDL-C, and TG which were higher in the DTG group, TG/HDL-C in the EFV group.

Protease inhibitors are mainly implicated in cardiovascular risk, through their ability to induce dyslipidemia and insulin resistance.²⁹ In contrast, integrase inhibitors have so far not shown consistent lipid abnormalities when used in antiretroviral-naïve patients.³⁰

It has also been noted in the literature that non-nucleoside reverse transcriptase inhibitors (NNRTIs) cause dyslipidemia, including total hypercholesterolemia and hypertriglyceridemia.³¹⁻³³

Except for DBP and blood glucose ($p>0.05$), all mean values of traditional and emerging risk factors as well as viral load and duration of treatment were significantly higher in the old regimen than in the new one diet.

Indeed, there is a relationship between antiretrovirals and the presence of a major level of cardiovascular risk. Exposure to

the lopinavir/ritonavir combination (protease inhibitors) is a factor increasing this risk. Marrakchi et al³⁴ made the same observation. Blumer et al³⁵ have shown that protease inhibitors only increase the risk of the onset of insulin resistance and possibly the risk of a cardiovascular event if they are combined with zidovudine and lamivudine. Several studies have found links between exposure to different classes of antiretrovirals and cardiovascular risk.^{14,35-37}

On the other hand, dyslipidemia in this study was frequent in patients on DTG. Several studies have shown the opposite Kamdem et al.¹³ Two randomized studies carried out in Africa, the New Antiretroviral and Monitoring Strategies in HIV-infected Adults in Low-income countries (NAMSAL) trial Blümer et al³⁸ and the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) trial Mingou et al³⁹ reported that people taking DGT-based treatment, mainly women, experienced significant weight gain. A new study, based on a cohort from 12 sites, African Cohort Study (AFRICOS), supported by the President's Emergency Plan for AIDS Relief (PEPFAR) (the United States Presidential Program for the Fight against HIV/AIDS) in Kenya, Nigeria, Tanzania, and Uganda confirms that a treatment based on DGT poses a significant risk of overweight to patients.⁴⁰ Viral load suppression was significant in the DTG arm. Several studies have also confirmed this.^{30,38-40}

The duration of exposure to ART greater than or equal to 9-years ($p=0.013$) was significantly associated with the presence of atherosclerosis as in the AM study Djalloh et al⁷ in Ivory Coast.¹²

Some recent studies report that newer ART decrease the prevalence of insulin resistance in HIV-infected patients compared to older ARVs.⁴¹⁻⁴³ The duration of exposure to ART is a determining factor in atherosclerosis.¹² On the other hand, the duration of DTG is short compared to other ART (deterministic and cumulative effect). Only married people, low socioeconomic level, duration of infection, duration of antiretroviral treatment beyond 9-years, and CT/HDL-C ratio were retained as independent determinants of atherosclerosis in multivariate analysis of the logistic regression type. On the other hand, Djalloh et al⁷ in Côte d'Ivoire¹² found the duration of exposure to ART, age, and hypertension as determinants of atherosclerosis in PLWHIV on ART.¹³

Despite the existence of a very effective treatment allowing PLWHIV to lead a relatively normal life, the chronic inflammation persists and is at the origin of the premature development of comorbidities related to age, such as CVD such as atherosclerosis. The low socio-economic level not only limits access to education, care, and training on the means of prevention against transmissible diseases⁴⁴ but also increases the risk of adopting risky sexual behavior.⁴⁴⁻⁴⁸ The CT/HDL-C ratio has been suggested as a statistically significant atherogenic risk.^{23,24} The present study reported an overall hospital prevalence (frequency) of subclinical atherosclerosis in PLWHIV on ART of 36.1%. This frequency seems lower than the study conducted by Djalloh et al⁷ in Côte d'Ivoire¹² which found a prevalence of 64.7% according to SPI and cIMT.

The results obtained cannot be generalized to all hospitals in the DRC and the hospital nature of the study does not

Table 5. Independent Determinants of Cardiometabolic Risk of Overall Subclinical Atherosclerosis in the Population of People Living with HIV on Antiretroviral Therapy

| Variables | OR 95% CI | p-value | ORaj 95% CI | p-value |
|--------------------------------------|----------------|---------|----------------|---------|
| Sex | | | | |
| Male | 1.2(0.7-2) | | | |
| Female | 1 | 0.303 | | |
| Age (years) | | | | |
| ≥60 | | | | |
| 43-59 | | 0.001 | | |
| <43 | | | | |
| Marital Status | | | | |
| Married | 10(4.2-23.7) | <0.0001 | 4(1.5-10.5) | 0.006 |
| Bachelor | 1 | | 1 | |
| Socio-Economic Level | | | | |
| Down | 18.4(4.4-77.1) | <0.0001 | 10.7(2.3-48.7) | 0.002 |
| Pupil | 1 | | 1 | |
| Duration of Infection (years) | | | | |
| ≥14 | 7.6(3.8-15) | | 6.6(2.8-16) | <0.0001 |
| 8-13 | 5.5(2.8-10) | <0.0001 | 4.1(1.9-9.2) | |
| <8 | 1 | | 1 | <0.0001 |
| Duration of Treatment (years) | | | | |
| ≥9 | | | 0.3(0.2-0.7) | 0.005 |
| 5-8 | | 0.013 | 0.7(0.3-1.5) | |
| <5 | | | 1 | 0.248 |
| Waist Circumference (cm) | | | | |
| ≥85 | 1.8(1.1-2.9) | | 0.012 | |
| <85 | 1 | | | |
| Hip Circumference (cm) | | | | |
| ≥100 | 1.7(1-3) | | 0.017 | |
| <100 | 1 | | | |
| BMI (Kg/m²) | | | | |
| ≥25 | 1.6(1-2.6) | | 0.024 | |
| <25 | 1 | | | |
| CRP (mg/L) | | | | |
| High ≥3 | 3(1.9-4.9) | <0.0001 | | |
| Down <3 | 1 | | | |
| Creatinine (mg/dL) | | | | |
| ≥1.5 | 3(1.8-5) | <0.0001 | | |
| <1.5 | 1 | | | |
| TG/HDL-C | | | | |
| ≥2.2 | 2(1.3-3) | | 0.002 | |
| <2.2 | 1 | | | |
| LDL-c/HDL-C | | | | |
| ≥2.52 | 1.5(0.9-2.3) | | 0.07 | |
| <2.52 | 1 | | | |
| CT/HDL-C | | | | |
| ≥4 | 4(2.3-7) | <0.0001 | 2(1.1-3.6) | 0.034 |
| <4 | 1 | 0.002 | | |

allow the conclusions to be generalized to the entire Congolese population in general. This constitutes the limits of our study. On the other hand, the present study has the merit of having identified the determinants of subclinical atherosclerosis in PLWHIV on ART without DTG, dyslipidemia under the diet with dolutegravir and having used the measurement of pulse pressure, SPI, and cIMT among PLWHIV in Kinshasa. Early screening for subclinical atherosclerosis in naïve PLWHIV and those on ART would be necessary; to conduct studies to determine the role of DTG in dyslipidemia in adults.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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