R E V I E W

Diabetes, metabolic syndrome and dyslipidemia in people living with HIV in Africa: re-emerging challenges not to be forgotten

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Background: The current challenge in managing people living with human immunodeficiency virus (PLWHIV) includes the identification and monitoring for comorbid health risks associated with HIV and its treatment and longer survival. Dyslipidemia, diabetes mellitus and metabolic syndrome are increasingly seen in PLWHIV.

Objective: In this narrative review, we aimed to summarize the current knowledge about diabetes, dyslipidemia and metabolic syndrome in PLWHIV in Africa and also to discuss the challenges that patients as well as health authorities in Africa may face.

Methods: PubMed and Google scholar published-English literatures concerning earlier mentioned entities regardless of time limit were critically reviewed.

Results: The prevalence of metabolic disorders in HIV population in Africa was estimated to range from 2.1% to 26.5% for diabetes and 20.2% to 43.5% for pre-diabetes, 13% to 58% for metabolic syndrome and 13% to 70% for dyslipidemia.

Conclusion: The management of metabolic disorders and cardiovascular disease risks related to HIV is complex especially in Africa due to healthcare resources, but our experience suggests that metabolic clinic is beneficial to patients and staff and should be an important part of HIV services especially as the older HIV population is increasing. In this context, cardiovascular risk assessment of HIV-infected patients will become an important component of care in developing countries in Africa and strategies are needed to deal with progressive increase in the epidemic of type 2 diabetes, dyslipidemia and metabolic syndrome.

Keywords: dyslipidemia, diabetes mellitus, metabolic syndrome, cardiovascular, NAFLD, HIV services, Africa, metabolic clinic

Introduction

Despite the fact that combined antiretroviral therapy (cART) for human immunodeficiency virus (HIV) has significantly prolonged the life span of people living with HIV (PLWHIV) and decreased morbidity and mortality, it is associated with an increase in diabetes, dyslipidemia and changes in fat distribution.[1] The prevalence of diabetes among HIV patients was estimated to be 14% in 60 adult HIV-infected Black South African individuals who were randomized to either standard-dose (30–40 mg) or low-dose (20–30 mg) stavudine (Bristol-Myers Squibb, New York, NY, USA) or tenofovir disoproxil fumarate (300 mg; Gilead Sciences, Foster City, CA, USA), each combined with lamivudine and efavirenz (Gilead Sciences), for 48 weeks.[2] HIV is a condition associated with insulin resistance and lipoatrophy. The risk of insulin resistance can be increased by cART, protease inhibitors (PIs) and some antiretroviral therapy (ART; stavudine and indinavir [Merck Sharp-Dohme, Kenilworth, NJ, USA]). HIV per se is

thought to lead to a chronic inflammatory state and this in part may lead to glucose intolerance, which adds to the risk of developing insulin resistance. Importantly, the combination of PIs and nucleoside analogs (NRTIs) was shown to increase the risk of type 2 diabetes.[3]

The issue of whether HIV infection is an independent risk factor for diabetes is a subject that requires further research.[4–6]

The Data Collection on Adverse Events of Anti-HIV Drugs (D.A.D.) multicenter study showed that 289 of the 2482 deaths were accounted for by cardiovascular disease (CVD) out of 33,308 patients with HIV.[7] In this study, they found that in patients with HIV, at baseline, 22% had total cholesterol ≥6.2 mmol/L, 34% had triglycerides ≥2.3 mmol/L and 26% had high-density lipoprotein cholesterol (HDL-c) ≤0.9 mmol/L. Furthermore, at baseline, only a few had hypertension (8.5%) and diabetes mellitus (DM; 2.5%). Dyslipidemia was recorded in 19.3% in patients with HIV worldwide. Several studies including meta-analysis concluded that HIV is associated with similar ranges of metabolic syndrome of 17%–47% as in general population.[8–10] This is important as metabolic syndrome is a strong predictor of CVD and type 2 diabetes.[11] The D.A.D. study showed a higher prevalence of CVD among HIV patients.

A gamut of variable literature has been published about metabolic syndrome in HIV patients in African nations that need to be grouped to clear the picture. Additionally, the services provided to HIV patients in some low-income African countries are suboptimal.

In this narrative review, we aimed to provide a comprehensive summary of the current knowledge about metabolic syndrome in HIV patients in Africa and discuss the challenges that African patients and authorities may face in providing good services for the aging HIV patients.

Methods
We reviewed the literature published in PubMed and Google Scholar using the following terms: dyslipidemia, diabetes mellitus, metabolic syndrome, cardiovascular risk and HIV, NAFLD, HIV services, Africa, metabolic clinic and HIV medications.

Diabetes in HIV/AIDS patients in Africa
Epidemiology and risk factors
The number of African people affected by and living with HIV/acquired immunodeficiency syndrome (AIDS) has increased due to the utilization of cART.[12,13] Though opportunistic infections in HIV patients may lead to serious illness and is one of the causes of mortality, the morbidity

and mortality from non-communicable diseases (NCDs) are increasingly becoming important as PLWHIV are surviving longer on therapy.[14] DM is a non-transmissible illness with a high prevalence around the world. However, its prevalence, risk factors, pathogenesis and burden in individuals living with or without HIV in Africa are not well studied.[15]

Several studies showed abnormal blood glucose levels or poor control in African HIV-infected patients.[16,17] The prevalence of disorders of glucose metabolic process in HIV patients was estimated to range from 2.1% to 26.5% for diabetes and 20.2% to 43.5% for glucose intolerance in some African countries.[18–22] The prevalence of type 2 DM was found to be 2.1 % (95 % CI 1.3%–3.2 %) amongst patients living with HIV/AIDS in a public sector facility in Zimbabwe.[22] The estimated prevalence of diabetes was higher in HIV-negative participants in data from surveyed people aged 50 years and over living with and without HIV in Uganda (471 studied, half of them were HIV positive).[15] Nevertheless, the prevalence was 5.8% for DM and 5.6% for impaired fasting glucose (IFG) among ART-naïve patients having HIV/AIDS in the main ART center in Guinea-Bissau.[18]

Similarly, Levitt et al compared the prevalence of dysglycemia (IFG, impaired glucose tolerance [IGT] or diabetes) in a cohort of South African participants from a community-based survey (CBS) and three gatherings of HIV/AIDS people not known to have diabetes.[17] They reported a prevalence of dysglycemia of 18.0%, 21.6%, 26.0% and 37.0% in CBS participants, ART-naïve patients, patients on non-nucleoside reverse transcriptase inhibitors (NNRTIs) as first-line ART in addition to NRTIs and patients on lopinavir/ritonavir-boosted PI with added NRTIs as second-line cART, respectively. The authors found that diabetes was comparative crosswise over these gatherings; however, IGT was three- to fourfold higher in second-line cART and CBS compared with ART-naïve and first-line ART groups.[17]

It was found that the duration of HIV infection, large abdominal circumference,[19] overweight/obesity, sedentary living, low income and lack of information were contributing factors for developing dysglycemia in African populations.[23] Higher baseline HIV 1 RNA and body mass index (BMI) were also established to be associated with greater risks.[24] Surprisingly, Tzur et al found that HIV-infected Ethiopians are more likely to develop DM at low BMI values compared to non-Ethiopians.[25]

There is some contradiction concerning older age and female sex as contributing factors for developing dysglycemia in HIV-infected patients. Levitt et al found that the enhanced risk of dysglycemia was related to older age, female

sex and HIV status (ART-naïve: odds ratio [OR] 2.31, with a 95% confidence interval [CI] 1.65–3.24; first-line ART: OR 2.47, 95% CI 1.80–3.38; and second-line ART: OR 4.10, 95% CI 2.54–6.61).[17] However, Tzur et al concluded that the comparatively raised prevalence of DM was age-independent but most detectable in those under 42 years.[25] Alternatively, it has been shown that HIV-infected women on NNRTI-based ART had higher-up glucose tolerance and lower levels of plasma metabolites linked to the developing of diabetes equated with men with alike metabolic disease risk profiles. The association between sex and plasma metabolite levels did not fundamentally differ according to HIV status amongst obese subjects, proposing the observed sex differences may not be HIV-specific.[26]

HIV medications and diabetes

Presently, cART predominantly used in the management of HIV/AIDS patients includes combinations of PIs and NRTIs, or NNRTIs and NRTIs or just NRTIs. These medications are discussed in relation to their consequences on glucose tolerance and their impact on increasing the risk of acquiring diabetes. There are two newer classes of cART, the CCR5 inhibitors and the integrase inhibitors;[27] which we have not included in the discussion in this paper.

In spite of its reduction in the burden on HIV/AIDS patients, cART is observed to be connected with insulin resistance, glucose intolerance and type 2 DM.[13,27–33] PLWHIV on cART have two- to fivefold greater risks for developing DM compared to cART-naïve patients.[28,34] Disrupted glycemic control in PLWHIV on cART is often attributed to PIs but Efavirenz (an NNRTI utilized as a part of first-line ART regimens in low- and center salary nations); zidovudine (ViiV Healthcare, Brentford, UK) and stavudine have also been associated with an increased risk of developing diabetes.[24,35–39] Nevertheless, a few studies revealed no significant association between cART duration and metabolic changes in African population.[24,31,40,41]

The increased glucose level in HIV patients on cART can be ascribed to pancreatic beta-cell lipotoxicity, which may represent drug-induced effects, or to the consequences of lipodystrophy or both.[42–44] In the homeostasis of blood glucose level, insulin supports glucose uptake by activating insulin receptors on cell surfaces. This sets up a course of phosphorylation of key cell substrates that results in translocation of glucose transporter 4 (GLUT4) from the cell cytosol to the surface of the cell, where it encourages glucose entry into the cell. Within this pathway, the action of insulin may be interrupted at numerous points, resulting in insulin resistance.[27] Several studies have demonstrated that use of the early PIs (such as indinavir) increases insulin

resistance.[24] A solitary dosage of the PI indinavir resulted in a 30% decrease in insulin resistance in healthy HIV-negative subjects,[45] while PLWHIV prior to the cART era indicated typical insulin activity.[46]

PIs increase insulin resistance through GLUT4-dependent or independent mechanisms. They interfere with the translocation of GLUT4 from the cell cytosol to the surface of the cell.[27] Furthermore, PIs inhibit adipocyte differentiation by altering adipogenic proteins, such as sterol regulatory element binding protein-1.[47] The differentiation of the adipocyte and the secretion of adipokines, (for example, adiponectin) are understood to modulate insulin sensitivity. Interestingly, associations have been additionally seen between leptin and obesity, blood lipids and insulin resistance in an HIV-negative Cameroonian population.[48] Insulin sensitivity in PLWHIV on cART demonstrates that lipodystrophy is also reduced[29,42,49] as expected, as lipodystrophy is a known insulin-resistant state.

A small study of PI-treated PLWHIV with lipodystrophy compared to PI-naïve PLWHIV without lipodystrophy (who were matched for age, BMI, and waist) showed increased insulin resistance in the PI-treated lipodystrophic group.[49] NRTIs additionally add to insulin resistance.[50] Furthermore, work in healthy HIV-negative controls showed that 4 weeks of stavudine reduced insulin sensitivity connected with decreased mitochondrial DNA and function in muscles.[51] Diminished expression of mitochondrial genes required for metabolism has likewise been shown in the adipocytes of stavudine-treated HIV-negative controls.[52] These studies propose that mitochondrial impacts may represent in any event a portion of the metabolic entanglements connected with cART, notwithstanding the notable mitochondrial-related neurological antagonistic impacts.

Adding to cART consequences on peripheral glucose uptake, there is likewise proving of cART impact on insulin secretion. In PLWHIV, who commenced a PI (at the meantime as initiating, or as of now getting, an NRTI), measurements of insulin secretion and beta-cell function decreased by 25%–50%.[53] Dysfunction of the beta cell (figured by insulin, proinsulin and C-peptide reactions to an oral glucose burden) is described in cART recipients equated with untreated PLWHIV.[54]

Studies of rodent islets and the MIN6 beta-cell culture line have additionally indicated that PIs inhibit glucose sensing and suppress insulin release.[55] Although mechanisms for these effects are not clear, GLUT2 is a nominee because it is considered to be required for glucose sensing, which is fundamental for the starting out of the pathway of insulin secretion.

Understanding of accessible information demonstrates that PLWHIV on cART are at expanded danger of DM,

partially added to by class-particular and medication particular antagonistic metabolic impacts, the impacts of lipodystrophy, and the impact of longer survival and increasing weight. Changes in the demographics of PLWHIV will likewise affect, with higher disease rates now occurring in populations who have hereditary liability to DM.[27]

With the enhanced survival of PLWHIV, NCDs are fast becoming an issue of concern in PLWHIV and also for health systems in Africa especially in low-income settings.[15,21,22,56–58]

Progressively diabetes and other NCDs are developing among low-wage populations that additionally are most burdened by social anxiety and disease.[59] PLWHIV are at particular risk.[58] Furthermore, DM commonly causes organ-specific damage with exacerbation of the socioeconomic burden.[13]

In the perspective of the expanded danger of dysglycemia in PLWHIV, screening for diabetes and other disorders of glucose metabolism ought to be founded in cART programs in Sub-Saharan Africa.[17,18,34] Increasing knowledge of health-related risk factors is of paramount importance. Further, it justifies equal research attention and financial commitment in the quest for well-being equity.[60]

Metabolic syndrome in HIV/AIDS patients in Africa

Epidemiology

Nguyen et al reported that there was no difference between the prevalence of the metabolic syndrome among HIV patients and the general population in a meta-analysis about global prevalence of metabolic syndrome among HIV patients in a total of 65 studies across the five continents.[8] Clinical features of the metabolic syndrome include obesity (including visceral obesity), dyslipidemia, hypertension and IGT. Their analysis showed that the prevalence of metabolic syndrome was 16.7%–31.3% among HIV patients and this was almost similar to the prevalence of metabolic syndrome in the general population. Importantly, the duration of diagnosed HIV infection, CD4+ counts, exposure to antiretroviral therapy and use of ART were considered as risk factors for the metabolic syndrome.[8] Table 1 provides a demonstration of the prevalence of metabolic syndrome in HIV patients in different African countries that ranges from 13% to 58%.

Risk factors for the metabolic syndrome among HIV patients

In South Africa, the prevalence of metabolic syndrome at diagnosis of HIV infection was found to be 8.7% and increasing to 19.2% over 36 months (*p*=0.001).

Table 1 The prevalence of the metabolic syndrome among HIV patients in some African countries

Reference	Country	Prevalence of metabolic syndrome
Gradidge and Crowther[61]	South Africa	42%
Sobieszczyk et al[62]	South Africa	19.2%
Muyanja et al[63]	Uganda	58%
Guira et al[64]	Burkina Faso	18%
Eholié et al[65]	Ivory coast	5.5%
Tesfaye et al[66]	Ethiopia	25%
Ayodele et al[67]	Nigeria	17.2%
Zannou et al[68]	Benin	13%

Abbreviation: HIV, human immunodeficiency virus.

The proportion of women with obesity increased from 34.4% to 47.7%; the proportion of women with abnormal waist circumference and elevated blood pressure increased from 33.5% to 44.3% and 23.8% to 43.9%, respectively. Predictors of metabolic syndrome were age, time post-infection and family history of diabetes.[62]

The prevalence of hypertension in patients on cART was twice (38%) that of the cART-naïve patients in Cameroon (19%), and risk factors were older age and male sex in the cART group and BMI-defined overweight in the cART-naïve group.[69] Importantly, in young black Africans, stroke is associated with clusters of the metabolic syndrome.[70] In Uganda, metabolic syndrome was detected in 58% of participants and 17% had a Framingham risk correlating to a 5% or greater risk for CVD within 10 years. Female sex and over 40 years of age were independently associated with having metabolic syndrome.[63] Metabolic syndrome was diagnosed in 18% patients from Burkina Faso. Associated factors were PI regimens, female sex, age >42 years (*p*=0.001) and lipodystrophy (*p*=0.01).[64]

The synergy between HIV, antiretroviral exposure and westernization of lifestyle in a cohort of HIV-infected patients of Sub-Saharan origin leads to a progressive increase in the risk of lipodystrophy, as demonstrated in a study in Ivory Coast (Côte d'Ivoire). The incidence of metabolic syndrome, insulin resistance and lipodystrophy was 5.5, 8.5 and 6.8 per 100 person-years of follow-up (cumulative incidence: 14.4%, 19.2% and 18.1%, respectively). Risk factors were living in France, female sex and overweight.[71]

Applying the International Diabetes Federation (IDF) criteria, metabolic syndrome was diagnosed in 25% of patients in Ethiopia receiving ART compared to 22.5% of the cART-naïve group. On the other hand, using the Adult Treatment Panel III (ATP) criteria, the prevalence of metabolic syndrome was 18.1% in the cART groups compared

to 15.6% in ART-naïve group. Patients receiving cART had significantly elevated cholesterol, triglyceride glucose and low-density lipoprotein cholesterol (LDL-c) levels but lower CD4+ cell counts than the cART-naïve groups. Being a female, having BMI of at least 25 kg/m², older age (i.e., age ≥45 years) and having total cholesterol of at least 200 mg/dl were significantly associated with the presence of metabolic syndrome.[66] In another study from Ethiopia, 18% had subclinical atherosclerosis; of whom 14% were ART-naïve whereas 24% were ART-treated. Independent predictors of subclinical atherosclerosis included age per 5-year increase in age, BMI and high LDL. High-sensitivity C-reactive protein was positively correlated with traditional cardiometabolic risk factors including waist circumference, triglycerides and total cholesterol:HDL ratio (TC:HDL) (r=0.225, p<0.001). Risk factors for lipodystrophy in Ethiopia were a history of smoking, cART regimen and duration of cART treatment.[72]

In this regard, longitudinal studies with longer follow-up showed a high prevalence of metabolic complications. For example, in Senegal, after a median of 9 years of cART, 37% had lipodystrophy, 28% had hypertension and 14% presented with diabetes.[73] Despite the fact that physical activity is regarded as a best treatment for metabolic syndrome, PLWHIV in Africa demonstrate low physical activity. For example, in Rwanda in a cohort of 407 patients with HIV, approximately 70% were inactive, 40% were obese and 43% were overweight. Obesity was strongly associated with inactivity. Lack of motivation and time, as well as fear of worsening the disease, were found to be barriers to participation in physical activity programs.[74] Therefore, high levels of metabolic complications are seen in an African population. For instance, in Cameroon, the high prevalence of diabetes, dyslipidemia, metabolic syndrome, arterial and aortic stiffness were noticed in PLWHIV in comparison with the general population.[75]

The use of different criteria in the diagnosis of metabolic syndrome is known as a cause for variations in the prevalence of metabolic syndrome. For instance, in a study in Nigeria, the prevalence of metabolic syndrome according to the ATP III, IDF and JIS criteria were 12.7%, 17.2% and 21.0%, respectively. Metabolic syndrome was significantly associated with female sex (all definitions), BMI (all definitions), increasing age and CD4 count (IDF definition). There was no significant association between metabolic syndrome and cART.[67] Furthermore, metabolic syndrome in Benin (IDF definition) appeared in 13% and was more common in women (19.2% versus 3.1% in men). Diabetes (8%) and hypercholesterolemia (35%) were also

observed. After adjustment, sex, young age (hazard ratio [HR] 0.45 [95% CI 0.22–0.90]; p=0.025), high BMI at inclusion (HR 1.53 [95% CI 1.28–1.83]; p<0.0001) and smoking (HR 28.0 [95% CI 2.5–307.4]; p=0.006) were significantly associated with lipohypertrophy. In this study, 30% patients developed lipodystrophy (lipoatrophy 9%, lipohypertrophy 24% and mixed pattern 2.5%). The incidence rate for lipodystrophy was estimated to 1.72 per person-month (95% CI 1.15–2.56) occurring after a median time of 11 months on cART.[68] Importantly, moderate-severe lipodystrophy affected one-third of West African patients on long-term cART, and stavudine administration was the only independent risk factor. Other associated risk factors were insulin resistance and central obesity and high triglyceride.[72,73,76]

Dyslipidemia in HIV/AIDS patients in Africa

Dyslipidemia is very common in PLWHIV and manifests as low HDL, high triglyceride, total cholesterol and LDL-c. Table 2 shows the prevalence and types of dyslipidemia associated with HIV drugs in some African countries. It is well established that cardiovascular risk assessment of HIV-infected patients is a critical element of care in developed countries, and health care systems that provide antiretroviral therapy in African countries would also benefit from lipid specialists in order to reduce CVD in HIV patients.

Among PLWHIV in South Africa, hypercholesterolemia was found in 32.2%, low HDL-c in 45.7% and elevated LDL-c in 9.5% (95% CI 6.2–12.8). TC and LDL-c were positively correlated with CD4+ cell count.[80] This is likely due to the effect of medications, as ART administration is associated with higher TG, TC, LDL-c and HDL-c than those who were ART-naïve.[81] Higher prevalence of dyslipidemia was also reported in other African countries. For instance, in Kenya, the prevalence of dyslipidemia was 63.1% and dysglycemia was 20.7%. HAART was associated with high total and LDL-c and high triglyceride levels. However, HAART is not associated with low HDL-c and had no effect on dysglycemia. In Nigeria, high cholesterol, LDL-c and triglyceride were seen in 28%, 24% and 35%, respectively. It is reported that PI worsens dyslipidemia.[82,83] In Tanzania, low HDL-c was prevalent in 67% and increased triglyceride in 28%. High triglyceride and low HDL levels were associated with low CD4+ counts (p<0.001).[77] The prevalence of dyslipidemia in Malawi, Ethiopia and Cameroon was estimated to be 31%, 56.9% and 70.2%, respectively.[72,77,78]

Dyslipidemia is largely related to CD4+ cell count, PI, fatty liver and use of ART. Importantly, HAART was

Table 2 The prevalence and type of dyslipidemia associated with HIV medications in some African countries.

Reference	Country	Type of study	Study population	Dyslipidemia	Prevalence	Main conclusion
Dave et al[80]	South Africa - Cape Town	A cross-sectional study	406 adult ART-naïve and 551 adult HIV participants receiving NNRTI*-based or PI**-based ART	High TG, TC, LDL-c and low HDL-c	90.0% and 85%, respectively	Dyslipidemia likely to occur with ART more than with ART-naïve
Julius et al[81]	South Africa - Johannesburg	A cross-sectional study	304 HIV adult patients on HAART for more than 1 year	High TG, TC, LDL-c and low HDL-c	Hypertriglyceridemia (>2.25 mmol (mL) in 15.8%, hypercholesterolemia (TC >5.00 mmol/mL) in 32.2%, low HDL-c (<1.20 mmol/mL) in 45.7% and elevated LDL-c (>4.10 mmol/mL) in 9.5%	ART administration is associated with dyslipidemia
Manuthu et al[40]	Kenya	A cross-sectional comparative group study	295 HIV adult patients; 134 (45%) were on HAART, 82% of whom were on stavudine, lamivudine and either nevirapine or efavirenz	High TG, TC, LDL-c and low HDL-c	Overall prevalence of dyslipidemia was 63.1% and dysglycemia was 20.7%. High TC occurred in 39.2% of HAART and 10.0% HAART naïve patients ($p<0.0001$), whereas high LDL-c occurred in 40.8% and 11.2%, respectively ($p<0.0001$, OR 5.43, 95% CI 2.973–9.917). HDL levels were low in 14.6% and 51.3% among HAART and HAART-naïve patients, respectively ($p<0.0001$, OR 0.16, 95% CI 0.091–0.29), while high TG occurred in 25.6% and 22.5%, respectively ($p=0.541$ OR 1.184 95% CI 0.688–2.037)	HAART was associated with high total cholesterol and LDL-c and high triglyceride levels. However, HAART was not associated with low HDL-c and had no effect on dysglycemia
Lesi et al[82]	Nigeria - Lagos	A prospective cross-sectional study	113 adult HIV patients on HAART therapy for 6–42 months	High TG, TC, LDL-c and low HDL-c	Fatty liver prevalence was 13.3%. High cholesterol, LDL-c and TG were seen in 28%, 24% and 35%, respectively	Hepatic steatosis was strongly associated with hepatomegaly and hyperlipidemia in subjects on long-term HAART
Salami et al[83]	Nigeria - Ilorin		127 HIV adult patients; 94 (29%) on PI and 233 (71%) on NNRTI regular treatment for at least 3 months	Low HDL, high triglyceride, cholesterol and LDL-c	The pretreatment metabolic changes in both groups (PI vs. NNRTI) were low HDL-c; 29 (31%) vs. 77 (33%), followed by hypertriglyceridemia; 16 (17%) vs. 38 (16%) and hypercholesterolemia; 6 (6%) vs. 10 (4%). After exposure to two different HAART regimens, hypertriglyceridemia and hypercholesterolemia became more prevalent especially with PI-based therapy than NNRTI; 74 (79%) vs. 108 (54%) and 58 (51%) vs. 72 (31%)	HARRT treatment, especially PI, worsened dyslipidemia (3 times)
Armstrong et al[77]	Tanzania	A cross-sectional study	12,513 ART-naïve, non-fasting HIV adult patients	High TG, TC, LDL-c and low HDL-c	Low HDL-c was prevalent in 67% and increased TG in 28%	Dyslipidemia was associated with low CD4 counts ($p<0.001$)

(Continued)

Table 2 (*Continued*)

Reference	Country	Type of study	Study population	Dyslipidemia	Prevalence	Main conclusion
Muronya et al[84]	Malawi	A cross-sectional study	174 HIV adult patients on long-term (>1 year) ART	High cholesterol	High TC levels (31.0%), raised blood pressure (45.9%), increased waist-hip ratio (45.4%)	Cardiovascular risk factors were common among long-term ART patients in Malawi
Feleke et al[72]	Ethiopia - Addis Ababa	A cross-sectional study	356 HIV adult patients on HAART for 1 year or more. 209 (59.7%) patients were on stavudine-based ART therapy and 135 (41.3%) were on zidovudine-based ART therapy	High TG, TC, LDL-c and low HDL-c	Prevalence of hyperlipidemia was 56.9%, prevalence of hypercholesterolemia was 38.2%, prevalence of high LDL-c 54.2%, prevalence of hypertriglyceridemia was 15.2%, prevalence of fasting hyperglycemia was 17.8%	Lipodystrophies occurred in majority of patients on ART treatment for longer than 1 year; hyperlipidemia and hyperglycemia were also seen commonly in Ethiopian HIV patients on HAART
Bekolo et al[78]	Cameroon	A cross-sectional study	114 HIV-infected persons aged 15 years or more and receiving first-line ART for at least 6 months	High TG, TC, LDL-c and low HDL-c	Prevalence of hyperlipidemia was 70.2%, prevalence of hypercholesterolemia was 29.8%, prevalence of high LDL-c was 30%, prevalence of hypertriglyceridemia was 51.8%	A high prevalence of dyslipidemia in HIV patients receiving first-line ART was found

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; HDL-c, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; LDL-c, low-density lipoprotein cholesterol; NNRTI, non-nucleoside reverse transcriptase inhibitor; OR, odds ratio; PI, protease inhibitor; TC, total cholesterol; TG, triglyceride.

associated with lipodystrophy, and the risk of developing type II diabetes among the HAART-experienced group was 5 times higher than the HAART-naïve group.[79]

Conclusion

PLWHIV live longer and are increasingly encountering a series of challenging metabolic disorders like diabetes, obesity, dyslipidemia and subsequent increase in the risk of CVD. Dyslipidemia can be due to HIV infection or induced by HIV medications. Furthermore, in African countries, CVD has become one of the major causes of death in HIV patients due to the high prevalence of diabetes, dyslipidemia and metabolic syndrome. Therefore, cardiovascular risk reduction and lifestyle modifications are essential components for the control program; and careful selection of the antiretroviral drugs according to underlying cardiovascular risk factors is of great importance. In the view of the fact that PLWHIV are an expanding and aging population to address, a metabolic clinic may be a good choice for African countries not only to meet the clinical demand for clinical services but also to provide a useful opportunity to collect data for future clinical research (see Ahmed et al[85] for further information about HIV metabolic clinic in Milton Keynes University Hospital, UK).

Disclosure

The authors report no conflicts of interest in this work.

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