

69% African Americans. The ART regimen of the cohort was mostly tenofovir/emtricitabine (44%), tenofovir/emtricitabine/efavirenz (19%) and zidovudine/lamivudine (6%). ABCA1 and HMGR were upregulated in cases compared with healthy controls ($P < 0.01$ and $P = 0.01$, respectively) (Figure 1).

Conclusion. ART might cause intracellular accumulation of cholesterol leading to upregulation of efflux gene, ABCA1. Perturbation of cholesterol biosynthesis may be in the causal pathway of ART-associated metabolic syndrome.

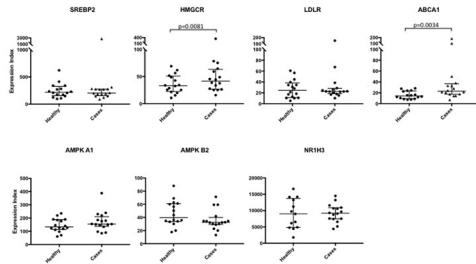


Figure 1. ART-induced perturbation of cholesterol regulation genes. ABCA1 and HMGR were upregulated in cases compared to healthy controls, while no statistical differences were observed in SREBP2, LDLR, AMPK A1, AMPK B2 and NR1H3.

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2248. Changes in Lipid Profiles for Patients to Tenofovir Alafenamide (TAF)-Containing Regimens: Perspectives from a Military HIV-Positive Cohort

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Background. Tenofovir alafenamide (TAF) was approved in 2015 for use in HIV-1. TAF decreases risk of renal and bone toxicity compared with tenofovir disoproxil fumarate (TDF). Early clinical trials reported median increases in low-density lipoprotein (LDL) of 20–29 and 9–13 mg/dL for total cholesterol (TC) following switch therapy from TDF-containing regimens at 48 weeks, raising concern for increased cardiovascular (CVD) risk over time. We assessed real-world changes in serum lipid concentrations following transition to TAF-containing regimens.

Methods. Eligible subjects in the U.S. Military Natural History Study, a longitudinal cohort of HIV-infected military beneficiaries, had been switched from TDF to TAF-based regimens, and had pre- and post-switch lipid profiles available. Antiretroviral therapy history, serum lipids, CD4 count and viral load were collected from the study database. Wilcoxon rank-sum test was used to compare lipid profile changes.

Results. As of January 1, 2018, 408 subjects on TDF switched to TAF; 238 had pre and post lipid profiles. Subjects were primarily male (95%), 45.4% African American, 70% were ≥ 40 years old at TAF start; 8% had CVD and 10% had diabetes. Changes in lipid profiles and CD4 count are presented in Table 1. No difference was seen when categorized by gender, race, or age. Lipid changes were not seen in subjects switched from an efavirenz (EFV) regimen. Increases in TC, HDL, and LDL were observed in those switched from rilpivirine (RPV) ($P = 0.002$, $P = 0.0404$, and $P = 0.0296$) or elvitegravir (EVG) ($P < 0.0001$, $P = 0.0003$, $P = 0.0040$) regimens.

Conclusion. We found significant changes in serum lipids, albeit lower than median changes observed in licensing trials. Changes were not observed in those switching from EFV, contrasting with those switching from RPV or EVG.

Table 1: Serum Lipid Profiles

	On TDF	After TAF Switch (>6 Weeks)	% Change	P-Value
TC*	174.0 [154.0–197.0]	184.0 [161.0–212.0]	6.6 [–5.4–18.6]	<0.0001
HDL	47.0 [39.0–57.0]	48.0 [41.0–57.0]	2.8 [–7.7–17.3]	0.007
LDL	107.0 [86.0–124.0]	112.5 [91.0–135.0]	6.5 [–10.3–22.0]	0.0007
TC:HDL	3.7 [2.9–4.4]	3.7 [3.0–4.5]	3.6 [–9.9–17.9]	0.03
CD4 (cells/ μ L)	676.0 [533.0–880.0]	704.0 [562.0–917.0]	6.6 [–8.0–20.1]	<0.0001

*Concentrations in mg/dL. Values are median [Q1–Q3].

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2249. Insulin Resistance Is Associated with Higher Viral Loads Among HIV-1-Infected Patients Initiated on 12 Months of First-Line Antiretroviral Therapy

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Background. As HIV-infected patients are living longer due to ART and decreasing mortality, the burden of noncommunicable diseases (NCDs) is expected to rise. With the implication of Insulin resistance (IR) and inflammation in the pathogenesis of Diabetes Mellitus (DM), DM is likely to be increasing in the HIV-infected patients in the Sub-Saharan Africa (SSA). HIV is characterized with systemic inflammation and markers which quickly decrease with ART initiation regardless of type of ARV regimen though they do not normalize. We thus assessed the relationship between IR and Virologic treatment failure among HIV-1-infected individuals at 12 months of first-line ART in the Zambian ART program.

Methods. We conducted a cross-sectional survey among HIV-1-infected individuals at 12 months (± 3 months) of first-line ART. Systematic sampling was performed and 20 clinics were selected based on the random starting-point, sampling interval and cumulative population size giving a sample size of 460. Eligible patients had their fasting blood specimens collected for VL, insulin, blood glucose, high sensitive c-reactive protein (hsCRP), tumour necrosis factor alpha (TNF α) and Lipogram. Anthropometric indices were also measured including visceral fat. Insulin resistance (IR) was determined using Homeostatic model assessment (HOMA). Proportions for each outcome at linearized standard error 95% confidence interval and summary estimates were determined. Viral Load suppression (VLS) was defined according to the detection threshold which was < 20 copies/mL and treatment failure was defined as VL $> 1,000$ copies/mL.

Results. Of the 473 patients enrolled, 142 (30%); 95% CI (26%, 34%) had IR. 19% of individuals with IR had treatment failure compared with 5.7% with treatment failure and without IR (P -value < 0.0001). Treatment success was associated with less likelihood of IR (OR 0.26 (0.14, 0.48), P -value < 0.0001). Among individuals with VLS, 82 out of 142 (58%) 95% CI (0.54%, 0.70%) had IR compared with 232 out of 331, (70%) 95% CI (65%, 75%) who did not have IR (P -value = 0.042)

Conclusion. Patients with poor virological outcomes at 12 months of first-line ART had increased likelihood of insulin resistance compared with those with treatment success. There was good evidence to suggest that the proportion of those with VLS and IR was less than those with VLS and no IR.

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2250. Metformin for Preventing Diabetes Mellitus in HIV-Infected Patients with Prediabetes: A Randomized Controlled Trial

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Background. Both HIV and diabetes mellitus (DM) increase the risk for cardiovascular diseases. Prediabetes (PreDM), a condition preceding DM, is commonly observed in HIV-infected patients receiving antiretroviral therapy (ART). Both metformin and lifestyle interventions have been shown to reduce risk of progression to DM in non-HIV-infected population. This study aimed to evaluate the efficacy of metformin for preventing DM in HIV-infected patients.

Methods. An open-label randomized controlled clinical trial was conducted in HIV-infected patients with PreDM. Patients were randomized into two groups: metformin group (received metformin) and control group (not received metformin). Patients in both groups were counseled regarding diet control and lifestyle modification and followed for 6 months. The primary endpoint was the development of DM. Fasting plasma glucose (FPG), 2-hour 75-gm oral glucose tolerance test, HbA1c, computer-based homeostatic model assessment index of β -cell function (HOMA β) and insulin resistance (HOMA-IR) were analyzed.

Results. Seventy-four patients were enrolled, 37 in each group. Mean age was 49.6 years and 68.9% were males. At baseline, mean CD4 cell count was 570 cells/mm³ and mean body mass index (BMI) was 24.6 kg/M². Baseline characteristics including age, sex, BMI, waist-hip (W/H) ratio, duration of ART, ART regimen, CD4 cell count and HIV RNA were similar between two groups ($P > 0.05$). Mean FPG, 2hPG, HbA1c, HOMA β and HOMA-IR at baseline were also similar between two groups ($P > 0.05$). At 6 months, one patient in metformin group and two in control group developed DM [risk reduction 2.70%; 95% CI, –9.09% to +15.20%]. Mean HbA1c significantly decreased from baseline only in metformin group. HOMA-IR at 6 months was significantly lower in metformin group (1.086 vs. 1.478, $P = 0.042$). However, BMI, W/H ratio, FPG, 2hPG, HbA1c, and HOMA β at 6 months were not significantly different between two groups ($P > 0.05$). No patient had adverse effects that led to discontinuation of metformin. No cardiovascular event was observed in study period.

Conclusion. Metformin appears to improve insulin resistance and prevent progression to DM in HIV-infected patients with PreDM. Further study with longer study period is needed to evaluate long-term benefit of metformin.

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