Endothelial Dysfunction Is Related to Monocyte Activation in Antiretroviral-Treated People With HIV and HIV-Negative Adults in Kenya

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Background. Residual monocyte activation may contribute to increased risk for endothelial dysfunction and subsequent atherosclerotic cardiovascular diseases (CVDs) among people with HIV (PWH) on antiretroviral therapy (ART). We examined the relationship between monocyte activation and endothelial activation in PWH in Kenya.

Methods. Serum levels of markers of endothelial activation (soluble/circulating intercellular [sICAM-1] and vascular [sVCAM-1] cell adhesion molecule–1), intestinal barrier dysfunction (intestinal fatty acid binding protein [I-FABP]), and monocyte activation (soluble CD14 [sCD14]) were measured in 275 PWH on ART and 266 HIV-negative persons. Linear regression was used to evaluate associations, adjusting for demographic and traditional CVD risk factors.

Results. Among 541 participants, the median age was 43 years, 50% were female, and most PWH were virally suppressed (97%). sICAM-1 and sVCAM-1 levels were significantly higher in PWH than in HIV-negative participants ($P < .001$ for both). After further adjustment for traditional CVD risk factors, HIV infection remained associated with 49% (95% CI, 33% to 67%) greater sICAM-1 and 30% (95% CI, 14% to 48%) greater sVCAM-1 relative to uninfected controls. Adjustment for sCD14 substantially attenuated the difference between PWH and HIV-negative individuals. In a stratified analysis of PWH, both sICAM-1 and sVCAM-1 were positively associated with sCD14 ($P < .001$).

Conclusions. Despite viral suppression, African PWH have evidence of enhanced endothelial activation associated with sCD14, suggesting that monocyte activation plays a role in atherosclerotic plaque development. Future studies are needed to determine mechanistic pathways leading to monocyte activation in this population.

Keywords. HIV; Africa; endothelial activation; sCD14; I-FABP; antiretroviral therapy; inflammation.

Cardiovascular disease (CVD) and HIV infection are the leading causes of death in Kenya [1, 2]. Additionally, people with HIV (PWH) on antiretroviral therapy (ART) have a 2-fold higher risk of incident CVD compared with their age- and sex-matched HIV-negative counterparts, even with effective viral suppression [3–5]. Much of the HIV burden is in Sub-Saharan Africa (SSA), and Kenya has an overall prevalence of 6% among adults [6]. The mechanism underlying this increased CVD risk is unknown but has been attributed to traditional CVD risk factors, off-target effects of ART, chronic immune activation, and vascular dysfunction [6, 7]. However, most studies of HIV and CVD are from US and European contexts, and there are limited data from SSA on the pathogenesis of CVD in PWH.

Endothelial dysfunction, a state of aberrant vascular endothelial cell activation, appears to be an important early step in the development of the fatty streak, a precursor of atherosclerotic plaque [8, 9]. When the endothelium is injured, the localized inflammatory response that ensues may lead to increased expression of endothelial surface receptors that mediate the adhesion and migration of immune cells into the vessel wall [9]. Elevated levels of endothelial activation molecules including soluble/circulating intercellular (sICAM-1) and vascular (sVCAM-1) adhesion molecule–1 have been shown to predict future CVD events in the general population and those with CVD [10, 11]. As a result, sICAM-1 and sVCAM-1 are widely used as markers of endothelial dysfunction.

HIV infection is characterized by chronic immune activation that persists despite viral suppression [12–17]. As such,

endothelial function is thought to be more impaired in those with HIV compared with HIV-negative individuals [17]. Evidence has been mixed, with some studies reporting normalization of endothelial dysfunction markers after treatment with ART [18, 19] and others reporting persistent endothelial dysfunction among PWH on ART [16, 20–25]. Most of these studies were limited by their inability to consider contributions of traditional CVD risk factors; they predominantly recruited men and individuals from Western countries who were mostly on protease inhibitor–based regimens.

Microbial translocation occurs in the gastrointestinal tract where there is a large HIV reservoir and has been linked to HIV-associated immune activation. Upon primary infection with HIV, gut blood barrier dysfunction following mucosal $CD4^+$ T-cell depletion results in chronic entry of microbial products such as lipopolysaccharide (LPS) into the systemic circulation. Soluble CD14 (sCD14) is secreted mainly by activated monocytes and macrophages (ie, Kupffer cells) upon stimulation with LPS [26, 27]. Persistent elevation of LPS, a gut epithelium damage marker (intestinal fatty acid binding protein [I-FABP]), and persistent elevation of sCD14 are often used as markers of microbial translocation and have been reported to predict overall mortality in PWH [28–31]. Although monocyte activation and endothelial activation have been implicated separately in the pathophysiology of CVD in studies conducted in Western high-income countries [31–39], very few studies have thoroughly investigated how monocyte activation affects endothelial activation in PWH on long-term ART treatment in the SSA region. Compared with Europe/US-based studies, the few studies looking at the association between immune activation and endothelial dysfunction conducted in African countries have been relatively small, have not directly evaluated the contribution of risk due to metabolic abnormalities vs HIV-associated inflammation/immune activation, and have not compared people with HIV with HIV-negative individuals. This comparison may be particularly relevant in developing countries, where all adults regardless of HIV status are at risk for inflammation and immune activation due to chronic exposure to bacterial and parasitic infections [40]. For these reasons, we believe that understanding these complex relationships in the presence of these exposures will be essential to understanding the pathophysiology of CVD in this setting.

In this study, we investigated the associations between marker of monocyte activation (sCD14) with circulating markers of endothelial activation (sVCAM-1 and sICAM-1) in PWLH and HIV-negative adults without a known history of CVD and examined whether these relationships differed according to HIV status. We hypothesized that sCD14 would be associated with markers of endothelial activation, independent of traditional CVD risk factors in ART-treated PWH.

METHODS

Study Population and Site

This study was part of a larger project to assess CVD risk factors among PWH on ART and HIV-negative men and women in Western Kenya [41]. This cross-sectional study conducted between July 2017 and May 2018 enrolled 300 PWH at the Kisumu District Hospital Comprehensive Care Center (KDH CCC) in Kisumu, Kenya. PWH were required to be in active care and on a stable ART regimen for at least 6 months. Simultaneously, 298 HIV-negative men and women were prospectively recruited from the voluntary HIV testing and counseling (HTC) center at Kisumu District Hospital, and all underwent routine confirmatory HIV testing. In both groups, participants were at least 30 years of age. The study cohort has been previously described in detail [41]. Participants were excluded if they were pregnant or lactating or if they had an acute infectious condition, cancer, or history of CVD such as stroke, peripheral vascular disease, or coronary arterial disease.

Data Collection

Data were collected by structured questionnaires, physical examination, and venous blood sampling. Data on sociodemographic, ART duration, type of ART, and nadir $CD4^+$ T-cell count were obtained from the participants and confirmed using medical records. CVD risk factor assessment was done using the World Health Organization noncommunicable disease STEP-wise approach to CVD risk factor surveillance tool (age, alcohol consumption and smoking status [previous and current], vegetable and fruit intake). Body mass index (BMI) was calculated from weight and height measurements. Blood pressure (BP) measurements were taken twice from each arm using an automated digital sphygmomanometer (Omron Hem 5, Omron Healthcare, Kyoto, Japan). Elevated BP was defined when the mean of the 4 readings showed systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg, or if there was current use of antihypertensives.

Sample Collection

Fasting blood samples were processed for serum and plasma then stored at –80°C until further analysis. Of the participants enrolled, only 541 had available stored samples for testing of soluble markers, as well as lipids, high-density lipoprotein (HDL), low-density lipoprotein, and triglyceride cholesterol (TG) and fasting blood glucose (FBG) measures. Plasma viral load (VL) was determined by Roche ultrasensitive reverse transcription polymerase chain reaction (RT-PCR; with a limit of detection of 20 copies/mL) and Roche Ultrasensitive RT-PCR (threshold 50 copies/mL). Undetectable VL was defined as <50 copies/mL, and viral suppression was defined as VL <1000 copies/mL, per Kenyan treatment guidelines [42].

Measurement of Endothelial Activation Markers and Other Soluble Biomarkers

Endothelial activation markers (sVCAM-1 and sICAM-1), our primary outcomes of interest, were measured in serum using multiplex enzyme-linked immunosorbent assay (ELISA; Meso-Scale Discovery, Rockville, MD, USA). Serum I-FABP and sCD14 were measured using commercially available ELISAs (Quantikine ELISA kit, R&D systems). A high-sensitivity C-reactive protein (hsCRP) test was performed using an automated Beckman Coulter AU5812. The interassay coefficients of variation were <20%. All samples were tested centrally at the University of Washington (Seattle, WA, USA). Assays were performed in duplicate and in accordance with manufacturers' protocols.

Statistical Analyses

Clinical characteristics and immunological parameters were compared between groups by sex and serostatus using the *t* test or Wilcoxon rank sum test for continuous data and the chi-square or Fisher exact test for categorical variables. Spearman's *rho* was used to assess correlations. To determine whether HIV serostatus is independently associated with endothelial activation, multivariable linear regression models were fully adjusted for demographics (age and sex) and CVD risk factors (BP, BMI, TG and HDL, smoking status [previous and current], alcohol consumption [previous and current], and FBG) and subsequently with each of the markers I-FABP and sCD14 in separate models.

We also conducted multivariable linear regression analysis to examine the association of sCD14 with endothelial activation in separate models for each biomarker. Models were fully adjusted for the demographics and CVD risk factors listed above. Analyses were further adjusted for current and nadir CD4⁺ T-cell count and ART duration for PWH. An interaction term between each serum biomarker and HIV status was introduced in the model to test the difference of these associations by HIV serostatus. All biomarker variables were log-transformed before model fitting due to their non-normal distribution. We performed secondary analyses excluding patients with detectable viral load and those with CD4 T-cell counts ≥500 cells/mm³ to better understand the effect of HIV infection on monocyte activation and endothelial activation during viral suppression and immuno-recovery. Variables were summarized using No. (%), mean (SD), or median (interquartile range). Significance was set at a *P* value <.05. Analyses were performed using STATA, version 13 (StataCorp, San Antonio, TX, USA).

Patient Consent Statement

The study was approved by the Ethics and Research Committee of Kenyatta National Hospital and the Institutional Review Board at the University of Washington. All participants provided written informed consent.

RESULTS

Participant Characteristics

This study included 541 adults: 275 PWH on ART and 266 HIV-negative adults. Clinical characteristics are shown in Table 1, stratified by sex and HIV serostatus. PWH were more likely to be older, with a lower BMI and lower prevalence of hypertension. Serum levels of I-FABP and sCD14 were significantly higher in PWH as compared with HIV-negative adults (*P* < .001 for all). PWH had long-standing disease (median time since diagnosis, 8 years), they were on ART for many years, and 80% had clinically undetectable viral loads (HIV RNA < 50 copies/mL). Women had significantly higher average CD4⁺ T-cell counts and nadir CD4⁺ T-cell counts compared with men (*P* < .001) (Table 1). All PWH were on co-trimoxazole prophylaxis regardless of their CD4⁺ T-cell count, and nearly all PWH were on an ART regimen that included a non-nucleoside reverse transcriptase inhibitor backbone of efavirenz (45%) or nevirapine (41%), in combination with lamivudine plus tenofovir or zidovudine; only 12% were on protease inhibitors.

Association of HIV With Endothelial Activation Biomarkers

sVCAM-1 and sICAM-1 levels were highly correlated (*r* = 0.79; *P* < .001) among PWH. Compared with the HIV-negative participants, PWH demonstrated higher median levels of sVCAM-1 (617 vs 416 ng/mL; *P* < .001) and sICAM-1 (613 vs 383 ng/mL; *P* < .001). The difference in the levels of these biomarkers persisted even among PWH with CD4 T-cell counts ≥500 cells/mm³; sVCAM-1 levels were 600 vs 416 ng/mL (*P* < .001) and sICAM-1 levels were 587 vs 383 ng/mL (*P* < .001) for PWH vs HIV-negative individuals, respectively. HIV infection remained associated with significantly higher sICAM-1 (49%; *P* < .001) and sVCAM-1 (30%; *P* < .001) relative to HIV-negative individuals in a multivariate analysis adjusted for age, sex, and traditional CVD risk factors (Table 2). Additional adjustment for sCD14 in the multivariable model used for Table 2 greatly diminished the association of HIV infection with sICAM-1 from 49% (*P* < .001) to 18% (*P* = .01) and with sVCAM-1 from 30% (*P* < .001) to 0% (*P* = .96). However, adjustment for I-FABP in the multivariable model in Table 2 had very little effect on the association of HIV with endothelial activation makers.

Association of Soluble Biomarkers With Markers of Endothelial Activation Biomarkers

The relationships between sCD14 with sICAM-1 and sVCAM-1 were also examined (Table 3). In the overall study population, higher sCD14 was independently associated with higher sVCAM-1 and sICAM-1 after adjusting for age and sex, and even after additional adjustment for CVD risk factors (fasting blood glucose, systolic BP, tobacco use status [previous and current], HDL, triglyceride, and alcohol intake; *P* < .001 for both) (Table 3). In stratified analyses, among PWH, sCD14 was positively associated with both sVCAM-1 and sICAM-1

Table 1. Characteristics of Study Participants (n = 541)

	Men HIV+ (n = 138)	Men HIV- (n = 132)	Women HIV+ (n = 137)	Women HIV- (n = 134)
Demographics				
Age, y	48 (41–54)[a]	44 (32–58)	43 (37–51)[c]	37 (31–49)
Cardiovascular risk factors				
Current smoker	8 (6)	6 (5)	0 (0)	2 (1)
Current alcohol use	29 (21)[a]	46 (34)	11 (8)	14 (10)
Diabetes	2 (1)	5 (3)	2 (1)	7 (5)
Overweight/obese	21 (15)[a]	33 (25)	52 (38)[b]	74 (55)
Elevated blood pressure	18 (12)	19 (13)	24 (16)[a]	39 (26)
Other characteristics				
SBP, mmHg	119 ± 16[a]	123 ± 18	116 ± 19[b]	124 ± 21
DBP, mmHg	74 ± 11	76 ± 12	71 ± 12[b]	76 ± 13
BMI, kg/m^2	22 ± 4[b]	23 ± 5	24 ± 5[c]	27 ± 6
Lab values				
HDL cholesterol, mg/dL	53 ± 16	50 ± 15	56 ± 16[b]	51 ± 10
LDL cholesterol, mg/dL	93 ± 31	92 ± 30	97 ± 32	100 ± 32
Triglycerides, mg/dL	87 (68–125)[a]	78 (63–100)	75 (58–99)	69 (54–90)
Total cholesterol, mg/dL	167 ± 37	159 ± 36	171 ± 40	167 ± 37
FBG, mg/dL	76 ± 16	77 ± 21	77 ± 21	79 ± 25
HIV-related characteristics				
Nadir CD4 T-cell count, cells/mm^3	349 ± 211		440 ± 260	
CD4$^+$ T-cell count, cells/mm^3	467 ± 206		565 ± 229	
Undetectable HIV RNA <50 copies/mL	109 (79)		111 (81)	
Total ART duration, y	9 (3–11)		8 (4–10)	
Current PI-based treatment	17 (12)		19 (14)	
Current NNRTI treatment	120 (87)		118 (86)	
Markers of endothelial activation and inflammation				
sICAM-1, ng/mL	638 (460–879)[c]	455 (309–647)	584 (417–800)[c]	350 (219–484)
sVCAM-1, ng/mL	624 (488–843)[b]	536 (332–878)	606 (411–830)[c]	358 (244–522)
hsCRP, mg/L	1.6 (0.7–3.4)	1.2 (0.5–3.3)	1.8 (0.7–4.3)	1.8 (0.8–3.2)
Markers of monocyte activation and intestinal barrier dysfunction				
I-FABP, pg/mL	3317 (1176–8252)[c]	2218 (1456–3355)	3181 (2072–4846)[c]	1668 (1237–2513)
sCD14, ng/mL	3290 (2150–4410)[c]	1553 (956–2367)	2965 (2167–4173)[c]	1393 (767–2295)

Data are reported as mean ± SD, No. (%), or median (interquartile range).

Abbreviations: BMI, body mass index; BP, blood pressure; DPB, diastolic blood pressure; HDL, high-density lipoprotein; hsCRP, high sensitivity C-reactive protein; I-FABP, intestinal fatty acid-binding protein; LDL, low-density lipoprotein; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PWH, people with HIV; sCD14, cluster of differentiation 14; SBP, systolic blood pressure; sICAM-1, soluble intercellular cell adhesion molecule–1; sVCAM-1, soluble vascular cell adhesion molecule–1.

[a]P < .05.

[b]P < .01.

[c]P < .001 for comparisons between PWH and HIV-negative participants (data were analyzed in women and men separately).

Table 2. Association of HIV Infection With sICAM-1 and sVCAM-1 Adjusted for Demographic, and CVD Risk Factors Plus Markers of Intestinal Barrier Dysfunction and Monocyte Activation

	Fully Adjusted[a] % Estimate (95% CI)	Fully Adjusted + I-FABP[b] % Estimate (95% CI)	Fully Adjusted + sCD14[b] % Estimate (95% CI)
sICAM-1			
HIV-	Reference	Reference	Reference
HIV+	49 (33 to 67)**	42 (26 to 60)**	18 (5 to 33)*
sVCAM-1			
HIV-	Reference	Reference	Reference
HIV+	30 (14 to 48)**	23 (8 to 41)*	0 (–13 to 15)

Table 2 shows the results of a multivariable linear regression analysis that assessed the associations between HIV serostatus with sVCAM-1 and sICAM-1. "% Estimate" inidcates percent differences.

Abbreviations: CVD, cardiovascular disease; HDL, high-density lipoprotein; I-FABP, intestinal fatty acid-binding protein; sCD14, cluster of differentiation 14; sICAM-1, soluble intercellular cell adhesion molecule–1; sVCAM-1, soluble vascular cell adhesion molecule–1.

*P < .05; **P < .001.

[a]The models are adjusted for age, sex, and CVD risk factors (fasting glucose levels, systolic blood pressure, body mass index, smoking and alcohol consumption status, triglycerides, and HDL cholesterol).

[b]The models are adjusted for age, sex, CVD risk factors, sCD14 or I-FABP.

in minimally adjusted models and after further adjustment for CVD risk factors (P < .001 for both) (Table 3). Similar associations were also observed for the HIV-negative participants in minimally and fully adjusted models (P < .001 for both), and no interactions were observed between sCD14 and HIV in relation to both endothelial activation markers (all $P_{interaction}$ > .05) (Table 3).

In a sensitivity analysis, serum median levels of sVCAM-1 (600 vs 416 ng/mL) and sICAM-1 (601 vs 383 ng/mL) remained significantly elevated after excluding PWH with detectable viremia compared with HIV-negative participants. Likewise, the magnitude of the association between sCD14 and these endothelial activation biomarkers persisted and even increased among virally suppressed PWH (data not shown).

DISCUSSION

In this cohort of African PWH on long-term ART and HIV-negative adults without a history of CVD in Kenya, we found that markers of endothelial activation were significantly elevated among virally suppressed PWH compared with HIV-negative individuals. Most importantly, we found that sCD14 was associated with greater endothelial activation in African PWH, independent of traditional CVD risk factors and HIV-related factors. To our knowledge, this is the first and the largest study in the SSA region to demonstrate an association between a monocyte activation marker, sCD14, and endothelial activation among persons on effective, long-term ART. Thus, our results suggest that despite effective ART, monocyte activation persists and is associated with endothelial activation, a risk factor for atherosclerotic plaque development. This residual

Table 3. Associations Between sCD14 and Endothelial Activation Markers by HIV Status

		sICAM-1		sVCAM-1	
		β (95% CI)	$P_{interaction}$[a]	β (95% CI)	$P_{interaction}$[a]
Minimally adjusted[b]			.30		.20
	ALL	0.33 (0.24 to 0.39)		0.34 (0.27 to 0.42)	
	HIV+[d]	0.26 (0.15 to 0.39)***		0.43 (0.29 to 0.59)***	
	HIV-	0.34 (0.24 to 0.44)***		0.29 (0.19 to 0.39)***	
			.38		.12
Fully adjusted[c]	ALL	0.32 (0.25 to 0.40)		0.38 (0.29 to 0.46)	
	HIV+[d]	0.28 (0.16 to 0.41)***		0.46 (0.32 to 0.62)***	
	HIV-	0.35 (0.26 to 0.44)***		0.31 (0.21 to 0.40)***	

Results are presented as β coefficients and 95% CIs. Interpret the coefficient as the percent increase/decrease in sICAM-1 or sVCAM-1 for every 1% increase in the biomarker of interest.
*$P < .05$; **$P < .01$; ***$P < .001$.
[a]$P_{interaction}$ sICAM-1 or sVCAM-1 (HIV status and biomarker).
[b]Minimally adjusted for age, sex, and HIV serostatus (for the entire population).
[c]Fully adjusted for age, sex, and CVD risk factors (fasting glucose levels, systolic BP, body mass index, smoking and alcohol consumption status, triglycerides, and HDL cholesterol).
[d]Analyses were further adjusted for current and nadir CD4 T-cell count and ART duration.

immune activation may be a therapeutic target to improve the vascular health of PWH of African descent.

Our study is the largest to evaluate endothelial activation among PWH on ART and HIV-negative adults in Africa. It builds upon prior work from Kenya [43], Botswana [40], South Africa [22], and the United States and Europe that reported persistent endothelial activation markers in the ART era [44–47]. However, our findings are in contrast to a US-based study that demonstrated normalization of these markers after 12 months of ART [18]. While the root drivers of persistent elevated endothelial activation during ART are unclear, the fact that most of our participants had an undetectable viral load suggests that factors beyond HIV viremia that are unique to PWH, including residual inflammation of the vascular endothelium related to co-infections, ART toxicity, and gut microbial translocation, are likely to be important contributors. Unfortunately, data from SSA are limited regarding potential causes and specific inflammatory pathways that may lead to endothelial damage in PWH.

An important finding in this study was that sCD14, a monocyte activation and an indirect marker of microbial translocation, was associated with endothelial activation in PWH independent of traditional CVD risk factors and HIV-related characteristics. These findings are important because sCD14 in particular can also predict risk for cardiovascular events and mortality in the general population [48, 49]. Moreover, several studies from high-income countries have also linked sCD14 with carotid atherosclerosis and mortality among PWH on stable ART [31, 33, 38, 50, 51]. Likewise, a recent study from Uganda also reported an increased risk of future subclinical atherosclerosis among PWH with elevated sCD14 after initiation of ART [52]. However, our study is the first to demonstrate a relationship between sCD14 and endothelial activation among virally suppressed PWH in SSA, an issue that warrants further investigation. However, our results confirm prior findings from

our collaborators in the United States that demonstrated an association between sCD14 and sVCAM-1 or sICAM-1 among PWH on suppressive ART [44, 46].

The source of monocyte activation (sCD14) remains unclear in this setting. CD14 receptors have been shown to participate in TLR-mediated immune responses to microbial products (LPS, lipoarabinomannan, and peptidoglycan) and viruses including cytomegalovirus [53, 54]. Likewise, proinflammatory cytokines including interleukin 6 have also been shown in vitro to induce sCD14 production comparable to LPS [54, 55]. To further explore potential contributors to monocyte activation and endothelial activation, we measured I-FABP, a systemic marker of gut epithelial cell death also used as a surrogate marker of gut microbial translocation. Contrary to our expectation, we did not find any correlation between I-FABP and sCD14. These findings contrast with those of other studies in the United States and Europe that demonstrated positive correlations between I-FABP with sCD14; however, this relationship was only demonstrated for PWH on stable ART with a history of AIDS and for untreated PWH [56]. This lack of an association between I-FABP and sCD14 in our cohort suggests that there is more than 1 pathway driving monocyte activation leading to endothelial activation in this setting [54]. It is also important to point out that unlike the previous studies, all our HIV-positive participants were on co-trimoxazole prophylaxis. Co-trimoxazole has been reported to reduce systemic and intestinal inflammation via antibiotic effects on the microbiome and by blunting immune and epithelial cell activation [57]. Likewise, I-FABP and sCD14 have not been reliably correlated in PWH on co-trimoxazole prophylaxis [58, 59]. It is therefore too early to exclude the role of microbial translocation in monocyte activation and endothelial activation in this setting. Further investigation using more

specific measures of microbial translocation (eg, 16sDNA and endoCab) is warranted to confirm these findings.

Our study has several strengths. It is the first study to assess the association between markers of monocyte activation and endothelial activation among both virally suppressed PWH and HIV-negative individuals in Africa. The relatively matched HIV-negative persons allowed for direct comparison between groups. Inclusion of women makes our results more generalizable. We acknowledge certain limitations to our study. For example, the use of I-FABP instead of LPS as a surrogate marker of microbial translocation as a measurement of LPS is technically difficult with high variability, as reported in previous studies. Additionally, this was a cross-sectional study, and therefore we cannot assume causality or control for unmeasured confounders.

CONCLUSIONS

Overall, we reported here that sCD14 is strongly associated with markers of endothelial activation in African PWH on stable ART. Our observations were independent of traditional CVD risk factors and suggest that monocyte activation may partially explain the heightened risk for endothelial dysfunction and subsequent CVD in this population. As we did not find significant interactions between sCD14 and HIV in relation to endothelial activation, we posit that similar immune activation pathways exist in PWH and HIV-negative adults in this setting. Future studies are needed to investigate potential drivers of monocyte activation among PWH of African descent.

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