GUT INTEGRITY MARKERS AND ASSOCIATIONS WITH ADIPOSITY IN PEOPLE WITH AND WITHOUT HIV

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ABSTRACT

Background: Fat accumulation after ART initiation remains a serious problem in people with HIV (PWH), but little is known about its pathogenesis. Gut barrier dysfunction may play a role, but data are inconsistent and lack adequate control groups. We compared gut integrity markers in PWH before and after ART to an uninfected control group and assessed associations between gut integrity markers and body composition.
Methods: Data from uninfected controls (matched by age, sex, and race) were prospectively collected and compared to data from participants prospectively enrolled in a treatment initiation study, ACTG A5260s, at 2 timepoints: pre-ART and 96 weeks after suppressive ART. Plasma levels of gut integrity markers, zonulin, intestinal fatty-acid binding protein (I-FABP), lipopolysaccharide binding protein (LBP) and beta-D-glucan (BDG), were measured by ELISA. Body composition was assessed by whole-body DXA. Groups were compared using logistic or linear regression with adjustment for matching factors, and associations among controls were assessed using linear regression models.
Results: 234 PWH and 116 controls were included. Groups were similar in age and race (PWH: mean 38 yrs, 65% white, non-Hispanic), but PWH included more men (90% vs 80%; P=0.01). PWH pre- and post-ART had significantly higher levels of I-FABP and zonulin (mean difference: 0.37 to 0.59 log10 pg/mL and 0.54 to 0.56 log10 ng/mL, resp), but lower levels of LBP (mean difference: 2.65 to 2.66 log10 ng/mL) vs controls (all P<0.001). PWH had similar levels of BDG pre-ART, but higher levels post-ART vs controls (mean difference: 0.14 log10 pg/ml, P=0.004). In all models for controls, LBP, I-FABP and BDG showed associations with body composition measures (Table); however, associations with SAT were slightly attenuated when adjusted for sex. In PWH post-ART, I-FABP was significantly associated with outcomes in both unadjusted and adjusted models with effect sizes larger in magnitude than in controls (Table); limited associations were observed with I-FABP at the pre-ART time point.
Conclusions: Levels of gut integrity markers, I-FABP and zonulin, were higher in PWH both pre- and post-ART, and BDG was higher in PWH post-ART. Gut integrity markers showed significant associations with several body composition measures in uninfected controls, but the strongest associations were seen with I-FABP among PWH on suppressive ART. I-FABP levels may help predict deleterious fat changes after ART initiation.

BACKGROUND

- Weight gain, fat accumulation (especially abdominal fat), and insulin resistance frequently occur in people with HIV (PWH), particularly with antiretroviral therapy (ART), and is a substantial threat to the success of modern treatment; however, the etiology of this phenomenon is ill-defined.
- HIV-associated inflammation and immune activation appear to play a role, as markers of immune activation are directly associated with visceral fat accumulation and incidence of diabetes among ART-treated PWH, but the relative drivers of the enhanced inflammatory state and resulting pathogenesis are poorly understood.
- In the general population, reduced gut barrier integrity and products of microbial translocation appear to play a role in the etiology of metabolic syndromes like obesity and diabetes.
- HIV induces a significant disruption in gut barrier integrity with subsequent increased microbial translocation that contributes to the inflammatory state among PWH.
- We previously showed that baseline levels of the gut integrity marker, I-FABP, were associated with increases in visceral adipose tissue, total adipose tissue, and body mass index over 96 weeks, regardless of treatment, and 96-week BDG levels were associated with changes in total and trunk fat over 96 weeks.
- To date, however, no study has compared markers of gut integrity in PWH, pre- or post-ART, to people without HIV or determined the differences in relationships between markers of gut integrity, inflammation/immune activation, and measures of body composition and insulin resistance.

OBJECTIVES

- To assess whether markers of gut integrity differ between people without HIV and PWH who are naïve to treatment or after ART-induced virologic suppression
- To compare associations between gut integrity markers and measures of body composition and insulin resistance among people without HIV to PWH, pre-and post-ART
- To compare associations between markers of gut integrity and systemic inflammation/immune activation among people without HIV to PWH, pre-and post-ART

METHODS

- **STUDY DESIGN / STUDY POPULATION**
  - A5260s is a metabolic sub-study of A5257, in which ART-naïve PWH were randomized to TDF/FTC + either ATV/r, DRV/r, RAL for 96 weeks.
  - 234 participants continued on their randomized treatment, achieved virologic by 24 weeks, remained suppressed through week 96, and were included in this current analysis.
  - People without HIV were enrolled and underwent similar testing and data collection for a single cross-sectional time point.
  - People without HIV were compared to PWH at two time points: prior to starting ART (pre-ART, week 0 from A5260s) and after suppressed on ART (supp ART, week 96 from A5260s).
- **STUDY ASSESSMENTS**
  - **Clinical and Laboratory Evaluation:** height/weight (for calculations of body mass index (BMI)), mid-waist circumference, fasting glucose and insulin (for calculations of insulin resistance by HOMA-IR), HIV RNA, CD4
  - **Gut Integrity Markers:** measured from stored plasma by enzyme-linked immunosorbent assays (ELISA)
    - **Zonulin:** marker of intestinal permeability
    - **Intestinal fatty acid binding proteins (I-FABP):** marker of enterocyte damage
    - **Lipopolysaccharide-binding protein (LBP):** marker of microbial (bacterial) translocation
    - **(1→3)-β-D-Glucan (BDG):** marker of microbial (fungal) translocation
  - **Body Composition:**
    - **Whole-body dual-energy absorptiometry (DXA):** total body fat, trunk fat
    - **Single-slice abdominal CT scan:** visceral adipose tissue (VAT), subcutaneous abdominal tissue (SAT)
  - **Soluble Inflammation/Immune Activation:** measured from stored plasma
    - **Interleukin-6 (IL-6)**: ELISA
    - **High-sensitivity C-reactive protein (hsCRP):** nephelometry
    - **D-dimer:** immunoturbidometric methods
    - **Soluble CD163 (sCD163):** ELISA
    - **Soluble CD14 (sCD14):** ELISA
  - **Cellular Inflammation/Immune Activation:** Cryopreserved PBMCs were assessed by flow cytometry and categorized based on size, granularity and the expression of specific phenotypes on the cell surface
    - **CD4+ T-cell activation:** CD38+HLA-DR+
    - **CD8+ T-cell activation:** CD38+HLA-DR+
    - **Inflammatory monocytes:** CD14+CD16+
    - **Patrolling monocytes:** CD14dimCD16+
- **STATISTICAL ANALYSIS**
  - Non-normal data were log-transformed on a log-10 scale
  - **Group comparisons:** appropriate two-sample and three-sample tests; no adjustments made for multiple testing; adjustments were made for age, sex, race where indicated
  - **Bivariate correlations:** Spearman correlation coefficients
  - **Regressions:** linear regression models with adjustment for confounding variables were used to quantify associations between gut markers and outcomes
  - P<0.05 considered significant for all analyses.

RESULTS

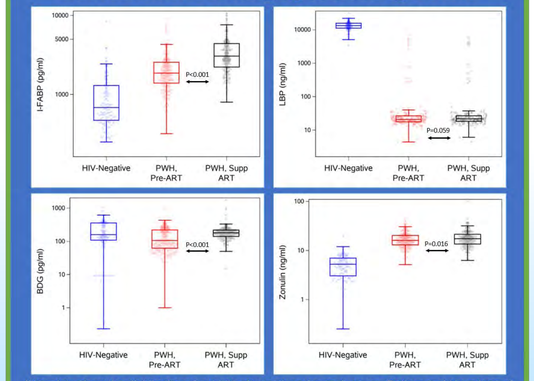
Baseline Characteristics

Mean (SD) or no. (%)	HIV-Negative (N=116)	PWH (N=234)	P
Clinical and Sociodemographics			
Age, years	39 (13)	38 (11)	0.270
Male sex	93 (80%)	210 (90%)	**0.013**
Black race	40 (34%)	70 (30%)	0.673
Hispanic (regardless of race)	6 (5%)	45 (19%)	**0.012**
Current smoking (30 days)	39 (34%)	77 (33%)	0.894†
Excessive alcohol use* (30 days)	24 (21%)	68 (29%)	**0.042†**
Current illicit drug use** (1 year)	39 (34%)	95 (41%)	0.206†
Physical Activity			
Low	0 (0%)	39 (17%)	**<0.001**
Moderate	0 (0%)	182 (78%)	
High	108 (93%)	0 (0%)	
HIV Variables			
CD4+ cell count, cells/mm^3	--	327 (178)	--
HIV RNA, copies/mL (log_{10})	--	4.5 (0.68)	--
Treatment			
ATV/r	--	68 (29%)	--
DRV/r	--	84 (36%)	
RAL	--	82 (35%)	

*Defined as having 4 or more drinks in a single occasion or having 8 or more drinks per week for women and 5 or more drinks in a single occasion or having 15 or more drinks per week for men. **Includes marijuana, cocaine, or amphetamines. †P values for smoking, alcohol use, drug use after adjusting for age, sex, and race = 0.990, 0.107, and 0.326, respectively. P values <0.05 are bold-faced.

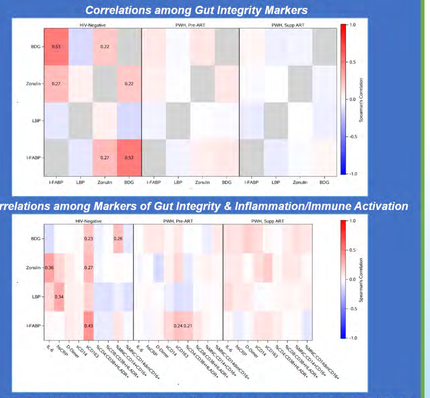
RESULTS

Distribution of Gut Integrity Markers by Cohort



Jitter plots show the distribution of gut integrity markers for each group. Bottom and top edges of the box represent 25th and 75th percentiles, respectively, the center horizontal line is drawn at the median, and the bottom and top vertical lines (whiskers) extend to the 10th and 90th percentiles, respectively.

Relationships between Gut Integrity Markers and Variables of Interest by Cohort



Heat map illustrating correlations by study group. Blue indicates negative correlations, and red indicates positive correlations. Only correlations reaching statistical significance ($P \leq 0.05$) are included in the figure.

Characteristics by Cohort

Characteristic	HIV-Negative	PWH, Pre-ART	PWH, Supp ART
	Mean (SD)	Mean (SD)	Mean (SD)
Gut Integrity Markers			
I-FABP, pg/mL (log_{10})	2.90 (0.30)	3.27 (0.22)	3.49 (0.21)
LBP, ng/ml (log_{10})	4.11 (0.14)	1.47 (0.55)	1.46 (0.50
Zonulin, ng/ml (log_{10})	0.66 (0.27)	1.21 (0.15)	1.24 (0.16)
BDG, pg/mL (log_{10})	2.11 (0.63)	2.04 (0.35)	2.24 (0.21)
Body Composition and Insulin Resistance			
VAT area, cm^2	88.61 (55.12)	91.90 (73.94)	96.41 (61.94)
SAT area, cm^2	209.57 (118.30)	231.24 (154.89)	254.11 (161.65)
Trunk fat, kg	11.86 (6.89)	10.31 (5.86)	11.91 (6.79)
Total fat, kg	25.40 (11.54)	20.20 (10.68)	22.69 (12.16)
BMI, kg/m^2	27.20 (5.87)	25.94 (5.19)	26.98 (5.89)
Avg mid-WC, cm	91.71 (15.67)	91.12 (13.18)	93.91 (14.87)
HOMA-IR (log_{10})	0.17 (0.31)	-0.10 (0.35)	0.15 (0.37)
Soluble Inflammation/Immune Activation Markers			
IL6, pg/mL (log_{10})	0.18 (0.41)	0.27 (0.29)	0.21 (0.36)
hsCRP, pg/ml (log_{10})	0.12 (0.64)	0.20 (0.48)	0.11 (0.54)
D-dimer, pg/ml (log_{10})	-0.56 (0.32)	-0.55 (0.48)	-0.74 (0.43)
sCD14, ng/ml (log_{10})	3.15 (0.09)	3.24 (0.11)	3.21 (0.10)
sCD163, ng/ml (log_{10})	2.64 (0.19)	3.04 (0.23)	2.79 (0.17)
Cellular Inflammation/Immune Activation Markers			
%CD4+ CD38+HLADR+	1.47 (0.86)	22.89 (16.41)	8.21 (6.41)
%CD8+ CD38+HLADR+	3.56 (3.15)	44.24 (15.60)	16.40 (9.62)
%MNC CD14dimCD16+	8.74 (6.42)	1.46 (2.75)	1.40 (4.85)
%MNC CD14+CD16+	10.88 (7.15)	10.33 (6.53)	9.12 (5.04)

Mean Differences in Characteristics between Cohorts

Characteristic	HIV-Negative v. PWH Pre-ART			HIV-Negative v. PWH Supp ART		
	Unadj Mean (95% CI)	P	Adj Mean (95% CI)†	Unadj Mean (95% CI)	P	Adj Mean (95% CI)†	P
Gut Integrity Markers							
I-FABP, pg/mL (log_{10})	-0.37 (-0.43, -0.32)	**<0.001**	-0.37 (-0.42, -0.31)	**<0.001**	-0.59 (-0.65, -0.54)	**<0.001**	-0.58 (-0.64, -0.53)	**<0.001**
LBP, ng/ml (log_{10})	2.64 (2.54, 2.74)	**<0.001**	2.64 (2.54, 2.74)	**<0.001**	2.65 (2.56, 2.74)	**<0.001**	2.66 (2.56, 2.75)	**<0.001**
Zonulin, ng/ml (log_{10})	-0.55 (-0.59, -0.5)	**<0.001**	-0.55 (-0.59, -0.5)	**<0.001**	-0.57 (-0.62, -0.53)	**<0.001**	-0.57 (-0.62, -0.52)	**<0.001**
BDG, pg/mL (log_{10})	0.06 (-0.04, 0.17)	0.238	0.07 (-0.03, 0.18)	0.180	-0.13 (-0.23, -0.04)	**0.005**	-0.12 (-0.22, -0.03)	**0.010**
Body Composition and Insulin Resistance								
VAT area, cm^2	6.71 (-5.16, 18.58)	0.267	5.78 (-4.86, 16.42)	0.286	-7.8 (-21.31, 5.72)	0.257	-8.42 (-20.62, 3.79)	0.176
SAT area, cm^2	-21.67 (-53.84, 10.5)	0.186	-39.13 (-69.12, -9.13)	**0.011**	-44.53 (-78.06, -11.01)	**0.009**	-60.16 (-92.75, -27.57)	**<0.001**
Trunk fat, kg	1.54 (0.15, 2.93)	**0.030**	1.01 (-0.32, 2.34)	0.137	-0.06 (-1.6, 1.48)	0.942	-0.5 (-2, 1.01)	0.516
Total fat, kg	5.19 (2.74, 7.65)	**<0.001**	3.96 (1.66, 6.26)	**<0.001**	2.71 (0.01, 5.4)	**0.049**	1.58 (-1.02, 4.17)	0.233
BMI, kg/m^2	1.26 (0.05, 2.47)	**0.041**	0.77 (-0.4, 1.95)	0.197	0.22 (-1.1, 1.54)	0.739	-0.24 (-1.53, 1.06)	0.720
Avg mid-WC, cm	0.59 (-2.56, 3.74)	0.712	-0.19 (-3.25, 2.86)	0.901	-2.2 (-5.61, 1.21)	0.205	-2.81 (-6.15, 0.53)	0.099
HOMA-IR (log_{10})	0.27 (0.19, 0.34)	**<0.001**	0.27 (0.19, 0.35)	**<0.001**	0.01 (-0.07, 0.09)	0.743	0 (-0.07, 0.08)	0.912
Soluble Inflammation/Immune Activation Markers								
IL6, pg/mL (log_{10})	-0.09 (-0.16, -0.01)	**0.023**	-0.11 (-0.18, -0.04)	**0.002**	-0.03 (-0.11, 0.06)	0.533	-0.05 (-0.14, 0.03)	0.192
hsCRP, pg/ml (log_{10})	-0.08 (-0.2, 0.04)	0.177	-0.09 (-0.22, 0.03)	0.122	0.01 (-0.12, 0.14)	0.897	-0.02 (-0.15, 0.1)	0.711
D-dimer, pg/ml (log_{10})	-0.01 (-0.11, 0.09)	0.832	-0.05 (-0.14, 0.04)	0.291	0.18 (0.09, 0.27)	**<0.001**	0.15 (0.06, 0.24)	**<0.001**
sCD14, ng/ml (log_{10})	0.09 (0.06, 0.11)	**<0.001**	0.09 (0.06, 0.11)	**<0.001**	0.06 (0.03, 0.08)	**<0.001**	0.06 (0.03, 0.08)	**<0.001**
sCD163, ng/ml (log_{10})	-0.4 (-0.45, -0.35)	**<0.001**	-0.4 (-0.45, -0.35)	**<0.001**	-0.15 (-0.19, -0.11)	**<0.001**	-0.15 (-0.18, -0.11)	**<0.001**
Cellular Inflammation/Immune Activation Markers								
%CD4+ CD38+HLADR+	-21.41 (-24.5, -18.33)	**<0.001**	-21.81 (-24.96, -18.67)	**<0.001**	-6.74 (-7.95, -5.53)	**<.001**	-6.85 (-8.08, -5.61)	**<0.001**
%CD8+ CD38+HLADR+	-40.68 (-43.64, -37.72)	**<0.001**	-40.68 (-43.69, -37.66)	**<0.001**	-12.84 (-14.7, -10.98)	**<.001**	-13.18 (-15.05, -11.3)	**<0.001**
%MNC CD14dimCD16+	7.28 (6.27, 8.29)	**<0.001**	7.25 (6.22, 8.28)	**<0.001**	7.34 (6.07, 8.61)	**<.001**	7.37 (6.07, 8.67)	**<0.001**
%MNC CD14+CD16+	0.55 (-1.01, 2.11)	0.492	0.25 (-1.33, 1.83)	0.757	1.76 (0.39, 3.12)	**0.012**	1.49 (0.12, 2.86)	**0.033**

†Adjusted for age, sex and race. P values <0.05 are bold-faced.

Regression Estimates for Associations between Outcome Measures and Gut Integrity Markers

I-FABP and LBP

Outcome	Uninfected Controls		PWH (Pre-ART)		PWH (Supp ART)	
	Estimate (95% CI)	P	Estimate (95% CI)	P	Estimate (95% CI)	P
I-FABP						
VAT Area (cm^2)	-7.34 (-17.5, 2.84)	0.16	-0.84 (-10.2, 8.50)	0.86	-4.57 (-16.6, 7.44)	0.45
SAT Area (cm^2)	-23.2 (-44.8, -1.58)	**0.04***	-14.4 (-42.2, 13.41)	0.31	-51.2 (-82.2, -20.2)	**0.001**
Trunk Fat (kg)	-0.95 (-2.22, 0.33)	0.14	-0.78 (-1.83, 0.27)	**0.15****	-2.12 (-3.38, -0.86)	**0.001**
Total Fat (kg)	-1.99 (-4.11, 0.12)	0.07	-1.45 (-3.38, 0.47)	**0.14****	-3.94 (-6.21, -1.68)	**<0.001**
BMI (kg/m^2)	-0.72 (-1.81, 0.37)	0.19	-0.69 (-1.62, 0.25)	**0.15****	-2.02 (-3.11, -0.92)	**<0.001**
WC (cm)	-2.28 (-5.17, 0.61)	0.12	-1.61 (-4.02, 0.80)	**0.19****	-4.57 (-7.32, -1.82)	**0.001**
HOMA-IR (log_{10})	0.01 (-0.05, 0.07)	0.74	-0.05 (-0.11, 0.02)	0.15	0.01 (-0.06, 0.07)	0.78
LBP						
VAT Area (cm^2)	26.07 (4.46, 47.68)	**0.02**	2.20 (-1.50, 5.89)	0.24	3.51 (-1.52, 8.53)	0.17
SAT Area (cm^2)	56.48 (10.12, 102.8)	**0.02**	-1.54 (-12.6, 9.51)	0.78	-3.45 (-16.9, 9.97)	0.61
Trunk Fat (kg)	3.72 (1.04, 6.40)	**0.007**	0.12 (-0.30, 0.54)	0.57	-0.08 (-0.64, 0.48)	0.78
Total Fat (kg)	5.80 (1.29, 10.31)	**0.01**	0.29 (-0.48, 1.05)	0.46	-0.28 (-1.28, 0.72)	0.59
BMI (kg/m^2)	2.74 (0.44, 5.05)	**0.02**	0.16 (-0.21, 0.53)	0.41	-0.21 (-0.69, 0.28)	0.40
WC (cm)	6.77 (0.60, 12.94)	**0.03**	0.30 (-0.65, 1.25)	0.53	0.01 (-1.20, 1.23)	0.98
HOMA-IR (log_{10})	0.10 (-0.02, 0.23)	0.10	-0.01 (-0.04, 0.01)	0.41	0.00 (-0.03, 0.03)	0.85

BDG and Zonulin

Outcome	Uninfected Controls		PWH (Pre-ART)		PWH (Supp ART)	
	Estimate (95% CI)	P	Estimate (95% CI)	P	Estimate (95% CI)	P
BDG						
VAT Area (cm^2)	-4.71 (-9.48, 0.07)	0.05	2.57 (-3.19, 8.33)	0.41	6.94 (-4.95, 18.84)	0.25
SAT Area (cm^2)	-8.84 (-19.1, 1.45)	0.09	-5.81 (-23.0, 11.42)	0.51	18.07 (-13.4, 49.49)	0.26
Trunk Fat (kg)	-0.45 (-1.05, 0.15)	0.13	-0.06 (-0.72, 0.59)	0.85	0.92 (-0.39, 2.23)	0.17
Total Fat (kg)	-0.81 (-1.82, 0.19)	0.13	-0.27 (-1.47, 0.93)	0.65	1.32 (-1.04, 3.68)	0.27
BMI (kg/m^2)	-0.54 (-1.05, -0.03)	**0.04***	-0.22 (-0.80, 0.36)	0.46	0.59 (-0.55, 1.73)	0.31
WC (cm)	-1.27 (-2.63, 0.09)	0.07	-0.38 (-1.86, 1.10)	0.61	1.80 (-1.06, 4.67)	0.22
HOMA-IR (log_{10})	-0.01 (-0.04, 0.02)	0.4	0.00 (-0.03, 0.04)	0.80	0.03 (-0.04, 0.10)	0.40
Zonulin						
VAT Area (cm^2)	0.55 (-10.6, 11.73)	0.92	6.07 (-7.15, 19.29)	0.37	14.06 (-0.99, 29.11)	0.07
SAT Area (cm^2)	8.27 (-15.7, 32.22)	0.50	17.40 (-22.0, 56.84)	0.39	29.21 (-10.9, 69.36)	0.15
Trunk Fat (kg)	0.82 (-0.57, 2.21)	0.24	0.68 (-0.82, 2.18)	0.37	1.11 (-0.57, 2.79)	0.19
Total Fat (kg)	1.14 (-1.19, 3.47)	0.33	0.66 (-2.08, 3.40)	0.64	1.55 (-1.47, 4.57)	0.31
BMI (kg/m^2)	0.79 (-0.39, 1.97)	0.19	0.36 (-0.97, 1.69)	0.60	0.59 (-0.87, 2.05)	0.43
WC (cm)	2.31 (-0.84, 5.46)	0.15	1.24 (-2.14, 4.61)	0.47	2.05 (-1.61, 5.71)	0.27
HOMA-IR (log_{10})	0.04 (-0.03, 0.10)	0.27	0.01 (-0.10, 0.08)	0.88	0.02 (-0.07, 0.11)	0.69

Non-normal data were log-transformed on the log-10 scale. Out marker estimates are presented as per 0.3 log_{10} units, which is equivalent to a 2-fold difference. P values <0.05 are bold-faced.
P values remained qualitatively the same (<0.05 or ≥0.05) after adjustments for age, sex, race, smoking, drug use and excessive alcohol use unless otherwise noted.
*P value no longer significant after adjustments. **P value significant after adjustments.

SUMMARY OF RESULTS

- I-FABP and zonulin, markers of enterocyte damage and intestinal permeability, respectively, were significantly higher in PWH, both pre-ART and after ART-induced virologic suppression, compared to people without HIV; whereas BDG, a marker of fungal translocation, was only significantly higher in PWH after ART-induced virologic suppression compared to people without HIV. On the other hand, LBP, a marker of bacterial translocation, was significantly lower in PWH, both pre-ART and suppressed on ART, compared to people without HIV.
- Among people without HIV, there were a number of significant correlations among gut integrity markers and between markers of gut integrity markers and inflammation/immune activation; however, there were few significant correlations in PWH. The only significant correlations were between I-FABP and sCD163 and %CD4+ T-cells expressing CD38+HLADR+ in PWH pre-ART.
- I-FABP was significantly negatively associated with all measures of body composition (with the exception of VAT area) in PWH on suppressive ART; whereas, similar significant associations were seen in PWH pre-ART but only after adjusting for confounders (except SAT area that remained non-significant). No other gut integrity markers were significantly associated with outcome measures in PWH.
- Among people without HIV, LBP was significantly associated with all measures of body composition. Few other gut integrity markers showed significant associations with outcomes measures except for I-FABP with SAT area and BDG with BMI (which were no longer significant after adjusting for confounders).

CONCLUSIONS

- Enterocyte damage and intestinal permeability are higher in PWH compared to people without HIV and persist even after virologic suppression with ART. In fact, enterocyte damage, intestinal permeability and fungal translocation appear to increase after successful ART treatment, whereas bacterial translocation remains relatively stable.
- In this population of people without HIV, bacterial translocation appears to be higher than in PWH, but may be related to the poor health/diet in this cohort that could negatively affect the gut microbiome and increase microbial translocation (as evidenced by the high median BMI and strong positive associations between LBP and all measures of body composition).
- A lack of strong correlations among gut integrity markers and between gut integrity markers and systemic inflammation/immune activation demonstrates the complex nature of the enhanced inflammatory state in PWH.
- However, fat accumulation in PWH appears to be strongly related to the degree of pre-treatment enterocyte damage, which suggests that initial HIV-related gut damage and loss of normal gut integrity are key drivers of adipocyte dysfunction.
- Measuring pre-treatment levels of I-FABP may help assess risk of abnormal fat accumulation in PWH or could be used to assess the effects of future treatments designed to treat HIV-associated gut injury.

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