I-FABP is Elevated and Inversely Related to Body Fat in People Living with HIV

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Background

- Chronic inflammation persists in people living with HIV (PLHIV) despite HIV viral suppression and improved peripheral CD4+ count and has been attributed to non-HIV/AIDS defining disease processes.
- The gastrointestinal mucosa has been identified as a harbor of residual viremia and intestinal CD4+ cells remain low despite ART, thus contributing to gut mucosal damage and chronic inflammation.
- Intestinal fatty acid binding protein (I-FABP) has been identified as a marker of intestinal damage and it has been associated with obesity in non-HIV populations.
- The aim of the study was to investigate if there is a relationship between GI mucosal damage and adipose tissue derangements in HIV-infected participants.

Methods

- Observational study of 154 men and women with chronic HIV infection (mean age 47±7) and 69 HIV-negative controls (mean age 46±7) from the same communities.
- Anthropometric measurements were measured using standardized methods by bionutritionists. A cross-sectional abdominal CT scan (at the L4 pedicle) was performed to assess visceral and subcutaneous adipose tissue areas (VAT and SAT respectively).
- I-FABP was measured by ELISA (R&D Systems).
- Nutritional data was obtained using 4-day food records analyzed by Nutrition Data System for Research (NDSR).
- Continuous and normally distributed variables were analyzed using student t test for 2 group comparisons. Non-normally distributed variables were analyzed using Wilcoxon rank sum test for 2 group comparisons, Kruskal-Wallis test for multi-group comparisons. Spearman rho was used to assess relationships with I-FABP as it was not normally distributed.

	HIV negative (n=69)	HIV infected (n=154)	*P* value
Demographics			
Age (mean, years)	45.8 ±7.0	46.9.1±6.9	0.28
Gender, male (%)	41 (59.4)	102(66.2)	0.33
Race n (%)			0.36
Asian	3(4.4)	1(0.7)	
White	34 (49.3)	77(50.0)	
Black/African American	24 (34.8)	54(35.1)	
American Indian	2(2.9)	4(2.6)	
Hispanic	4(5.8)	16(10.4)	
More than one race	2(2.9)	2(1.3)	
Active smoker (%)	37.7	42.5	0.50
Systolic BP (mmHg)	116.7 ±14.4	118.5 ±13.2	0.38
Diastolic BP (mmHg)	76.0 ±9.3	75.8 ±8.9	0.90
HIV related Parameters			
Length since diagnosis of HIV (years)		14.1 ±6.30	
Absolute CD 4 count (cells/m3)		552.8 ±290	
Viral load (median, copies/mL)[a]		49 [47,49]	
Currently on ART (%)		96.1	
Suppressed Viral load (%)		82	
Metabolic Parameters			
BMI (kg/m2)	27.7 ±4.80	26.8 ±5.1	0.20
VAT (cm2)	127 ±100	138 ±106	0.48
SAT (cm2)	270 ±154	218 ±135	0.02*
Hemoglobin A1c (%)	5.65 ±0.55	5.51±0.78	0.14
Total cholesterol (mg/dL)	181 ±35	181 ±40	0.94
LDL (mg/dL)	107±31	103±33	0.32
HDL (mg/dL)	53±15	52 ±18	0.72
Triglycerides (median, mg/dL)	84 [63, 126]	96 [75, 168]	0.006*
Statins (%)	4	13	0.07
I-FABP (median, pg/mL)	1633 [1149, 2127]	3373 [1976, 4527]	<.0001*

Table 1: baseline characteristics of HIV infected and HIV negative controls. ᵃ The limit of detection for our assay changed during the course of the study from 50 to 48 copies/mL. Thus, those with undetectable viral load were inputted as having the 47 or 49 copies/mL. * Symbolizes significant correlation with a p value <0.05.

	ρ	*p*
MCP-1		
All participants	0.19	0.005*
HIV+	0.12	0.15
HIV-	0.21	0.20
CXCL10		
All participants	0.30	0.008*
HIV+	0.17	0.25
HIV-	0.32	0.11
sCD14		
All participants	0.13	0.06
HIV+	0.07	0.41
HIV-	0.11	0.38
IL-6		
All participants	-0.07	0.37
HIV+	-0.03	0.74
HIV-	-0.13	0.38
sCD163		
All participants	0.26	<0.0001*
HIV+	0.08	0.31
HIV-	0.30	0.01*
LPS		
All participants	0.16	0.03*
HIV+	0.05	0.61
HIV-	0.19	0.16
Adiponectin		
All participants	0.20	0.02*
HIV+	0.20	0.04*
HIV-	0.20	0.22
Duration of statin use		
All participants	-0.12	0.09
HIV+	-0.21	0.02*
HIV-	-0.07	0.58

Table 3: correlation between serum I-FABP and inflammatory markers, adiponectin, and duration of statin use. * Symbolizes significant correlation with a p value <0.05.

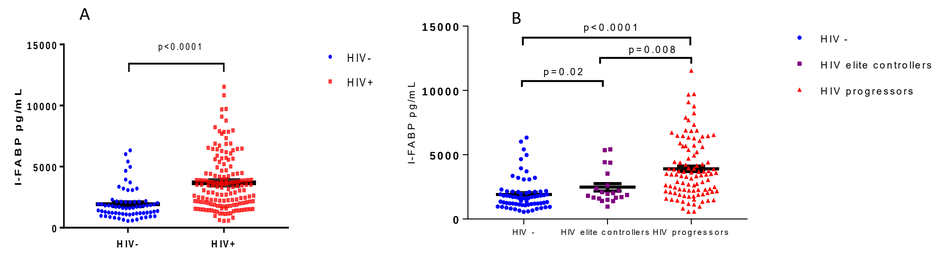


Figure 1:A. serum I-FABP and HIV status. Figure 1B Serum I-FABP in HIV negative, HIV Elite Controllers, and HIV Progressors

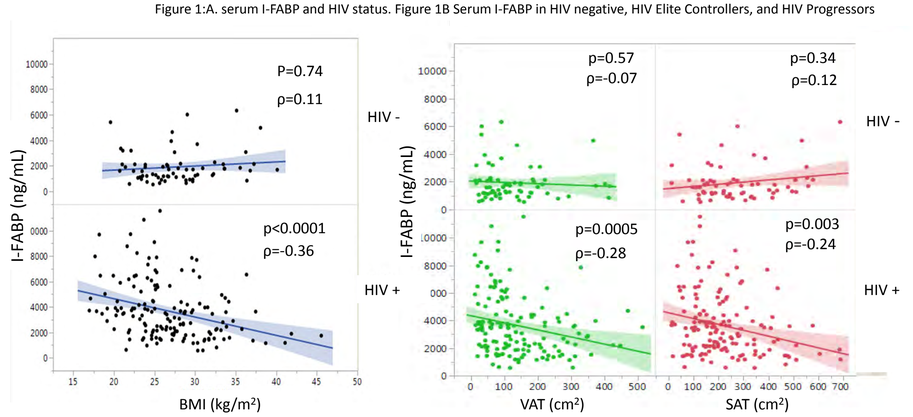


Figure 2:Serum I-FABP is Inversely correlated to BMI, VAT, and SAT in HIV

Nutritional Intake	HIV negative Median [IQR]	HIV infected Median [IQR]	p value
Total energy (kcal)	1946 [1334, 2570]	2077 [1576, 2793]	0.28
Total fat (g)	78 [47, 111]	81 [60, 109]	0.40
Total carbohydrate (g)	219 [165, 296]	247 [181, 340]	0.05
Total protein (g)	89 [62, 118]	86 [66, 114]	0.90
Total cholesterol (mg)	280 [188, 384]	288 [192, 400]	0.48
Total SFA (g)	26 [16, 35]	28 [20, 36]	0.19
Total MUFA (g)	29 [19, 42]	31 [22, 40]	0.60
Total PUFA (g)	15 [10, 21]	16 [10, 22]	0.70
Total sugar (g)	77 [46, 112]	104 [73, 156]	0.007*
Added sugar (g)	45 [30, 70]	63 [38, 107]	0.008*
Sucrose (g)	31 [18, 41]	38 [26, 66]	0.006*
Fructose (g)	15 [8, 28]	22 [12, 33]	0.03*

Table 4: Comparison of nutritional data based on food records between HIV negative controls and HIV infected individuals. * Symbolizes significant correlation with a p value <0.05.

Nutritional Intake	HIV negative, ρ	p value	HIV positive, ρ	p value
Total energy (kcal)	-0.11	0.41	0.10	0.26
Total fat (g)	-0.11	0.41	0.12	0.17
Total carbohydrate (g)	-0.11	0.40	0.12	0.18
Total protein (g)	-0.17	0.23	-0.06	0.55
Total cholesterol (mg)	-0.23	0.09	0.005	0.95
Total SFA (g)	-0.11	0.45	0.14	0.13
SFA 4:0	0.01	0.94	0.21	0.02*
SFA 6:0	-0.01	0.95	0.21	0.02*
SFA 8:0	-0.06	0.68	0.24	0.008*
SFA 10:0	-0.04	0.76	0.19	0.03*
SFA 12:0	0.01	0.97	0.20	0.03*
SFA 14:0	-0.03	0.83	0.16	0.09
SFA 17:0	-0.06	0.69	0.19	0.04*
SFA 20:0	-0.05	0.72	0.21	0.02*
SFA 22:0	-0.01	0.96	0.20	0.02*
Total MUFA (g)	-0.06	0.65	0.10	0.30
Total PUFA (g)	-0.15	0.27	0.20	0.03*
Total sugar (g)	-0.04	0.80	0.16	0.07
Added sugar (g)	-0.03	0.85	0.22	0.03*
Sucrose (g)	0.08	0.56	0.27	0.003*

Table 5: correlation between serum I-FABP and nutritional intake among HIV infected individuals and HIV negative controls. * Symbolizes significant correlation with a p value <0.05.

Conclusions

- People living with HIV have significantly elevated I-FABP compared to non HIV controls. HIV progressors have significantly higher I-FABP compared to elite controllers.
- Serum I-FABP was positively related to MCP-1, CXCL10, sCD163, LPS, and adiponectin among all participants.
- To our knowledge, this is the first report of the inverse relationship of serum I-FABP to BMI, VAT, and SAT in HIV infected individuals.
- There were no significant differences in total caloric, carbohydrate, protein, and fat intake between HIV infected and HIV negative groups. HIV-infected group had higher median intake of total and added sugar compared to HIV negative individuals. There was a positive correlation between serum I-FABP and added sugar and saturated fat intake in the HIV-infected group.

Limitations

- The cross-sectional design does not allow us to determine the direction of causality.

Future Directions

- Further research is needed to further understand the mechanism of the inverse relationship of I-FABP to BMI and adipose tissue in PLHIV.
- The role of added sugar and high saturated fat diet as a contributor of further gut mucosal damage in PLHIV will need to be evaluated.
- Effects of therapeutic strategies to ameliorate gut mucosal damage such as probiotics and glucagon-like peptide 2 (GLP-2) on body composition and I-FABP will further help elucidate mechanisms of the relationship between I-FABP and body fat and weight.
- GLP-2 is known to improve gut mucosal integrity and intestinal absorption animal studies and in people with short bowel syndrome. Thus, GLP-2 agonist is currently being investigated to assess its effects on intestinal integrity and body composition in PLHIV.

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