MARKERS OF IMMUNE ACTIVATION AND FUNCTION IN OBESE AND NON-OBESE SUBJECTS WITH HIV

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Background

- Obesity is an emerging health issue in people with HIV (PWH), with increasing prevalence described in cohorts from both high- and low-income countries[1,2].
- Both obesity and HIV are associated with systemic inflammation, contributing to the development of non-AIDS related complications, such as metabolic and cardiovascular co-morbidities[3-5].
- The additional impact of obesity on immune-mediated inflammation in PWH and the underlying molecular pathways are still poorly understood.

Objectives

- To explore associations between biomarkers of inflammation, immune activation and immune function and the obese phenotype in obese and non-obese PWH.

Methods

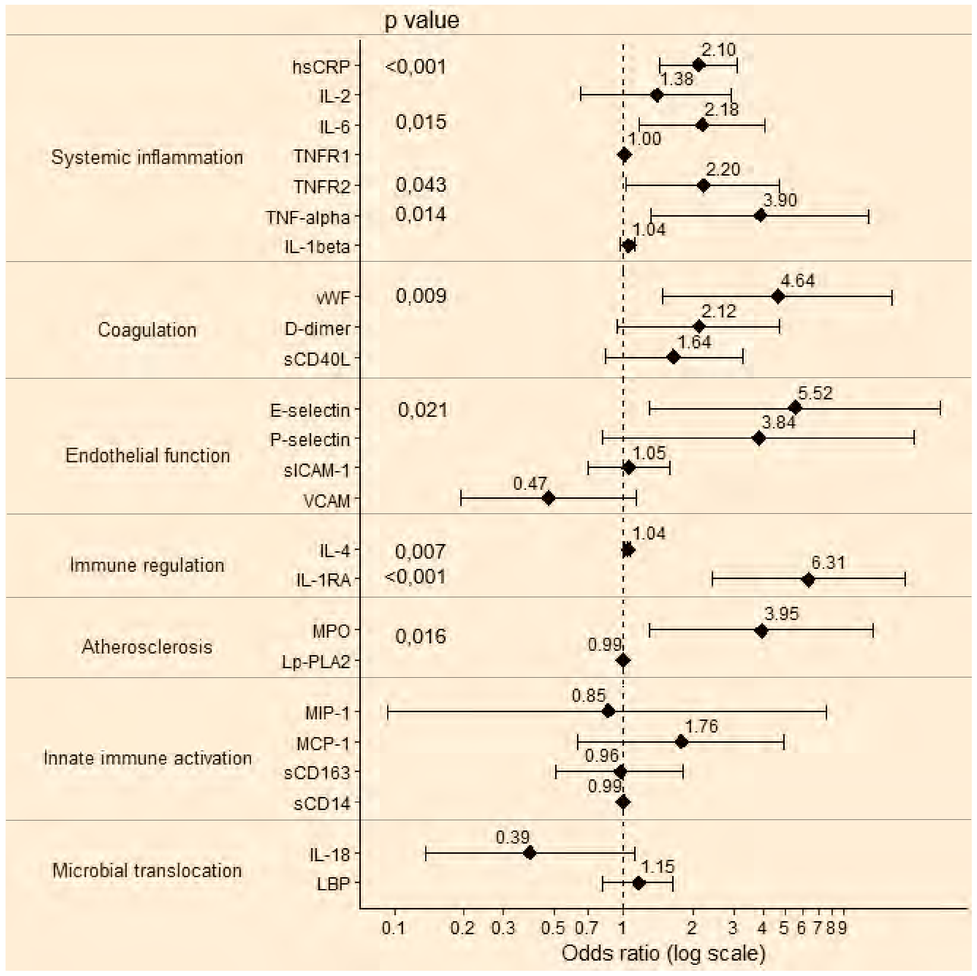
- Cross-sectional analysis conducted on plasma samples from PWH enrolled in the UCD Infectious Diseases (ID) Cohort, a multicentre prospective cohort.
- Obese and non-obese participants recruited in a 1:2 ratio for obese vs non-obese, matched for age, gender and ethnicity.
- 25 biomarkers covering pathways related to systemic inflammation and the development of co-morbidities in PWH were analysed on plasma samples using a bead-based, multiplex, quantitative ELISA assay (Luminex, R&D Systems).

Biomarkers functional group	Biomarkers analysed
Markers of systemic inflammation	hsCRP, IL-2, IL-6, TNFR1, TNFR2, TNF-α, IL-1β
Markers of coagulation	vWF, D-dimer, sCD40L
Markers of endothelial function	E-selectin, P-selectin, sICAM-1, VCAM
Markers of atherosclerosis	MPO, Lp-PLA2
Markers of immune regulation	IL-4, IL-1RA
Markers of innate immune activation	MIP-1α, MCP-1, sCD163, sCD14
Markers of microbial translocation	IL-18, LBP

- Associations between the obese phenotype and biomarkers were evaluated using logistic regression adjusted for age, gender, ethnicity, smoking status, NRTI backbone and use of INSTI.

Results

- 99 PWH on ART were included in the analysis, 33 obese and 66 non-obese:
  - ✓ Median [IQR] BMI was 33.63 [31.10; 36.06] for the obese group and 24.87 [23.34; 26.88] for the non-obese group
  - ✓ Obese and non-obese PWH were well matched for age, gender and ethnicity (table)
  - ✓ Overall, 63% of subjects were heterosexual, 18% MSM and 8% IDU
  - ✓ Use of INSTI was significantly higher in the obese compared to the non-obese group, whereas use of TDF/FTC was significantly higher in the non-obese compared to the obese group



Results (cont)

Patients' characteristics n (%) or median (IQR)	Obese (n=33)	Non-obese (n=66)	p value
Gender: Male	18 (54.54%)	37 (56.06%)	0,886
Age (years)	41 (36, 48)	41 (37.5, 48)	0,707
Ethnicity: African	15 (45.45%)	30 (45.45%)	1
Heterosexual	28 (84.85%)	52 (78.79%)	0.895
Duration of HIV (years)	10 (3.5, 14.5)	9 (3.75, 15.0)	0,876
Viral load, current (cp/mL)	40 (40, 40)	40 (40, 40)	0,649
CD4, current (cells/μL)	698 (501.5, 964.5)	606 (426.5, 764)	0,051
CD4, baseline (cells/μL)	320 (196.0, 590.0)	367.5 (227.25, 507.5)	0,967
Use of TDF/FTC	12 (36.36%)	38 (57.58%)	<0.001
Use of INSTI	19 (57.58%)	25 (37.88%)	<0.001

- 9 markers were significantly associated with obesity in adjusted analyses: hsCRP, IL-6, TNF-α, TNFR2, vWF, E-selectin, MPO, IL-4 and IL-1RA.
- Obese phenotype was characterised by increases in markers of systemic inflammation and immune regulation, and some of the markers of coagulation, endothelial function and atherosclerosis.
- In contrast, markers of innate immune activation and microbial translocation were not associated with the obese phenotype.

Conclusions

- In the first study of multiple biological patterns of inflammation in obese PWH, we observed changes in obesity associated with systemic inflammatory, vascular and coagulation pathways.
- In contrast, innate immune activation and microbial translocation, which have been previously associated with HIV infection, were not associated with the obese phenotype.
- How these distinct patterns of inflammation and immune activation contribute to the development of comorbidities in obese PWH remains to be determined.

References & Acknowledgments

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