INFLAMMATORY MARKERS SHOW DYNAMIC CHANGES IN ACUTE HIV AND PREDICT COGNITIVE OUTCOMES

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BACKGROUND

HIV-Associated Neurocognitive Disorder (HAND):

- Continues to be prevalent in persons who have achieved virologic suppression.
- Has been linked to inflammation in blood and CSF.

Our study analyzed relationships between viral load (VL), inflammatory cytokine levels in CSF and plasma, interval since estimated date of infection (I-EDI), and longitudinal Neurocognitive Performance Testing (NPT) in an early infection cohort with well-defined timing of HIV acquisition.

METHODS

Data Collection:

- In the *Sabes* study, HIV-negative participants were monitored for incident HIV infection, and randomized to immediate or deferred ART upon diagnosis.
- At diagnosis participants provided samples of plasma (N = 88) and CSF (N = 30), analyzed for levels of 33 proinflammatory biomarkers, as well as peripheral and CSF viral load.
- We calculated the estimated date of detectable infection; we used this and the enrollment date to provide an estimate of I-EDI.
- Participants underwent NPT at 12, 24, 48, 72, and 96 weeks.
- Longitudinal analyses of NPT included only participants who began ART immediately, and their baseline biomarker levels (plasma = 43, CSF = 13).

Statistics: Single linear regressions between:

- I-EDI as predictor of Log10-transformed baseline plasma and CSF VL, biomarker levels.
- Baseline biomarker levels as predictors of change in standardized NPT score from baseline (ΔNPT).
- Benjamini-Hochberg adjustment (BH) for multiple comparisons of biomarkers and ΔNPT.

Table 1: Cohort Characteristics

	Complete cohort	Immediate ART	Deferred ART
N	88	43	45
Mean Age (Years)	27.06	27.38	26.76
Mean I-EDI (days)	43.3	42.6	44
Mean Baseline Plasma VL (log 10)	4.45	4.47	4.44
Mean Baseline Blood CD4 Count	434	416	460
Provided CSF sample	29	13	16
Sexual orientation:			
Cis-MSM	39	36	39
Transgender Woman	13	7	6

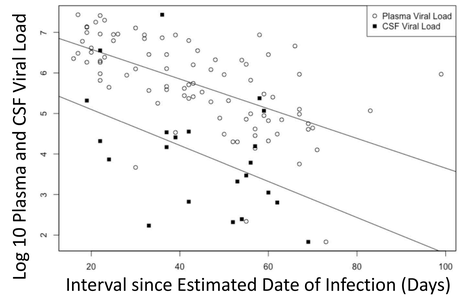
RESULTS:

Plasma and CSF biomarkers Associated with Time Since Infection

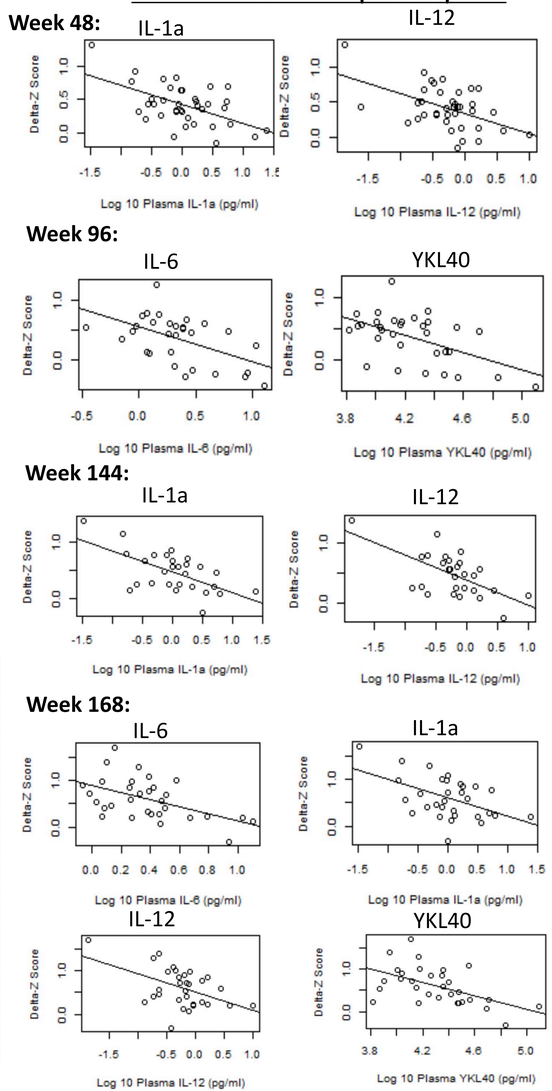
Analyte	B-Coefficient (Δ in log 10 ug/ml analyte/week of infection)	Benjamini-Hochberg-adjusted p-value
Negatively Associated Plasma Biomarkers		
IFN-y	-0.0100	0.005
IL-10	-0.0080	0.002
VCAM-1	-0.0060	0.0003
MCP-1	-0.0030	0.03
Negatively Associated CSF Biomarkers		
Total Protein	-0.2380	0.03
IFN-y	-0.0150	0.02
IL-6	-0.0100	0.005
Neopterin	-0.0090	0.02
MIP-1a	-0.0070	0.0003
Neurofilament Light Chain	-0.0070	0.05
VCAM-1	-0.0060	0.02
CD-163	-0.0050	0.002
IL-2	-0.0040	0.05
TNF-α	-0.0040	0.05
Positively Associated Plasma Biomarkers		
CD-163	0.0040	0.05
MMP-9	0.0050	0.005
YKL40	0.0050	0.03

Biomarkers Measured in Plasma, CSF	
TNF-b	IL-12p70
SDF-1a	IFN-y
MIP-1b	IL-10
MCP-1	APP-BR39
IL-8	CD163
IL-4	Osteopontin
IL-23p40	S100B
IL-1b	VCAM-1
IL-16	YKL40
IFN-a2a	TIMP-1-BR76
TNF-a	MMP2
MIP-1a	MMP9
IP-10	Abeta-1-40
IL-7	A-beta42
IL-6	T-tau
IL-2	Neopterin
IL-1a	Neurofilament Light Chain

CSF, Plasma VL are Negatively Associated with I-EDI



Baseline levels of Four Biomarkers Associated with Decline in NPT at Multiple Timepoints



1. Time since estimated date of infection was negatively associated with viral load in CSF and plasma, & 14 Inflammatory biomarkers.

2. Plasma IL-1a, IL-12, IL-6, and YKL40 at diagnosis were associated with a decline in neurocognitive function between baseline and multiple time points, despite immediate initiation of ART.

CONCLUSIONS:

- In ART-naïve patients, both VL and inflammatory biomarker levels in plasma and CSF are higher closest to date of infection. These elevated markers decrease over time, even prior to ART initiation.
- High baseline levels of several inflammatory markers were associated with lower neurocognitive performance over time.
- High levels of inflammation occurring during early HIV infection may influence subsequent neurocognitive outcomes, providing a rationale for early diagnosis and treatment, as well as possible anti-inflammatory treatment in early HIV.

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