Changes in Inflammatory Biomarkers Among Youth Living with Perinatal HIV Infection and Exposure

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BACKGROUND

HIV infection is associated with systemic immune activation. We sought to:

- Evaluate and compare changes in levels of circulating inflammatory biomarkers over time in youth with perinatal HIV (PHIV) and those perinatally HIV-exposed but uninfected (PHEU)
- Among PHIV participants, to evaluate the associations of changes in inflammatory biomarkers with the initial antiretroviral therapy (ART) regimen and HIV viral load, and the duration of combination ART (cART).

METHODS

In a longitudinal sub-study of cardiac status among youth in the Pediatric HIV/AIDS Cohort Study, we measured 8 inflammatory biomarkers (Interleukin [IL]-1β, IL-6, IL-8, IL-10, IL-18, tumor necrosis factor-α [TNF-α], soluble TNF receptor 2 [sTNF-R2], and high-sensitive C-reactive protein [hsCRP]) at the start of the sub-study (T1) and ~11 years later (T2) among 99 PHIV and 59 PHEU participants with paired samples.

Among PHIV, univariate and multivariate linear regression models were used to evaluate the associations of biomarker levels at T2 with specific cART regimens, CD4 count, and viral load (VL).

- At baseline, PHIV participants receiving cART and PHEU had similar median levels of inflammatory biomarkers with the exceptions of IL-18 and TNF-α, which were significantly higher in the PHIV group.
- Most biomarkers decreased over ~11 years in both groups.
- There was a greater decrease among PHIV than PHEU for IL-6, IL-8, IL-10, and TNF-α.
- After 11 years, only the median TNF-α level was significantly higher in the PHIV group.
- Among PHIV, better control of HIV was associated with lower median IL-18 and sTNF-R2 levels at 11 years.

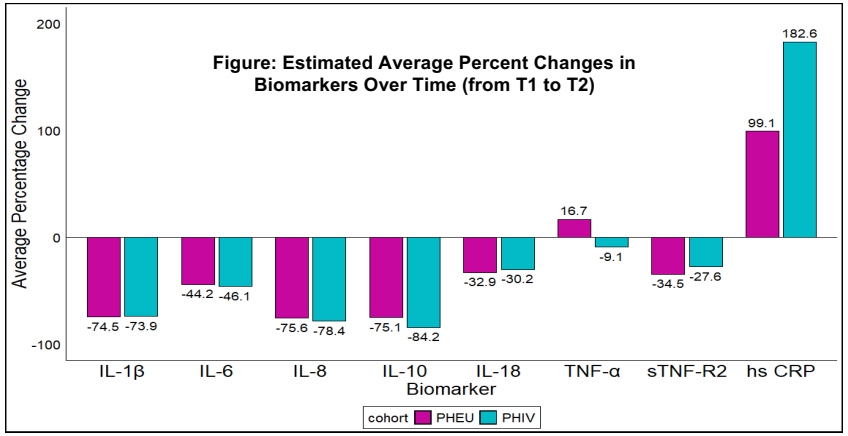
RESULTS

Participant Characteristics

At T1, the median age of the PHEU and PHIV participants was 11.2 and 13.0 years, respectively, with a median duration of 11.2 years between T1 and T2 in both groups; 56% and 64%, respectively, were female; and 71% of both groups were Black. Among the PHIV, 93% were receiving cART at T1 and 92% at T2; 72% had a VL<400 copies/mL at T1 and 81% at T2; and 81% and 64%, respectively, had a CD4 count > 500 cells/mm^3.

Baseline Inflammatory Biomarkers
Median (IQR)

	YPHIV (N=99)	YPHEU (N=59)	P-Value
Interleukin-1β (pg/mL)	0.80 (0.60, 1.59)	0.90 (0.50, 1.40)	0.57
Interleukin-6 (pg/mL)	0.96 (0.50, 2.40)	1.10 (0.60, 1.70)	0.91
Interleukin-8 (pg/mL)	7.85 (4.80, 25.7)	7.10 (4.30, 12.8)	0.43
Interleukin-10 (pg/mL)	3.50 (1.90, 4.80)	2.80 (1.50, 4.20)	0.19
Interleukin-18 (pg/mL)	258 (199, 330)	216 (177, 265)	0.02
TNF-α (pg/mL)	8.30 (5.05, 13.9)	6.00 (4.30, 8.00)	0.01
sTNF-R2 (pg/mL)	2,570 (2,170, 3,340)	2,600 (2,120, 3,35)	0.71
hsCRP (mg/L)	0.30 (0.20, 0.80)	0.50 (0.20, 2.10)	0.12



Changes Over Time of Inflammatory Biomarkers

At T1, the PHIV and PHEU groups had similar median levels of inflammatory biomarkers with the exceptions of IL-18 and TNF-α, which were significantly higher in the PHIV group. (Table).

The median levels of most inflammatory biomarkers in both groups decreased from T1 and T2, except for TNF- α (increased in the PHEU group) and hsCRP (increased in both groups) (figure). There was a greater decrease among PHIV than PHEU for IL-6, IL-8, IL-10, and TNF-α. At T2, only the median sTNF-R2 level was significantly higher in the PHIV than PHEU group (1,880 pg/mL vs. 1,600 pg/mL, p=0.04).

Relationship of Mean Biomarker Levels at T2 With HIV Disease Status

- A nadir CD4 <15%, as compared to those with a nadir CD4% >25%, was associated with a 31% lower median IL-8 level (95% CI -60% to +17%).
- A CD4 count ≤500 cells/ mm^3 was associated with 52% higher IL-18 levels (95% CI 11% to 110%);
- A VL ≥400 was associated with 91% higher sTNF-R2 levels (95% CI 22% to 200%);
- Integrase inhibitor use was associated with a 5%/year increase in IL-10 levels (95% CI 0.03% to 9.6%).

CONCLUSIONS

Over time, inflammatory biomarker levels decreased in both groups, with a greater decrease among PHIV participants receiving cART, approaching levels in the PHEU group.

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