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Advanced maternal HIV is associated with increased inflammatory biomarkers in infants

TABLE 3. Geometric mean (95%CI) immune biomarker concentration (pg/mL) in HEU infants by maternal viral load closest to delivery.

	Week	Maternal HIV RNA <400 copies/mL	Maternal HIV RNA ≥400 copies/mL	p-value
IL-2	48	110 (76-160)	188 (152-234)	0.031
IL-10	6	3629 (2965-4442)	5444 (4109-7213)	0.024
IL-10	48	1902 (1395-2593)	3247 (2241-4705)	0.029

BACKGROUND

- Most infants born to mothers living with HIV are HIV-exposed but uninfected (HEU).
- HEU infants have demonstrated immune dysfunction compared to HIV-unexposed (HUU) infants.
- In utero exposure to inflammation from maternal HIV is a proposed mechanism.
- This study compared inflammatory markers in HEU and HUU infants over the first year of life.

METHODS

- HEU plasma samples: infants enrolled in the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) protocol P1025 (multiple US sites; 2002-2013).
- HUU plasma samples: infants enrolled in 3 separate studies (CO, US; 2016-2022).
- MesoScale Discovery platform was used to measure biomarkers.
- Statistical analysis: multivariable regression analysis adjusting for sex, race/ethnicity, delivery mechanism, gestational age, birth weight, and HEU maternal CD4 count and viral load at delivery

Anti-inflammatory	Pro-inflammatory chemokines	T cell activation & differentiation	Macrophage activation	B cell activation
IL-10	MCP-1 (CCL2) MDC (CCL22) MIP-1α (CCL4) IL-8 (CXCL8) MIP-1β (CCL3) IP-10 (CXCL10)	IL-2 IFNγ IL-17A IL-12p70	TNFα IL-1β IL-6	IL-4 IL-5

FIGURE 1. Plasma markers measured

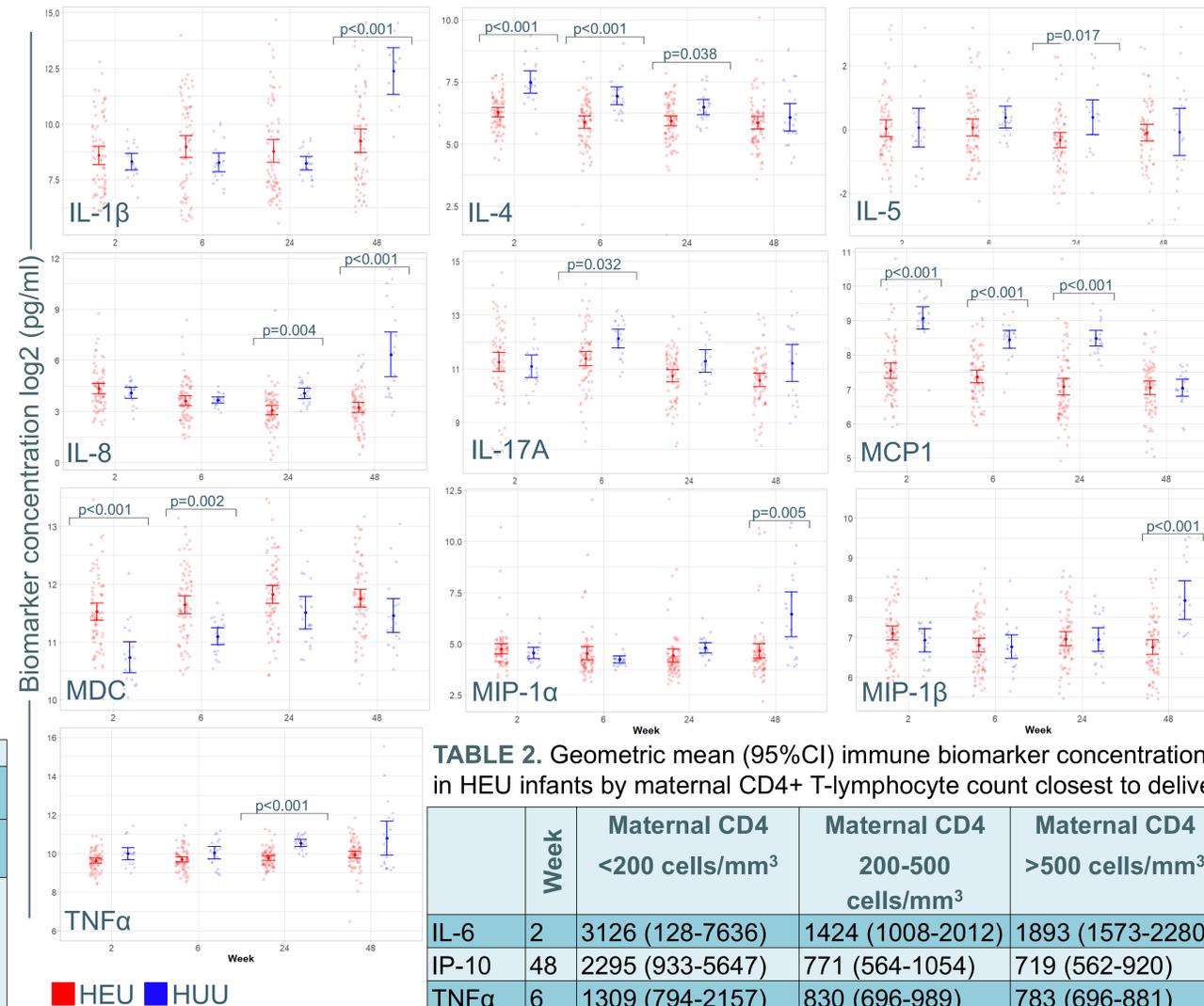


FIGURE 2. HEU vs HUU biomarker concentration (pg/ml) at weeks 2, 6, 24, 48. Multiple biomarker concentrations were lower in HEU infants. One biomarker was higher in HEU infants: MDC at weeks 2 and 6.

TABLE 2. Geometric mean (95%CI) immune biomarker concentration (pg/mL) in HEU infants by maternal CD4+ T-lymphocyte count closest to delivery.

	Week	Maternal CD4 <200 cells/mm ³	Maternal CD4 200-500 cells/mm ³	Maternal CD4 >500 cells/mm ³	p-value
IL-6	2	3126 (128-7636)	1424 (1008-2012)	1893 (1573-2280)	0.028
IP-10	48	2295 (933-5647)	771 (564-1054)	719 (562-920)	0.007
TNFα	6	1309 (794-2157)	830 (696-989)	783 (696-881)	0.015
TNFα	48	1830 (941-3558)	944 (798-1118)	883 (727-1074)	0.018
MIP1α	2	60 (15-244)	25 (19-32)	24 (21-28)	0.007
MIP1α	6	75 (8-728)	23 (17-31)	19 (15-25)	0.006
MIP1α	24	47 (6-352)	23 (17-32)	17 (14-22)	0.037
MIP1α	48	122 (8-1880)	27 (18-42)	19 (16-23)	<0.001
MIP1β	48	128 (52-314)	121 (99-149)	86 (72-103)	0.035

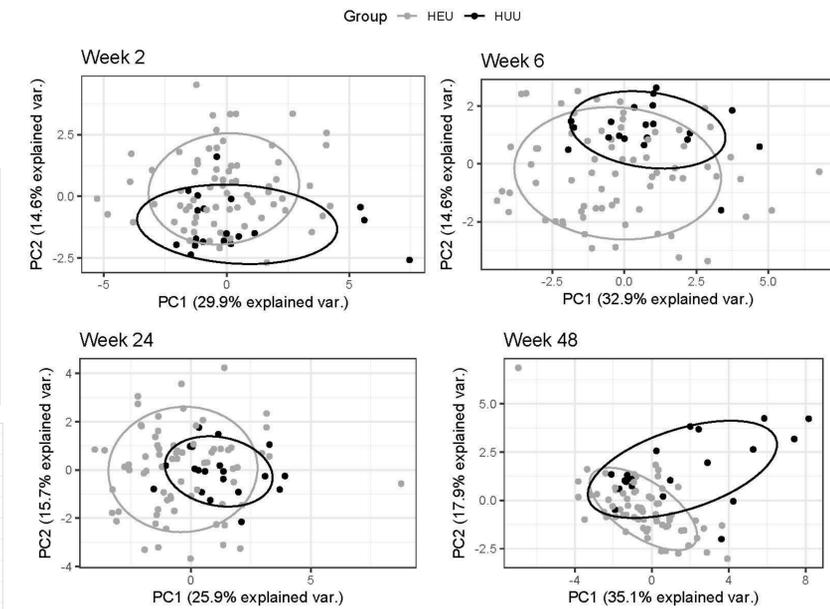


FIGURE 3. Inflammatory biomarker variance at weeks 2, 6, 24, and 48.

CONCLUSIONS

- HEU infants had lower inflammatory biomarker concentrations than HUU, possibly resulting from immune regulation or exhaustion
- Among HEU, higher concentrations of inflammatory biomarkers were associated with:
 - Lower maternal CD4+ T-lymphocyte count at delivery
 - Higher maternal HIV viral load at delivery
- Findings suggested an association between advanced/uncontrolled maternal HIV infection and increased infant inflammation in the first year of life

RESULTS

TABLE 1. Demographics

Median (IQR)	level	HEU (n=135)	HUU (n=51)	p-value
Sex (%)	Female	61 (45.2)	27 (52.9)	0.411
	Male	74 (54.8)	24 (47.1)	
Birth Weight (grams)		3044 [2800-3325]	3220 [2928-3510]	0.019
Race/ethnicity (%)	Asian non-Hispanic	0 (0.0)	3 (5.9)	<0.001
	Black non-Hispanic	66 (48.9)	5 (9.8)	
	Hispanic	52 (38.5)	17 (33.3)	
	White Non-Hispanic	13 (9.6)	21 (41.2)	
	Other/Unknown	4 (3.0)	5 (9.8)	
Delivery Mode (%)	Cesarean	66 (48.9)	15 (29.4)	0.014
	Vaginal	69 (51.1)	35 (68.6)	
	Unknown	0 (0.0)	1 (2.0)	
Gestational age		38 [37-39]	39 [38.5-40]	<0.001
Breastfed (%)	Exclusive until 6 months	0 (0.0)	15 (29.4)	<0.001
	Some breastfeeding	0 (0.0)	33 (64.7)	
	Not breastfed	135 (100.0)	3 (5.9)	