ASSOCIATION BETWEEN MATERNAL INFLAMMATION AND GROWTH OF CHILDREN WHO ARE HIV-EXPOSED AT AGE 2 YEARS: ROLE OF BREASTFEEDING

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BACKGROUND

Children who are HIV-exposed (CHE) are at increased risk of poor growth outcomes in resource limited settings. Breastfeeding may mitigate these effects through anti-inflammatory pathways. We evaluated whether the association between second trimester maternal inflammation and growth in CHE at 2 years differed by breastfeeding duration.

Breastfeeding duration was found to modify the association between inflammation and CHE growth outcomes. IL-6 and sCD163 showed consistent negative associations with growth among African and Indian CHE whose mothers breastfed ≤12 months and mothers who breastfed ≥12 months respectively.

METHODS

- We leveraged growth and associated data from a study nested within the IMPAACT 1077BF/FF trial with maternal plasma inflammation data (IFN-γ, IL-6, TNFα, sCD14, sCD163, and I-FABP) measured at antepartum study entry (t0) and four weeks later (t4).
- Continuous variables of Length-for-Age Z-score (LAZ), Weight-for-Age Z-score (WAZ), and Weight-for-Length (WLZ) at 2 years were analyzed using multivariable linear regression models, with inflammatory marker concentrations and changes between t0 and t4 treated as continuous growth predictors.
- Separate analyses were conducted by breastfeeding duration (≥ 12 months or < 12 months), and adjusted parameter estimates and 95% robust confidence intervals (CI) corresponding to a 0.25 log10-unit increase in biomarker concentration were reported.

TABLE 1. Associations of Maternal Inflammatory Marker Concentration and child Weight-for-Length Z-score at 2 Years by Breastfeeding Status at 12 Months

Biomarker	Breastfeeding ≥ 12 months?	AP Week 0 Estimate (95% CI)	P-value	AP Week 4 Estimate (95% CI)	P-value	Change (AP Week 4 - AP Week 0) Estimate (95% CI)	P-value
I-FABP	No	0.35 (0.09, 0.62)	0.009	0.18 (-0.05, 0.41)	0.13	0.10 (-0.15, 0.35)	0.45
	Yes	-0.14 (-0.49, 0.20)	0.41	-0.11 (-0.69, 0.47)	0.70	-0.06 (-0.66, 0.55)	0.86
IFNγ	No	-0.11 (-0.36, 0.14)	0.38	-0.15 (-0.33, 0.03)	0.11	-0.13 (-0.33, 0.07)	0.21
	Yes	0.04 (-0.15, 0.22)	0.70	0.12 (-0.17, 0.41)	0.42	0.13 (-0.18, 0.43)	0.42
IL-6	No	-0.15 (-0.39, 0.08)	0.20	-0.21 (-0.47, 0.05)	0.11	-0.19 (-0.51, 0.13)	0.25
	Yes	0.06 (-0.36, 0.47)	0.79	-0.21 (-0.51, 0.09)	0.17	-0.26 (-0.62, 0.10)	0.16
TNFα	No	0.12 (-0.26, 0.50)	0.53	0.12 (-0.24, 0.49)	0.50	0.11 (-0.42, 0.63)	0.69
	Yes	-0.25 (-0.62, 0.13)	0.20	-0.34 (-0.80, 0.11)	0.14	-0.35 (-0.92, 0.23)	0.23
sCD14	No	-0.23 (-0.84, 0.37)	0.45	-0.17 (-0.63, 0.28)	0.46	-0.00 (-0.54, 0.54)	0.99
	Yes	0.09 (-0.46, 0.64)	0.75	0.23 (-0.51, 0.97)	0.55	0.35 (-0.76, 1.46)	0.53
sCD163	No	0.34 (-0.11, 0.78)	0.14	0.23 (-0.22, 0.68)	0.31	-0.10 (-0.64, 0.44)	0.71
	Yes	0.06 (-0.33, 0.44)	0.78	0.20 (-0.29, 0.69)	0.42	0.31 (-0.29, 0.91)	0.31

RESULTS

Analyses included 252 mother-child pairs, including three children who acquired HIV. Results were similar when these children were excluded from each analysis.

Table 2: Associations of Maternal Inflammatory Marker Concentration and child Length-for-Age Z-score at 2 Years by Breastfeeding Status at 12 Months

Biomarker	Breastfeeding ≥ 12 months?	AP Week 0 Estimate (95% CI)	P-value	AP Week 4 Estimate (95% CI)	P-value	Change (AP Week 4 - AP Week 0) Estimate (95% CI)	P-value
I-FABP	No	-0.03 (-0.49, 0.42)	0.88	-0.19 (-0.51, 0.13)	0.25	-0.19 (-0.51, 0.14)	0.26
	Yes	0.06 (-0.13, 0.25)	0.55	0.15 (-0.12, 0.42)	0.29	0.16 (-0.13, 0.45)	0.29
IFNγ	No	0.16 (-0.09, 0.40)	0.21	0.12 (-0.12, 0.36)	0.34	0.09 (-0.20, 0.37)	0.55
	Yes	0.08 (-0.05, 0.21)	0.22	-0.04 (-0.19, 0.12)	0.64	-0.10 (-0.25, 0.05)	0.20
IL-6	No	0.06 (-0.25, 0.37)	0.70	-0.24 (-0.60, 0.12)	0.18	-0.68 (-1.13, -0.23)	0.003
	Yes	0.00 (-0.24, 0.24)	0.98	0.01 (-0.23, 0.25)	0.96	-0.01 (-0.24, 0.22)	0.93
TNFα	No	0.44 (0.16, 0.72)	0.002	0.10 (-0.30, 0.51)	0.62	-0.57 (-1.18, 0.05)	0.073
	Yes	0.29 (0.08, 0.51)	0.007	0.36 (0.10, 0.62)	0.007	0.29 (-0.10, 0.67)	0.14
sCD14	No	0.33 (-0.34, 0.99)	0.34	0.28 (-0.26, 0.81)	0.31	0.18 (-0.59, 0.96)	0.64
	Yes	-0.03 (-0.41, 0.34)	0.86	-0.01 (-0.44, 0.42)	0.96	0.00 (-0.72, 0.72)	>0.99
sCD163	No	-0.07 (-0.62, 0.49)	0.81	-0.08 (-0.59, 0.43)	0.76	-0.10 (-0.69, 0.49)	0.74
	Yes	-0.32 (-0.57, -0.07)	0.013	-0.48 (-0.77, -0.18)	0.002	-0.51 (-0.89, -0.14)	0.008

Table 3: Table 2: Associations of Maternal Inflammatory Marker Concentration and child Weight-for-Age Z-score at 2 Years by Breastfeeding Status at 12 Months

Biomarker	Breastfeeding ≥ 12 months?	AP Week 0 Estimate (95% CI)	P-value	AP Week 4 Estimate (95% CI)	P-value	Change (AP Week 4 - AP Week 0) Estimate (95% CI)	P-value
I-FABP	No	0.23 (-0.10, 0.56)	0.18	0.04 (-0.22, 0.29)	0.77	-0.02 (-0.30, 0.27)	0.91
	Yes	-0.02 (-0.22, 0.17)	0.82	0.12 (-0.08, 0.32)	0.25	0.17 (-0.05, 0.39)	0.13
IFNγ	No	0.01 (-0.22, 0.24)	0.94	-0.04 (-0.21, 0.13)	0.63	-0.05 (-0.26, 0.17)	0.65
	Yes	0.04 (-0.06, 0.15)	0.44	0.02 (-0.13, 0.17)	0.79	-0.00 (-0.17, 0.16)	0.97
IL-6	No	-0.11 (-0.32, 0.11)	0.33	-0.34 (-0.55, -0.14)	<0.001	-0.53 (-0.85, -0.21)	0.001
	Yes	-0.04 (-0.20, 0.12)	0.63	-0.15 (-0.43, 0.12)	0.28	-0.16 (-0.45, 0.13)	0.29
TNFα	No	0.31 (-0.05, 0.67)	0.088	0.10 (-0.31, 0.51)	0.62	-0.25 (-0.69, 0.20)	0.28
	Yes	0.04 (-0.14, 0.21)	0.69	0.03 (-0.17, 0.22)	0.80	-0.03 (-0.39, 0.33)	0.87
sCD14	No	0.01 (-0.43, 0.46)	0.96	-0.00 (-0.37, 0.36)	>0.99	0.01 (-0.59, 0.61)	0.96
	Yes	-0.01 (-0.33, 0.30)	0.93	0.01 (-0.32, 0.35)	0.94	0.03 (-0.47, 0.54)	0.90
sCD163	No	0.19 (-0.21, 0.59)	0.34	0.10 (-0.28, 0.48)	0.60	-0.17 (-0.63, 0.30)	0.48
	Yes	-0.18 (-0.40, 0.04)	0.10	-0.19 (-0.46, 0.08)	0.17	-0.12 (-0.50, 0.26)	0.54

CONCLUSIONS

- We observed significant differences in associations between specific biomarkers and growth by breastfeeding duration.
- Shorter breastfeeding was characterized by inverse associations between IL-6 and growth, whereas longer breastfeeding showed consistent inverse associations between sCD163 and growth.
- Higher TNFα was positively associated with LAZ regardless of time breastfed.

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