ASSOCIATION BETWEEN ANTEPARTUM MATERNAL INFLAMMATION AND GROWTH OUTCOMES AMONG CHILDREN WHO ARE HIV-EXPOSED

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BACKGROUND

In resource limited settings, children who are HIV-exposed (CHE) are at increased risk of poor growth outcomes. Contributors to poor growth in CHE are not well-understood. We evaluated whether second trimester maternal inflammation is associated with CHE growth at age 2 years.

Inflammation was found to be associated with CHE growth outcomes. Increased monocyte activation marker sCD163 and cytokine IL-6 were associated with decreased growth although this was not consistent for all time-points.

METHODS

- This was a secondary analysis of a nested case-control study evaluating maternal inflammation within the PROMISE 1077BF/FF trial conducted in Southern and East Africa and India.
- Six inflammatory markers (IFN-γ, IL-6, TNFα, sCD14, sCD163, and I-FABP) were measured in maternal plasma samples during the second trimester: at entry into PROMISE (t0) and four weeks later after ART initiation (t4).
- Length and weight were measured at age 2 years.
- Weighted multivariable linear regression models assessed the association between maternal inflammation and WHO length-for-age z-scores (LAZ), weight-for-age z-scores (WAZ), and weight-for-length z-scores (WLZ) at age 2 years.
- Adjusted parameter estimates and 95% robust confidence intervals (CI) were reported.

TABLE 1. Maternal Characteristics

Characteristic		Total
		(N=252)
Country	South Africa Malawi	41% 35%
Maternal age	Median (Q1, Q3)	25.3 (21.9, 28.8
WHO clinical stage	Stage 1	96%
Gestational age	Median (Q1, Q3)	37.0 (36.0, 38.5)

RESULTS

Analyses included 252 mother-child pairs with growth data at age 2 years. Median gestational age at birth was 37.0 (36.0, 38.5) weeks. Among newborns, 132 (52%) were female. Median birth-length was 47.6 (46.0, 49.0) cm and median birth-weight 2.7 (2.3, 3.1) kg. There were no statistically significant associations between any inflammatory markers and child WLZ (results not shown). Analyses included 3 children living with HIV and 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

Biomarker	Week 0 Estimate (95% CI)	P-value	Week 4 Estimate (95% CI)	P-value	Change (Week 4 - Week 0) Estimate (95% CI)	P-value
I-FABP	0.01 (-0.17, 0.19)	0.87	-0.03 (-0.23, 0.18)	0.81	-0.02 (-0.25, 0.20)	0.83
IFNγ	0.11 (-0.01, 0.22)	0.062	0.02 (-0.11, 0.15)	0.80	-0.04 (-0.18, 0.10)	0.59
IL-6	0.04 (-0.14, 0.22)	0.65	-0.07 (-0.28, 0.13)	0.48	-0.15 (-0.37, 0.08)	0.21
TNFα	0.32 (0.14, 0.50)	<0.001	0.22 (-0.03, 0.48)	0.089	-0.07 (-0.50, 0.36)	0.74
sCD14	0.04 (-0.32, 0.39)	0.85	0.07 (-0.28, 0.41)	0.70	0.10 (-0.45, 0.66)	0.72
sCD163	-0.22 (-0.51, 0.08)	0.15	-0.31 (-0.57, -0.04)	0.025	-0.29 (-0.62, 0.05)	0.091

Weighted linear regression models adjusted for country, maternal HIV treatment arm, maternal age, maternal HIV-1 RNA, maternal hemoglobin, maternal CD4, maternal BMI, maternal education, and home tap water status.
Models of change additionally adjusted for baseline inflammation.
All estimates are for a 0.25 $\log_{10}$-unit increase in biomarker concentration.
Results with p-value < 0.05 highlighted in light grey.

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

Biomarker	Week 0 Estimate (95% CI)	P-value	Week 4 Estimate (95% CI)	P-value	Change (Week 4 - Week 0) Estimate (95% CI)	P-value
I-FABP	0.03 (-0.11, 0.17)	0.71	0.07 (-0.10, 0.25)	0.42	0.08 (-0.13, 0.30)	0.45
IFNγ	0.03 (-0.07, 0.14)	0.55	0.01 (-0.11, 0.12)	0.89	-0.01 (-0.14, 0.13)	0.92
IL-6	-0.06 (-0.20, 0.08)	0.39	-0.21 (-0.39, -0.03)	0.021	-0.24 (-0.45, -0.03)	0.024
TNFα	0.11 (-0.08, 0.30)	0.27	0.03 (-0.20, 0.26)	0.79	-0.14 (-0.46, 0.18)	0.40
sCD14	-0.08 (-0.36, 0.21)	0.60	-0.04 (-0.33, 0.24)	0.76	0.03 (-0.40, 0.46)	0.90
sCD163	-0.05 (-0.29, 0.19)	0.69	-0.10 (-0.32, 0.13)	0.40	-0.12 (-0.43, 0.19)	0.45

Weighted linear regression models adjusted for country, maternal HIV treatment arm, maternal age, maternal HIV-1 RNA, maternal hemoglobin, maternal CD4, maternal BMI, maternal education, and home tap water status.
Models of change additionally adjusted for baseline inflammation.
All estimates are for a 0.25 $\log_{10}$-unit increase in biomarker concentration.
Results with p-value < 0.05 highlighted in light grey.

CONCLUSIONS

- We observed that higher maternal sCD163 at t0 and IL-6 levels at t4 and change from t4-t0 were associated with lower CHE LAZ and WAZ, respectively at age 2 years, while higher TNFα was associated with higher LAZ.
- Future studies are needed to confirm these findings and investigate whether reducing specific inflammatory markers could improve CHE growth outcomes.

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