Investigating the relationship between infant feeding practices and immune biomarkers of one-year-old infants in the CHILD Cohort Study

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BACKGROUND

Human breast milk satisfies infant nutritional requirements and contains components associated with supporting early life immune system development (1,2).

Nuances in infant feeding practices – such as human milk feeding (HMF) duration, exclusivity, and feeding method (e.g. directly from the breast, or pumped and bottled) – have been associated with immune-related health outcomes (e.g. infections and asthma) (3,4).

The relationship between infant feeding practices and early life immune system development is unknown.

OBJECTIVE

To understand the relationship between infant feeding practices and immune system development in the first year of life.

METHODS

We studied 670 one-year-old infants from the CHILD Cohort Study. 32 infants were outside the "normal" range of one-year-old white blood cell count (6000 – 17500 mm^3) (5) and were excluded from analysis.

Figure 1. The CHILD Cohort Study: An ongoing longitudinal pregnancy-based cohort developed to study genetic and environmental determinants of child health and chronic disease. 3455 families were recruited from 2008-12 across four Canadian sites (Vancouver, Edmonton, Winnipeg, Toronto). www.childstudy.ca

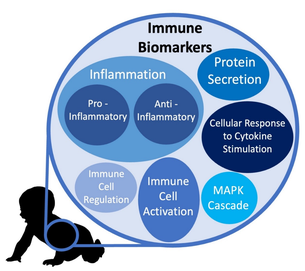

Figure 2. Biological processes associated with the Olink Target 96 Inflammation Panel (6).

Infant human milk feeding (HMF) duration, exclusive HMF duration, and feeding method at 3 months of age were derived from CHILD questionnaires and medical records.

The Olink Target 96 Inflammation Panel measured the normalized protein expression (Olink's arbitrary protein level unit) of 92 inflammation-associated biomarkers in serum collected at one year of age.

The collective level of these biomarkers indicate immune system activity (6) and can reflect immune system development.

Relationships were tested using linear regression modelling, Kruskal-Wallis one-way analysis of variance, and Wilcoxon rank-sum tests, with Benjamini-Hochberg adjustment for multiple comparisons.

References:
1) Dawod B *et al. Curr Opin Gastroenterol* 2021. 37(6): 547-56; **2)** Victora CG *et al. Lancet* 2016. 387(10017): 475-490; **3)** Oddy WH. *J Asthma* 2004. 41(6): 605-21; **4)** Fehr K *et al. Cell Host Microbe* 2020. 28(2): 285-297; **5)** Nathan DG *et al. United Kingdom, Saunders* 1987; **6)** Olink Target 96 Inflammation. https://www.olink.com/products-services/target/inflammation/.

RESULTS

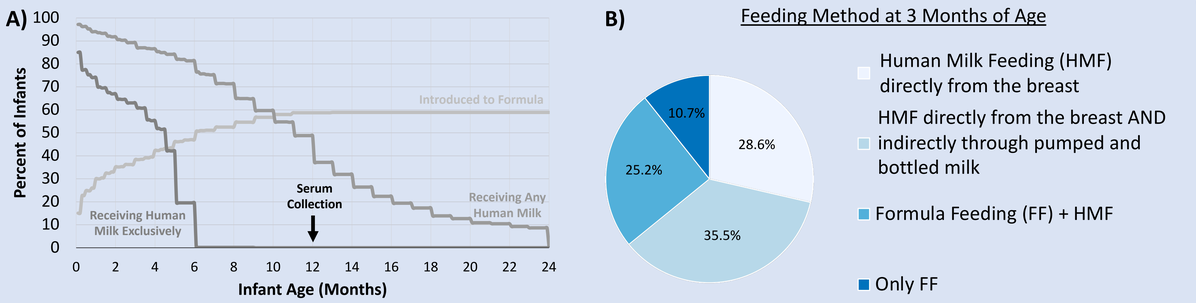

Figure 3. Infant feeding practices for one-year-old infants (N = 638). (A) Percentage of infants introduced to formula (mean age introduced to formula: 2.7 ± 3.1 months old), receiving human milk exclusively with no formula or solid food (mean duration receiving human milk exclusively: 3.4 ± 2.3 months), and receiving any human milk (mean duration receiving human milk: 11.3 ± 6.5 months). **(B)** Distribution of feeding methods at 3 months of age.

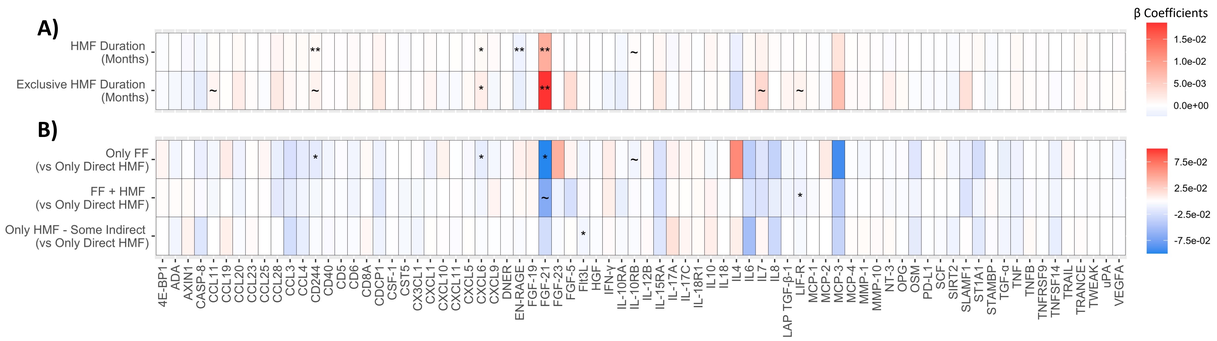

Figure 4. Feeding practices are associated with inflammation-associated serum biomarkers in one-year-old CHILD infants. Values are β coefficients from linear regressions to predict serum biomarker levels using **(A)** HMF Duration or Exclusive HMF Duration (in months), and **(B)** feeding method at 3 months, using "Only Direct HMF" as the reference group. The Benjamini-Hochberg method was used to adjust for multiple comparisons. ~p<0.1, *p<0.05, **p<0.01

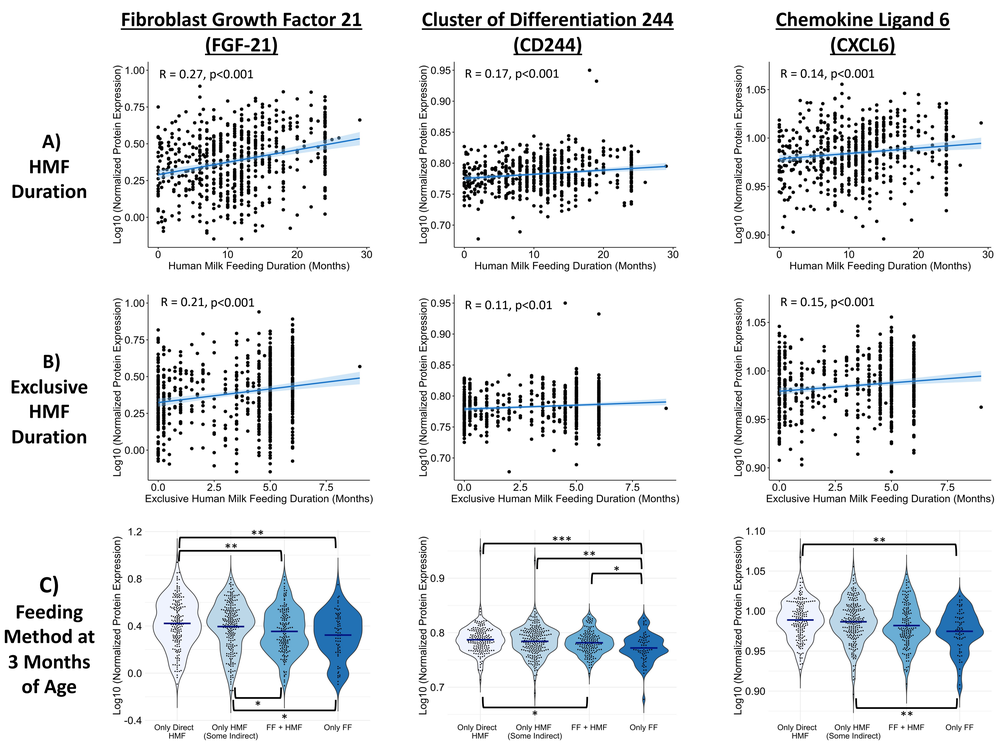

Figure 5. HMF duration, exclusive HMF duration, and feeding method (at 3 months of age) are associated with the level of FGF-21, CD244, and CXCL6. (A) Linear regression results between HMF duration and biomarker normalized protein expression. R is the correlation coefficient between HMF duration and biomarker normalized protein expression. **(B)** Linear regression results between exclusive HMF duration and biomarker normalized protein expression. R is the correlation coefficient between exclusive HMF duration and biomarker normalized protein expression. **(C)** Results of Wilcoxon rank-sum tests comparing median normalized protein expression between feeding method groups. *p<0.05, **p<0.01, ***p<0.001

KEY FINDINGS

- Feeding method at 3 months of age was positively associated with CD244, CXCL6, FGF-21, Flt3L, LIF-R, and LAP-TGF-β-1 serum levels in one-year-old infants.
- HMF duration was positively associated with CD244, CXCL6, FGF-21, and IL-10RB serum levels in one-year-old infants, but was negatively associated with EN-RAGE levels.
- Exclusive HMF duration was positively associated with CD244, CXCL6, FGF-21, CCL11, IL-7, and LIF-R serum levels in one-year-old infants.

CONCLUSIONS (SO FAR)

Feeding method at 3 months of age, HMF duration, and exclusive HMF duration are associated with the level of select inflammation-associated serum biomarkers at one year of age.

SIGNIFICANCE

This research will:

- Advance knowledge about how infant feeding practices are related to early life immune system development.
- Help us understand how human milk shapes the infant immune system and how to provide the best start to life for infants.

NEXT STEPS

- Determining if different infant feeding experiences are associated with distinct biomarker clusters within one-year-olds' serum.
- Including other variables associated with early life immune system development in statistical analyses.

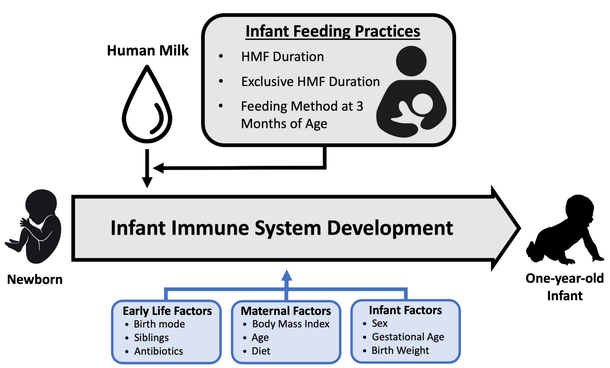

Figure 6. Variables associated with early life immune system development.

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