

Differences in Gut Microbiome in HIV-Infected versus HIV-exposed, Uninfected Infants

Wei Li A. Koay^{1,2}, Hyunwook Koh³, Mutsa Bwakura-Dangarembizi⁴, Adriana Weinberg⁵, Myron J. Levin⁵, Ni Zhao³, Deborah Persaud⁶



¹Division of Infectious Diseases, Children's National Medical Center, Washington DC, USA; ²School of Medicine and Health Sciences, George Washington University, Washington DC, USA; ³Department of Biostatistics, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, USA; ⁴Colleges of Health Sciences, University of Zimbabwe, Harare, Zimbabwe; ⁵Division of Infectious Diseases, University of Colorado School of Medicine, Denver, CO, USA; ⁶Department of Pediatrics, Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, MD, USA

BACKGROUND

- Increased inflammation and immune activation are features of HIV-1 infection, for which gut dysbiosis is implicated in adults with HIV.
- Little is known about the gut microbiome in HIV-1-infected (HIV+) infants, who also have persistent inflammation and immune activation.
- Our previous studies show that markers of intestinal integrity (zonulin, intestinal fatty acid binding protein) do not differ between HIV+ and HIV-exposed uninfected (HEU) infants at 3 months of age, but HIV+ infants had higher concentrations of cytokines (IFN γ , IL-1 β , IL-2, IL-6, IL-8, IL-10, TNF α) compared with HEU infants.
- Using residual stool extracts from a rotavirus vaccine trial in sub-Saharan Africa (IMPAACT P1072), we profiled fecal bacterial populations to define HIV-associated gut dysbiosis in HIV+ and HEU infants at 3 months of age, who were breastfed (BF) and non-breastfed (NBF).

METHODS

- 40 infants (20 HEU, 20 HIV+) on co-trimoxazole prophylaxis were selected from a rotavirus vaccine trial, in whom we previously characterized inflammation, immune activation and intestinal integrity markers profiles.
- Infants were selected based on stool availability and breastfeeding with matched HEU control infants.
- 16S rRNA (V3/V4) sequences from stool DNA were assigned organizational taxonomic units (OTU) with QIIME.
- Alpha (Chao1, abundance coverage estimator (ACE), Shannon, Simpson) and beta (Bray-Curtis, Jaccard, unweighted and weighted UniFrac) diversity, and differentially abundant taxa (linear discriminant analysis effect size (LEfSe)) were analyzed.
- Multivariate analysis adjusted for HIV status, breastfeeding and gender (results not shown).
- p<0.05 indicated statistical significance.

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RESULTS

Table 1a. Characteristics of participants by HIV-1 infection status

	HEU		HIV+		p-value	HEU		HIV+		p-value	
	Male, n (%)	Female, n (%)	Male, n (%)	Female, n (%)		CD4%, median (SD)	WHO weight-for-age Z-score, median (SD)	CD4%, median (SD)	WHO weight-for-age Z-score, median (SD)		
Total	10 (52.6)	9 (47.4)	4 (20)	16 (80)	0.048	39.9 (7.8)	32.5 (12.3)	0.032	-0.52 (0.86)	-1.1 (1.33)	0.042
Non-breastfed	6 (66.7)	3 (33.3)	4 (40)	6 (60)	0.37	42.8 (7.7)	35.6 (14.6)	0.211	-0.2 (0.76)	-0.69 (1.38)	0.307
Breastfed	4 (40)	6 (60)	0 (0)	10 (100)	0.087	37.3 (7.3)	29.5 (9.1)	0.059	-0.81 (0.89)	-1.52 (1.21)	0.143

Table 1b. Characteristics of participants by breastfeeding status

	Non-breastfed (NBF)		Breastfed (BF)		p-value	NBF		BF		p-value	
	Male, n (%)	Female, n (%)	Male, n (%)	Female, n (%)		CD4%, median (SD)	WHO weight-for-age Z-score, median (SD)	CD4%, median (SD)	WHO weight-for-age Z-score, median (SD)		
Total	10 (52.6)	9 (47.4)	4 (20)	16 (80)	0.048	39.0 (12.1)	33.4 (9.0)	0.06	-0.46 (1.13)	-1.16 (1.1)	0.144
HEU	6 (66.7)	3 (33.3)	4 (40)	6 (60)	0.37	42.8 (7.7)	37.3 (7.3)	0.153	-0.2 (0.76)	-0.81 (0.89)	0.182
HIV+	4 (40)	6 (60)	0 (0)	10 (100)	0.087	35.6 (14.6)	29.5 (9.1)	0.19	-0.69 (1.38)	-1.52 (1.21)	0.405

BETA DIVERSITY:

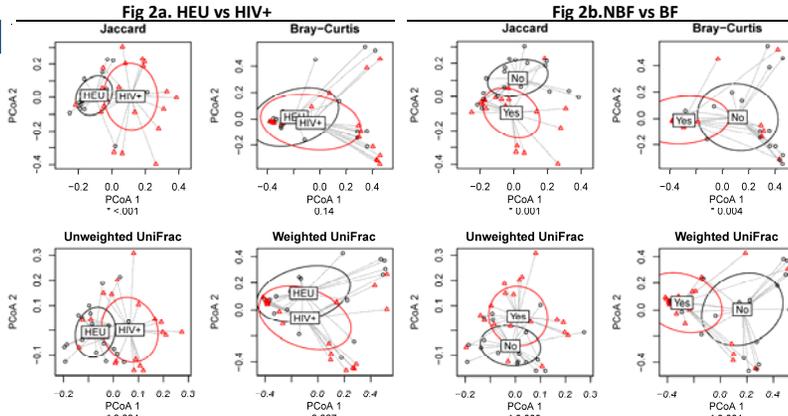


Fig 2. a: HEU (O) vs HIV+ (Δ). Jaccard and unweighted UniFrac (both not abundance based), but not Bray-Curtis or weighted UniFrac (both abundance based) showed significant difference between HEU and HIV+. **b: NBF (O) vs BF (Δ).** All measures of beta diversity show significant difference between NBF and BF infants.

CONCLUSIONS

- Significant differences between the microbiome of HEU and HIV+ infants from sub-Saharan Africa are observed.
- Although multivariate analysis did not show an impact of breastfeeding and gender, effect changes may not be evident due to the small sample size.

ALPHA DIVERSITY:

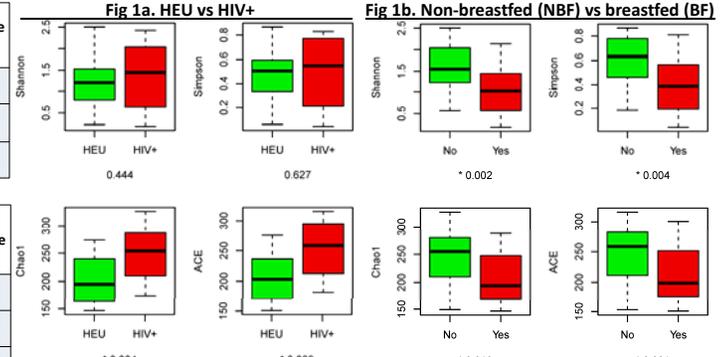


Fig 1. a: HEU (green) vs HIV+ (red). Chao1 and ACE (both take into account the number of species or richness), but not Simpson or Shannon (both take into account abundance of species and richness), show significantly higher α -diversity in HIV+ compared with HEU. **b: NBF (green) vs BF (red).** All measures show significantly lower α -diversity in BF compared to NBF infants.

DIFFERENTIAL ABUNDANCE:

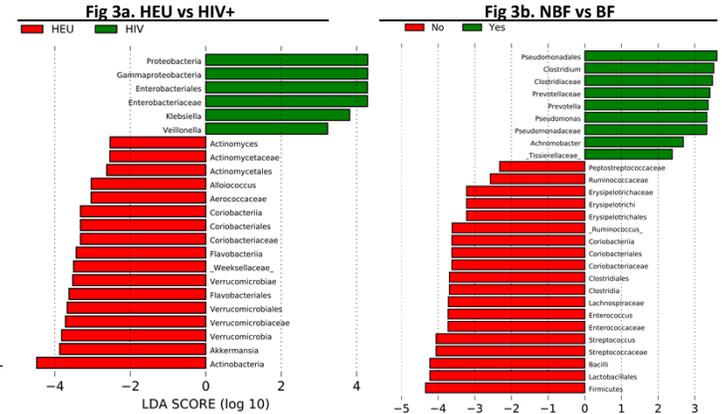


Fig 3. Differentially abundant microbial taxa through phylum, class, order, family and genus for a. HEU (red) vs HIV+ (green), where taxa enriched in HEU infants are shown in red and taxa enriched in HIV+ are shown in green and **b. NBF (red) vs BF (green),** where taxa enriched in NBF infants are shown in red, and taxa enriched in BF infants are shown in green.

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