

Global variation in gut microbiome composition in healthy infants Akshaya Vasudevan¹, Padmanaban Venkatesan²



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Introduction

- Early life gut microbiome composition is implicated in various disease states in childhood, while also having lasting effects well into adulthood
- important factor • Geographical variation is an contributing to differences in gut microbiome composition as different regions have distinct lifestyles,



- *Figure 1: Distribution of phyla across regions*
- 25 genera with relative abundance > 5% relative abundance were present (total genera - 1770), mainly belonging to 5 phyla, with phylum Firmicutes having the maximum number of genera

Beta diversity

• Participants from same regions, especially Africa and South America tended to cluster together on Principle Coordinate Analysis using Bray-Curtis distance





Figure 6: Campilobacterota in different regions



FDR: 7.294e-03

breastfeeding practices and dietary preferences are some of the most important influences that vary by geography

• Analysis of gut microbiome of healthy individuals from different regions, with focus on infancy and early childhood, is needed to understand normal gut microbiome composition

Methods

- Data sources: Microbiome DB an open-source data repository and open-access data from the AFRIBIOTA consortium
- 16S rRNA sequencing taxonomic data and participant metadata for healthy participants
- 302 participants (aged between 0-12 months) from 4 studies conducted across 11 countries grouped into 4 regions (North America (USA), South America (Peru, Brazil), Asia (Bangladesh, India, Malaysia) and Africa(Mali, Niger, South Africa, Kenya, The Gambia))

Statistical analyses

- Relative abundance at genus and phylum levels
- Analysis of variance (ANOVA) of alpha (Shannon index) diversity between groups



Figure 2: Mean relative abundance of genera across regions

- South American participants had an overwhelming preponderance of genus *Bifidobacterium* (belonging to phylum Actinobacteria) - over 56%, while Africa had just under 3%
- African and South Asian participants had similar profiles of relative abundance of certain genera belonging to phyla Firmicutes (Lactobacillus, Proteobacteria Streptococcus), (Escherichia/Shigella) Bacteroidetes and (*Bacteroides*)
- African subjects had higher relative abundance of *Prevotella* (16.6%) while USA had higher abundance of *Bacteroides*, both belonging to the phylum

Figure 4: Principle Coordinate Analysis (PCoA)

• PERMANOVA based on Bray-Curtis distance, adjusted for age and study effects, showed statictically significant results, with region accounting for 11% of the differences (p value = 0.001)

Relative abundance across regions Mixed effects model

• Linear mixed effects model comparing relative abundance of phyla, with age as fixed effect and study as random effect, showed that relative abundance of Bacteroidota increased with age (β = 1.1, Q value < 0.003) across all regions



Discussion

- Genus *Prevotella* has been shown to be associated with plant-based diets, which are a staple in sub-Saharan Africa
- Considering that breastmilk and other milk products/substitutes would dominate the diet in infants, all regions show a higher relative abundance of lactic acid bacteria (particularly genera *Bifidobacterium* and *Lactobacillus*), but South America had a significantly higher abundance, possibly indicative of a higher preference for milk-based diets
- Certain phyla comprise of disease-causing pathogens, which had higher relative abundance in Africa
- Analysis of gut microbiome datasets from publically available databases revealed considerable differences in gut microbiome composition in healthy infants under 12 months of age between regions of the world
- Dietary practices and disease states maybe key contributors

Further research

• Establishment of normative gut microbiome composition data for various populations to compare and contrast with various disease states, both gastrointestinal and beyond

- Principal coordinate analysis (PCoA) and statistical significance in beta diversity (Bray-Curtis dissimilarity matrix) using PERMANOVA
- Mixed effects model to study differences in relative abundance distributions amongst the groups, adjusted for age (fixed effects) and study (random effects)
- Programming language R Programming language 'phyloseq', 'Maaslin2', packages with 'MicrobiomeSeq', 'Vegan', 'Adonis2' and 'ggplot2'



• Median age of children across all regions was 7 months

Relative abundance

- 6 phyla with relative abundance > 5% (total phyla -66) across all samples were present
- Phyla Fusobacteria and Campilobacterota had the least abundance across all regions
- Relative abundance of phylum Actinobacteria was highest in South American population

Bacteroidetes

Alpha diversity

- Samples from South America had the lowest alpha diversity based on Shannon diversity index
- Statistically significant differences between regions were observed in pairwise ANOVA comparisons, however a linear mixed effects model adjusted for age and sex showed no significant associations



Figure 5: Association of Bacteriodota with age

• South Asia (β = -2.24, Q value = 0.004) and South America (β = -2.93, Q value = 0.004) had lesser relative abundance of Campilobacterota when compared to Africa in the linear mixed model

- Population-based studies on both compositional data and associated factors • Robust curated databases
- Microbiota directed feeds as a mode of treatment for treatment of dysbiosis related to various gastrointestinal diseases

References

- 1. MicrobiomeDB [Internet]. [cited 2024 Oct 23]. Available from:
- https://microbiomedb.org/mbio/app
- 2. Vonaesch P, Araújo JR, Gody JC, Mbecko JR, Sanke H, Andrianonimiadana L, et al. Stunted children display ectopic small intestinal colonization by oral bacteria, which cause lipid malabsorption in experimental models. Proc Natl Acad Sci. 2022 11;119(41):e2209589119.
- 3. Sheng Y, Wang J, Gao Y, Peng Y, Li X, Huang W, et al. Combined analysis of cross-population healthy adult human microbiome reveals consistent differences in gut microbial characteristics between Western and non-Western countries. Comput Struct Biotechnol J. 2024 1;23:87–95.

Figure 3: Comparison of alpha diversity across regions



