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Investigating the Infant Gut Microbiome Associated with Child Growth Failure in Early life

Ankita Maddheshiya[1], Sunita Taneja[2], Nita Bhandari[2], Partha Pratim Majumder[1], Ranadip Chowdhury[2], and Souvik Mukherjee[1]*

Presenting Author: Ankita Maddheshiya; *Correspondence to: Dr. Souvik Mukherjee, Associate Professor, NIBMG, Kalyani, West Bengal

[1]Human Microbiome Research Laboratory, National Institute of Biomedical Genomics, Kalyani, West Bengal, India

[2]Society for Applied Studies, Kalu Sarai, New Delhi, India

E-mail- Ankita Maddheshiya: am5@nibmg.ac.in; Dr. Souvik Mukherjee: sm2@nibmg.ac.in

INTRODUCTION

WHAT IS **THE MICROBIOME?** Community of microbes

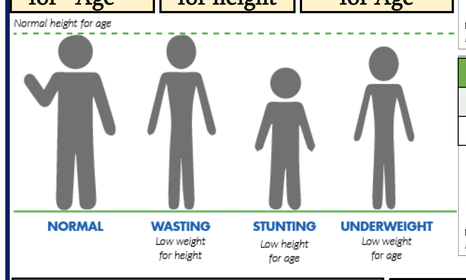
Human microbiome: Collective genome of all the microbes or community of microbes in the human body

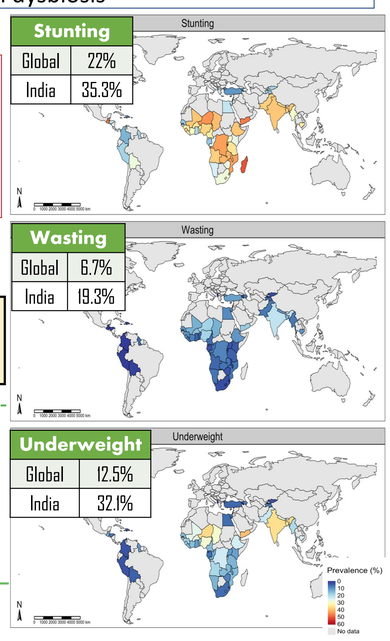
Gut microbiome

The composition of the intestinal microbiome: It affects health from the prenatal period throughout childhood, and many diseases have been associated with dysbiosis

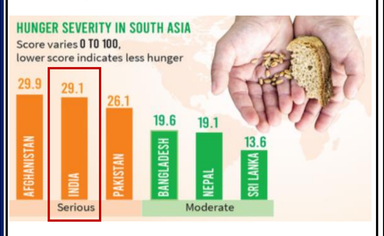
Child Growth failure (CGF)

Expressed as stunting, wasting, or underweight in children <5 years of age which is <-2 SD the WHO reference standard median for each (WHO & UNICEF, 2009)





Child Growth Failure: A major concern in INDIA



The GHI looks at four main indicators: Undernourishment, **Child Wasting, Child Stunting**, and Child Mortality

Early infancy Child Growth failure

- Period from birth through the completion of the 6th month of life
- Highest rates of undernutrition among 0-6 months old infants were reported (1)
- Incident of stunting and wasting during this early infancy period are of great concern as it is associated with increased risk of chronic diseases in later life (2,3)
- The pathophysiology associated with growth failure after 6 months of age begin in early life (4)

HYPOTHESIS AND OBJECTIVE

HYPOTHESIS

Gut microbiome dysbiosis is a predictor of early childhood growth failure (CGF)

RESEARCH OBJECTIVE

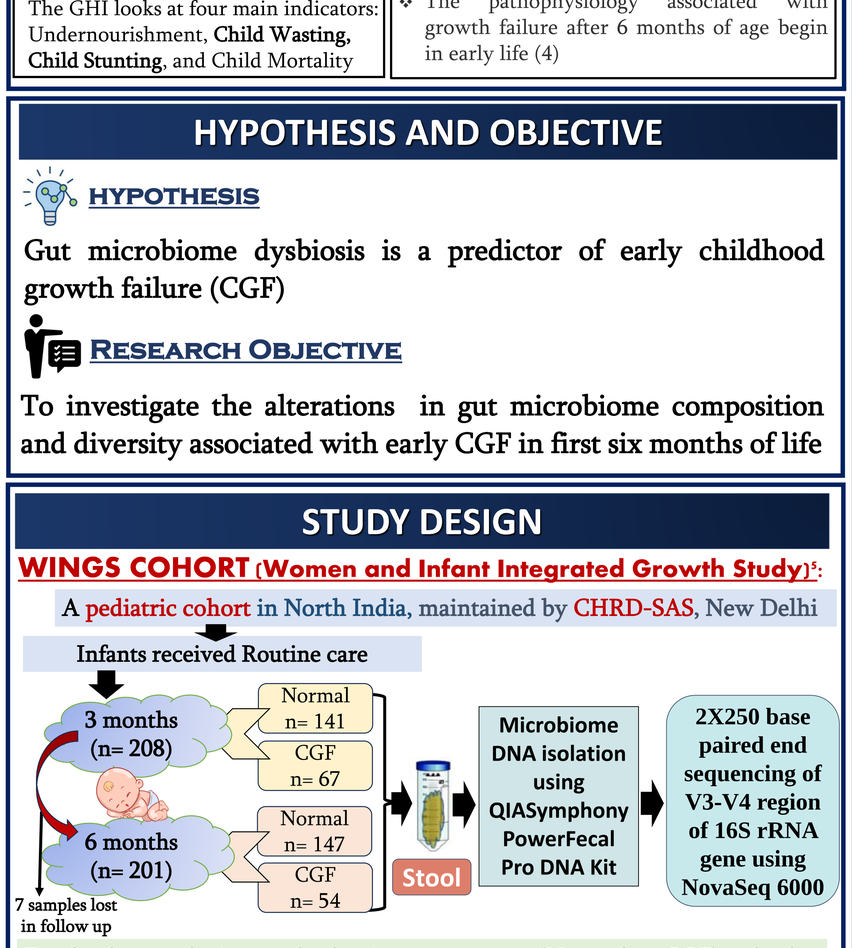
To investigate the alterations in gut microbiome composition and diversity associated with early CGF in first six months of life

STUDY DESIGN

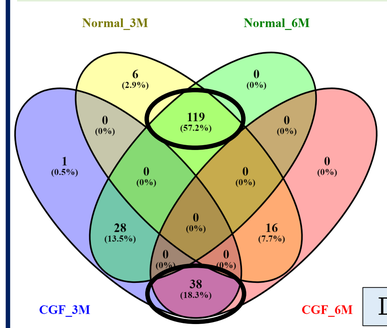
WINGS COHORT (Women and Infant Integrated Growth Study)[5]:

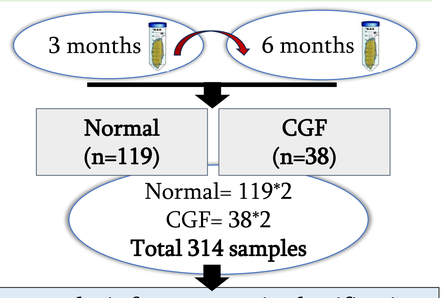
A pediatric cohort in North India, maintained by CHRD-SAS, New Delhi

Infants received Routine care



For further analysis samples having same status (Normal or CGF) at both the time point (3 and 6 months) have been chosen (n = 157)





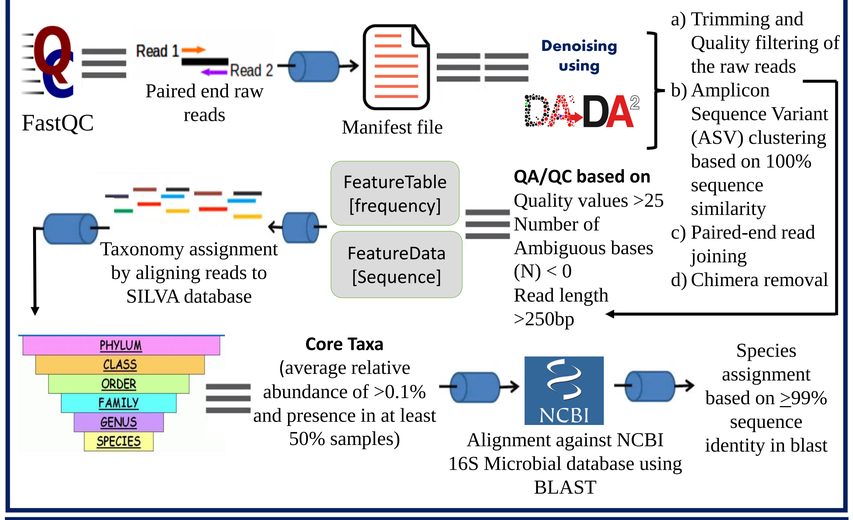
Data analysis for taxonomic classification

Inclusion criteria
- No antibiotics prior to one month of sample collection
- Clinically healthy infants with no signs of infection

Exclusion criteria
- Plan to move out of Delhi in next 3 months
- Non consent for participation by parents

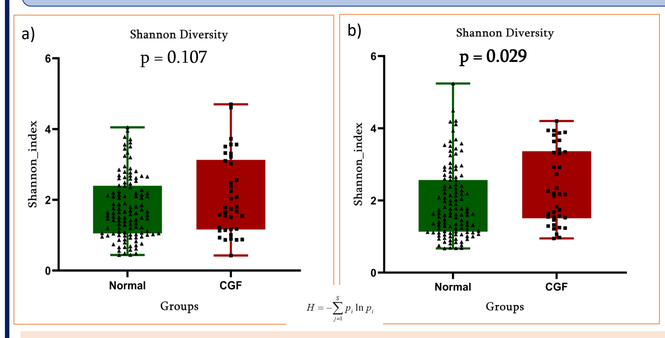
METHODOLOGY

Data Analysis using QIIME2: ASV based clustering (100% sequence similarity)



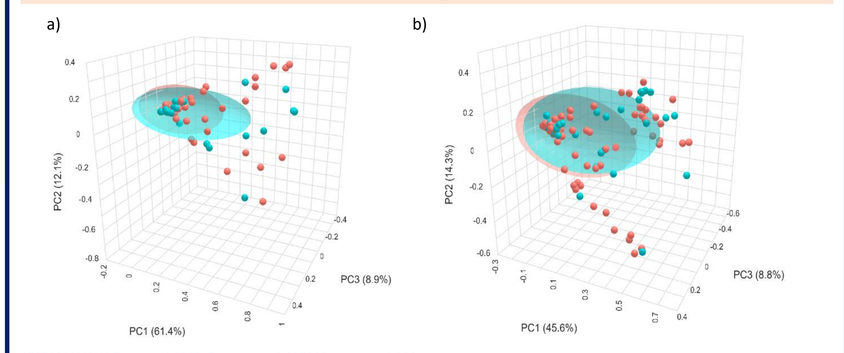
RESULTS

Alpha and Beta Diversity Estimation



Shannon diversity (Richness and Evenness) is significantly higher in CGF group of infants as compared to Normal group at 6 months of age

Diversity is higher in CGF group which may be due to the increase in pathogenic bacterial species and subsequently decrease in the corner stone member of the infant gut microbiota (*Bifidobacterium*)

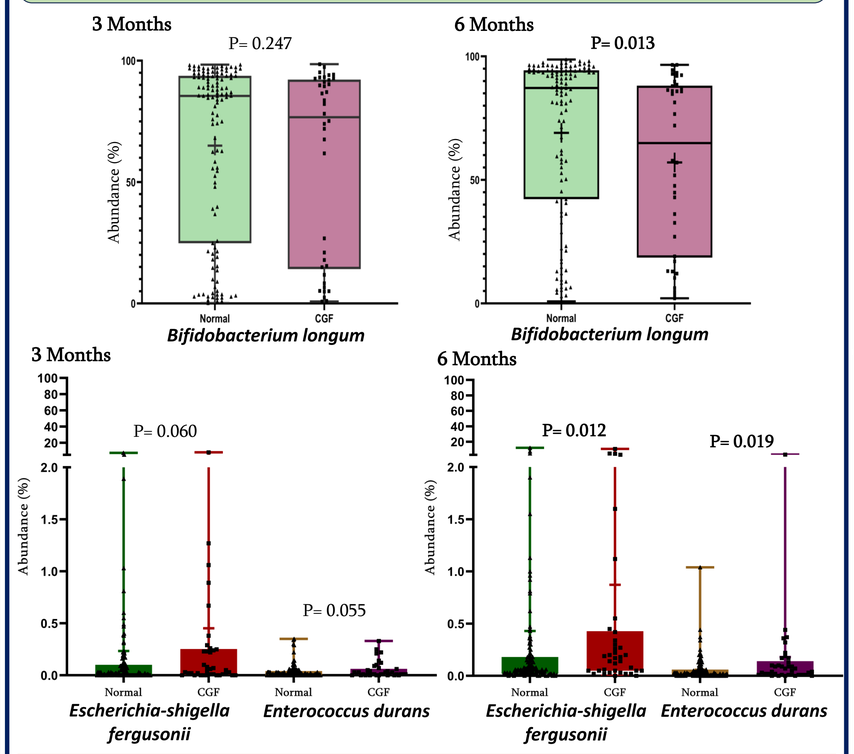


[PERMANOVA] F-value: 4.0222; R-squared: 0.025293; p-value: 0.022

[PERMANOVA] F-value: 2.3112; R-squared: 0.014692; p-value: 0.062

Principal coordinate analysis (PCoA) plots generated using Bray-Curtis dissimilarity index shows higher inter-individual variability across CGF group of infants as compared to Normal group whose microbiome composition is mostly similar across individuals at both a) genus and b) species levels at 6 months of age

Significantly different taxa in Normal and CGF group of infants



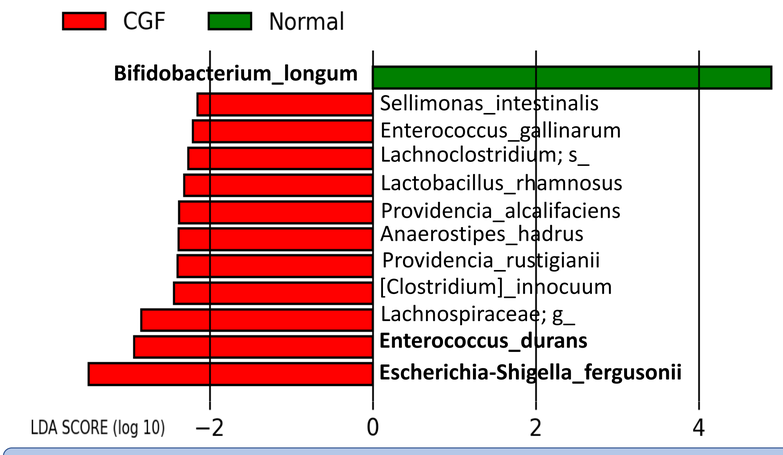
At 6 Months of age

1. Abundance of *Bifidobacterium longum* has been significantly increased in Normal group
2. Abundance of *Escherichia-shigella fergusonii*, and *Enterococcus durans* has been significantly increased in CGF group

RESULTS

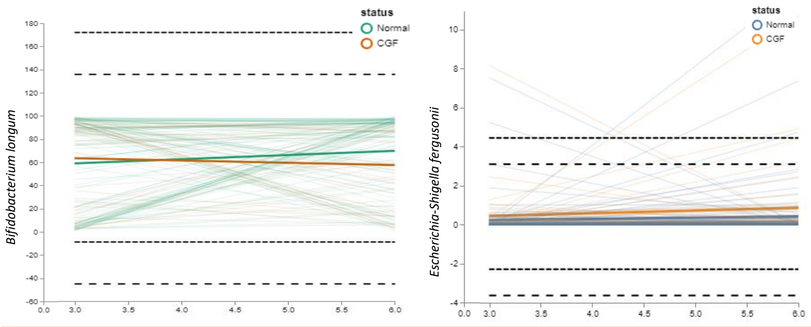
Linear Discriminant Analysis Shows:

1. *Bifidobacterium longum* is the most discriminant taxa in Normal group
2. *Escherichia-Shigella fergusonii* and *Enterococcus durans* are the most discriminant taxa in CGF group at 6 months of age



Longitudinal Analysis

Linear Mixed Effect (LME) has been performed using q2-longitudinal plugin in QIIME2 to check the effect of age (3 and 6 Months) and child status (CGF/Normal) on the relative abundance of genera and their species level data



1. *Bifidobacterium longum* is **increasing with age in Normal** group of infants and **decreasing in CGF** group
2. *Escherichia-Shigella fergusonii* is significantly **increased with age in CGF** group of infants

DISCUSSION AND CONCLUSION

Bifidobacterium — Core health-promoting organisms due to the ability to utilize human milk oligosaccharides

A reduction in the abundance of *Bifidobacterium sp.* in infants has been shown to increase the prevalence of obesity, diabetes, metabolic disorder, and all-cause mortality later in life (6)

Escherichia-shigella — A major contributor to diarrheal illness and dysentery in children younger than 5 years of age in low- and middle-income countries

The gut microbiota dominated by the *Escherichia/Shigella sp.* correlates with low SCFA concentrations and an increase in metabolic pathways related to diarrheal pathogens in pediatric populations of South Asia (7)

Enterococcus — Facultative pathogens that can cause a variety of infections

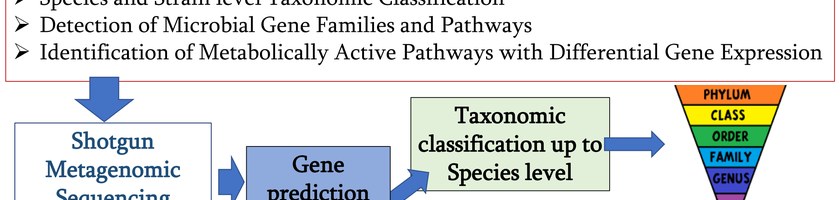
- ✓ The differences in microbial communities may have important health consequences as *Bifidobacterium* is one of healthy commensal, important for human milk oligosaccharides metabolization in infants
- ✓ *Escherichia-Shigella* and *Enterococcus* have pathogenic potentiality, that can cause gut dysbiosis which eventually leads to CGF
- ✓ These differences in microbial communities can act as predictive biomarkers of early infancy CGF that can be modulated by prebiotic/probiotic approaches in future

KEY MASSAGES

- ➢ Significant differences in gut microbiome composition and diversity are visible at 6 months of age
- ➢ *Bifidobacterium sp.* are important for proper growth of infants

Future Scope

Limitations of 16S rRNA gene sequencing:
- ➢ Species and Strain level Taxonomic Classification
- ➢ Detection of Microbial Gene Families and Pathways
- ➢ Identification of Metabolically Active Pathways with Differential Gene Expression



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7. *Lancet. 2013 Jul 20;382(9888):209-22.*

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Human Microbiome Research Team @ NIBMG

@smlab_NIBMG

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