Distinct Gut Microbiota in Small-, Appropriate-, and Large-for-Gestational-Age Infants

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Abstract

This study compared the gut microbiomes of small (**SGA**), appropriate (**AGA**), and large-for-gestational-age (**LGA**) infants to identify compositional and temporal differences. Forty-three neonates were classified into six subgroups based on weight and sampling time (early (< 14 d) *vs.* late (≥ 14 d of life). Although overall phylum- and genus-level abundances were similar, ***Streptococcus salivarius*** and ***Streptococcus sp.*** were enriched in late LGA infants. **α-diversity** was higher in late SGA infants, while **β-diversity** showed clear microbial separation among groups. **Co-occurrence network analysis** indicated a more stable microbial community in LGA infants. These findings highlight distinct developmental trajectories of the gut microbiome across SGA, AGA, and LGA infants.

Introduction

Abnormal fetal growth, including SGA and LGA conditions, increases the risk of neonatal morbidity, mortality, and long-term health complications. The gut microbiome plays a pivotal role in immune and metabolic development and is strongly influenced by maternal and perinatal factors.

Previous studies have primarily focused on low birth weight or preterm infants, leaving the gut microbiome characteristics of term SGA and LGA infants largely unexplored.

This study compared the **gut microbiome composition among SGA, AGA, and LGA infants born after 35 weeks of gestation to identify microbial differences** related to growth status.

Methods

Study Population and Fecal Sampling

- 43 late preterm and term infants admitted to newborn nursery or NICU at Hanyang University Hospital (Seoul, Korea) between Sep 2021 and Jan 2024 were prospectively enrolled (IRB 2023-04-047, NCT06812091).

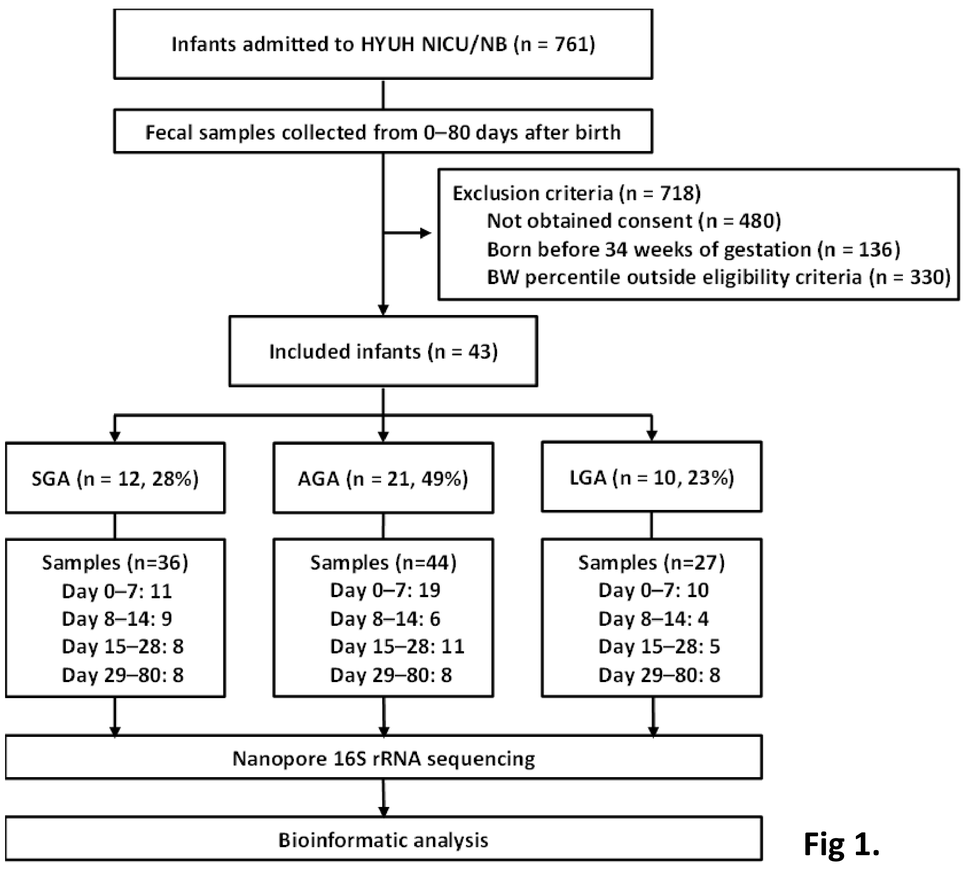

Fig 1.

Table 1. Baseline characteristics

	SGA (12)	AGA (21)	LGA (10)	*p*-value
GA (weeks, mean ± SD)	37.9 ± 1.8	38.1 ± 1.5	37.2 ± 1.6	0.318
BW (gram, mean ± SD)	2338 ± 411	3145 ± 323	3921 ± 241	<0.001
Male, n (%)	6 (50.0)	13 (61.9)	8 (80.0)	0.347
Cesarean section, n (%)	7 (58.3)	14 (66.7)	7 (70.0)	0.831
Exclusive whole milk, n (%)*	2 (16.7)	8 (38.1)	2 (10)	0.173
Use of antibiotics, n (%)	8 (66.7)	8 (38.1)	9 (90.0)	0.018
Ponderal index	2.26 ± 0.40	2.62 ± 0.29	2.79 ± 0.23	<0.001

Fecal DNA Extraction and Sequencing

- DNA extraction using ZymoBIOMICS DNA Miniprep Kit
- Full-length 16S rRNA gene (V1–V9) was amplified and sequenced using the Oxford Nanopore MinION

Bioinformatics and Statistical Analysis

- Raw FASTQ files were processed using QIIME2 (v2022.2) and SILVA reference database for taxonomic classification (85% identity).
- Statistical analyses were conducted using SAS v9.4 and GraphPad Prism v10.0.4, with $p < 0.05$ significance.

Results

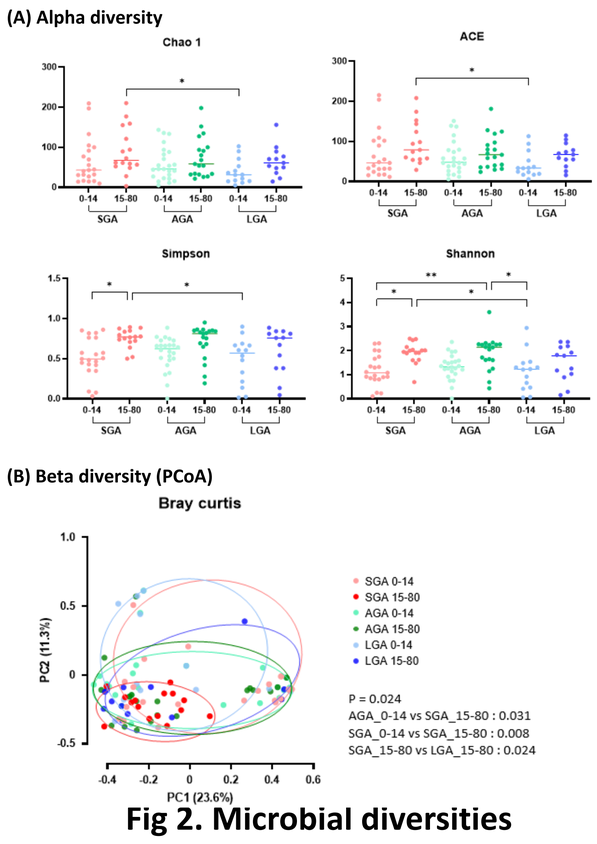

Fig 2. Microbial diversities

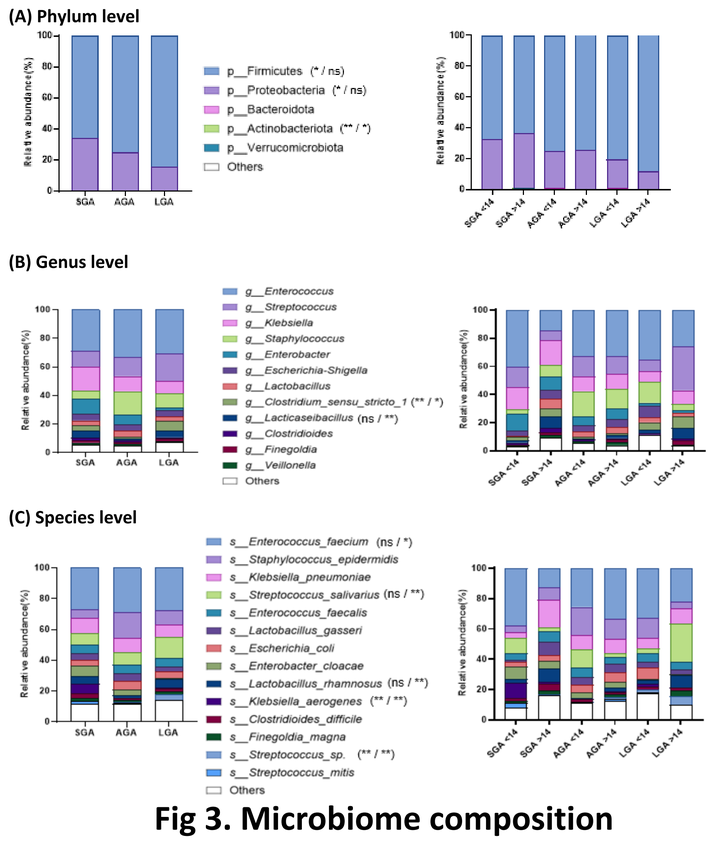

Fig 3. Microbiome composition

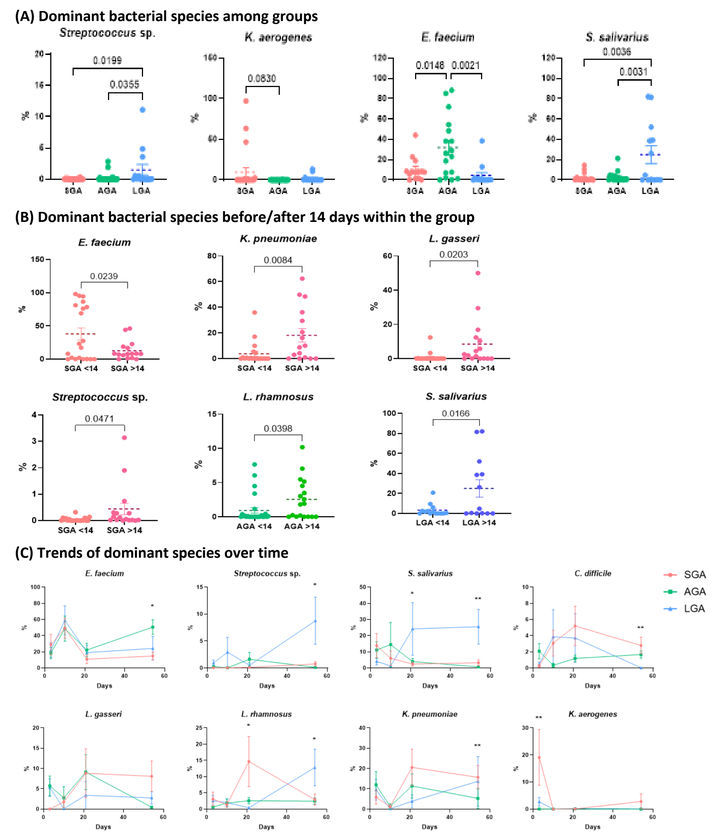

Fig 4. Dominant bacterial species

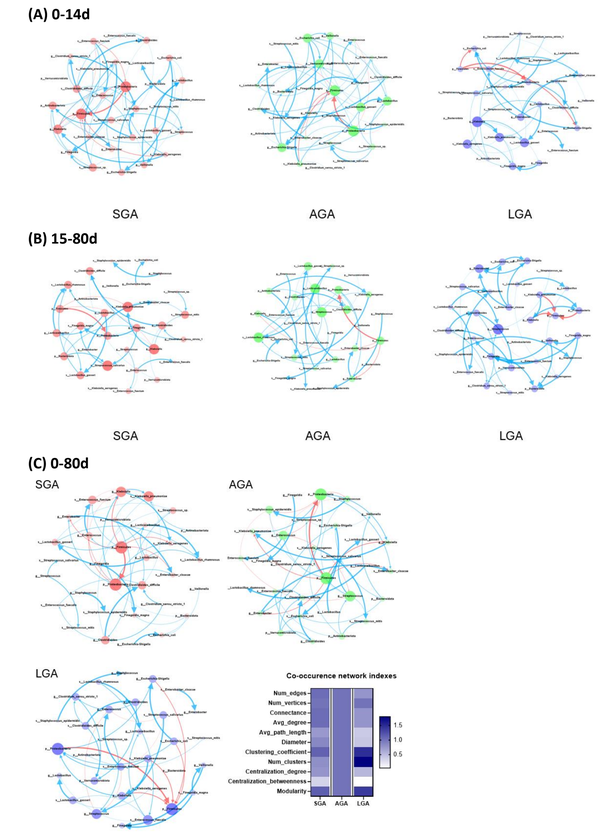

Fig 5. Co-occurrence network

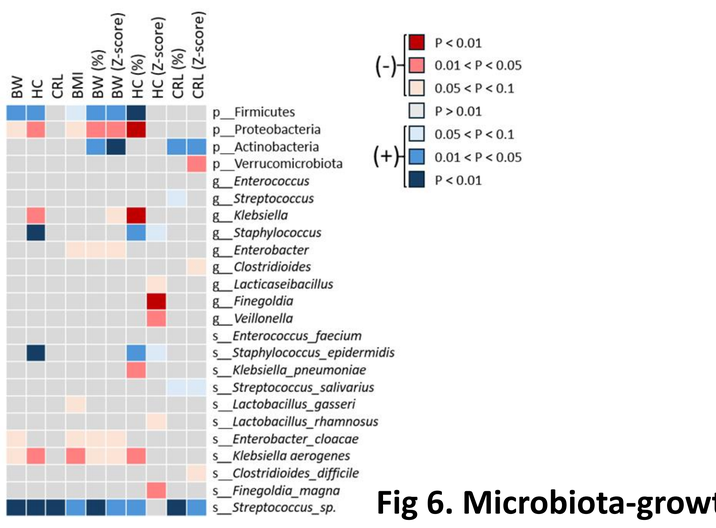

Fig 6. Microbiota-growth

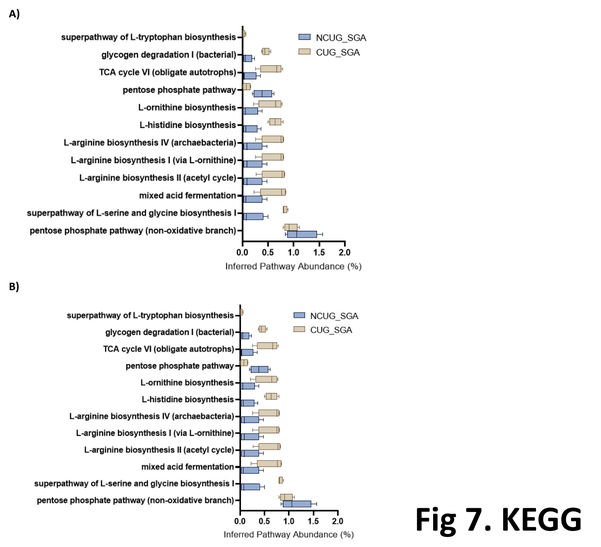

Fig 7. KEGG

Discussion

- This study provides the first longitudinal comparison of gut microbiota among SGA, AGA, and LGA infants using nanopore sequencing and network analysis.
- Microbial richness increased over time in SGA and AGA infants but remained low in LGA infants, suggesting distinct colonization dynamics linked to growth patterns.
- Firmicutes were associated with favorable growth and intestinal stability, while Proteobacteria predominated in early SGA infants, indicating potential dysbiosis.
- Functional analyses revealed enrichment of amino acid and energy metabolism pathways supporting catch-up growth, and tryptophan biosynthesis pathways potentially influencing neurodevelopment.
- Overall, these findings highlight early-life microbiome differences as potential targets for probiotic or metabolic interventions to improve long-term health outcomes.

References

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3. Reyman M, van Houten MA, Watson RL, Chu M, Arp K, de Waal WJ, et al. Effects of early-life antibiotics on the developing infant gut microbiome and resistome: a randomized trial. Nat Commun 13:893 (2022).