Microbiome-associated growth faltering in HIV-exposed but uninfected children



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Children born to pregnant women with HIV who are HIV-exposed but uninfected (HEU) are at an increased risk of growth stunting, morbidity, and mortality compared to HIV-unexposed children. The biological mechanisms driving growth deficits in HEU children remain poorly understood but may be linked to differences in the composition and function of the gut microbiome. In a prospective cohort of 168 HEU and HIV-unexposed children, we analyzed longitudinal quarterly growth measures from child aged 3 months to 2 years, stool shotgun metagenomic data at 3 months' age, and paired maternal rectal swab metagenomics for 75 participants pairs. While maternal HIV serostatus was not a major determinant of overall infant microbiome composition, it was associated with disturbances of potential opportunistic pathogens. Slower length growth was linked to enriched Streptococcus pneumoniae and Dolosigranulum pigrum, both known to cause infections. A random forest model showed that the infant microbiome corresponded with 7.3% of the variation (95% CI: 7.0%-7.5%) in the individual length growth slopes. Finally, a greater abundance of *Bifidobacterium breve* was associated with greater length growth in children born to HIV-seronegative mothers, compared to those born to HIV-seropositive mothers, suggesting that maternal HIV serostatus may modulate the effects of microbiome on growth. Our findings expand the understanding of microbiome-related mechanisms underlying growth in HEU children and offer promising targets for interventions.





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tested for anemia, malaria



MaAsLin3: Log2/TSS transformed, generalized linear mixed models testing for both abundance and prevalence associations microbiome features ~ hiv status + total reads



Interaction model: Imer(length value ~ hiv status × PCo2/microbial feature + time + (1 | id))



Conclusion

Our findings support a HIV-microbiome interaction relevant to growth in HEU children during early life. Understanding the microbiome-related mechanisms could lead to new avenues to support healthy growth in this population.

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Slower infant growth is associated with differences in gut microbiome composition, such as enriched Streptococcus pneumoniae and Dolosigranulum pigrum, both known to cause infections



Random slope: Imer(length value ~ time + (time | id)) **MaAsLin3:** microbiome features ~ length slope + total reads

Most common species shared across mominfant pairs

