The Relationship Between NICU Experience of VLBW Infants and Their Microbiome at 2-3 Years Old

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References:

Dogra, S., Sakwinska, O., Soh, S.-E., Ngom-Bru, C., Brück, W. M., Berger, B., . . . Chong, Y.-S. (2015). Dynamics of infant gut microbiota are influenced by delivery mode and gestational duration and are associated with subsequent adiposity. MBio, 6(1), e02419-02414.


Abstract Summary:
The study explored the relationships between prenatal and NICU factors experiences and characteristics of VLBW infants with their gut microbial taxa at 2-3 years of age.

Learning Activity:
| LEARNING OBJECTIVES | EXPANDED CONTENT OUTLINE |
The learner will be able to identify relationships between NICU experiences and characteristics of VLBW infants with their bacterial taxa at 2-3 years of age.

Evidence shows that maternal characteristics, the NICU environment, common use of antibiotics, and effect of mother’s own milk can contribute to development of the child's microbiome at 2-3 years of age.

The learner will be able to describe the importance of gastrointestinal flora in physiological and pathophysiological health outcomes.

Phyla composition of gut microbiome influences health outcomes.

Abstract Text:
The infant gastrointestinal microflora is likely to significantly contribute to the core community that makes up the adult ‘signature microbiome’, which may participate in physiological and pathophysiological interactions with the host. In addition, the literature indicates multiple consequences of very low birth weight on health outcomes (Caesar et al., 2016; Eichenwald & Stark, 2008). This study examined the association of variables initially studied as VLBW infants in the Neonatal Intensive Care Unit (NICU) with their gastrointestinal microflora collected when they were 2-3 years of age. The gut microbiome was measured longitudinally during their NICU stay and then later when they reached 2-3 years of age. **Objective:** The proposed study explored the relationship between NICU experience and characteristics of VLBW infants with their bacterial taxa at 2-3 years of age. **Methods:** These data are from a parent study of a cohort of VLBW infants with measures of gut microbiome, human milk intake, milk immunology, fecal calprotectin levels and later health outcomes collected when they reached 2 years of age. We followed VLBW infants (<1500 Gms) during 6 weeks of the NICU stay and followed up with home visits and stool collection at 2-3 years of age on 18 toddlers. This study analyzed measures collected while the infants were in the NICU (gestational age, antibiotic intake, amount of human milk, birth type, and infections) with their bacterial taxa at 2-3 years old. Stool swab samples were stored at -80°C prior to use. Microbial genomic DNA was extracted using the PowerSoil-htp 96 Well Soil DNA Isolation Kit (MoBio). DNA Samples were forwarded to the lab of Dr. Jack Gilbert (Argonne National laboratory and University of Chicago). The microbial content was profiled with 16S rRNA sequencing. PCR of the 16S rRNA V4 region (515F–806R) was performed and sequenced using the Illumina MiSeq platform to generate ~100,000 250 bp paired end reads per sample. Approval for this study was obtained from the university Institutional Review Board. All participants gave informed written consent to access their electronic health records and donate their children’s stool samples prior to their participation. **Results:** The study consists of 18 VLBW infants with a mean gestational age of 27.9 weeks (range 25.3 to 30.4), and a mean birth weight of 1088.59 gms (range 675-1485 gms). The gender distribution was equal. Length of stay mean was 73.06 days, with a range of 42 to 123 days. Twelve (66%) of the sample suffered respiratory distress syndrome and the mean days on oxygen were 26.13 days (range of 0-101 days). This study analyzed 18 stool samples from these children when they reached 2-3 years of age (the oldest is 45 months old) so far. As VLBW infants, the dominant phyla was Proteobacteria. As preliminary results, the microbial phyla of toddlers showed predominance of Firmicutes and Bacteroidetes, followed by Actinobacteria, Proteobacteria, and Verrucomicrobiota. This represents a huge developmental shift of gut microbiome from infant to toddler. Principal Component Analysis of microbiome showed a potential genetic effects as twins tended to cluster together. Prenatal factors included maternal steroids. In addition, some of the sequences identified in the founding microbiome of infants were still present in the toddler. **Discussion:** The preterm infant microbiomes described in our study are largely consistent with other findings(Karlsson, Molin, Cilio, & Ahrné, 2011; Sharon et al., 2013), confirming an association between low gestational age and the microbiota profile. The predominance of Proteobacteria characterizes a dysbiosis that is linked with detrimental outcomes for preterm infants (Dogra et al., 2015; Groer et al., 2014). In addition, the hospital environment, common use of antibiotics, and the use of infant formula rather than mothers own milk can contribute to dysbiosis (Groer et al., 2015). Oligotyping of the Enterobacteriaceae and Bifidobacteria found that certain substrains present in the stool in infancy were retained in the toddlers’ stools. Enterobacteriaceae
consists of virulent organisms capable of producing human disease (gram-negative bacteria that includes *Salmonella, Escherichia coli, Serratia, and Citrobacter*), and increased proportions are found after antibiotic use (Hollister, Gao, & Versalovic, 2014). **Conclusions:** Toddlers show increased alpha diversity retaining some of the same Enterobacteriaceae "oligotypes" from infancy. Pre and post-natal factors significantly influence later childhood phyla composition. Feeding status is not predictive of community composition, but effect of antibiotics may be predictable. As an important regulator of physiological and pathophysiological effects, it is relevant to develop intervention approaches to decrease dysbiosis and increase diversity in the VLBW. In pursuit of appropriate interventions, studies which explore microbial influence, diversity and succession are crucial.