June 2022

Identifying Predictors for Inflammation-Induced Preterm Birth: A Murine Study

Tzu Ning Liu BS
Wayne State University School of Medicine, Department of Obstetrics and Gynecology,
tzu.ning.liu@med.wayne.edu

Jose Galaz MD
Wayne State University School of Medicine, Department of Obstetrics and Gynecology; Perinatology Research Branch, Division of Obstetrics and Maternal-Fetal Medicine, Division of Intramural Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, U.S. Department of Health and Human Services (NICHD/NIH/DHHS), jgalaz@wayne.edu

Nardhy Gomez-Lopez PhD
Wayne State University School of Medicine, Department of Obstetrics and Gynecology; Perinatology Research Branch, Division of Obstetrics and Maternal-Fetal Medicine, Division of Intramural Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, U.S. Department of Health and Human Services (NICHD/NIH/DHHS), ngomezlo@med.wayne.edu

Introduction: Preterm birth is the leading cause of neonatal morbidity and mortality worldwide. A large proportion of preterm deliveries is affected by intra-amniotic inflammation, which can occur in the presence (intra-amniotic infection) or absence (sterile intra-amniotic inflammation) of microbes. Studies have shown an association between intra-amniotic inflammation, cervical shortening, and changes in the cervicovaginal microbiome. However, their causal relationships are unknown. This study aims to determine the causality of intra-amniotic inflammation, cervical shortening, and cervicovaginal microbiome alterations.

Methods: Pregnant C57BL/6 dams received an ultrasound-guided intra-amniotic injection of an endotoxin lipopolysaccharide (LPS) or the alarmin interleukin-1α (IL-1α) on 16.5 days post-coitum (n = 6-8 per group) to model intra-amniotic infection- or sterile intra-amniotic inflammation-associated preterm birth. Control dams were injected with saline (n=6-8). Cervical length was measured by ultrasound at time zero and 6-hours post-injection. In a second cohort of injected dams, cervical and vaginal tissues were collected 6 hours post-injection (n = 6 per group) for cervicovaginal microbiome analyses via 16S rRNA sequencing.

Results: Dams that received intra-amniotic injections of LPS and IL-1α showed greater percentage of cervical shortening when compared to controls. Microbiome analyses showed taxonomic differences in the bacterial profiles of the cervical and vaginal tissues. However, there were no differences in bacterial profile richness/heterogeneity, composition/structure, and bacterial taxa abundance between the two contrasting groups using generalized linear models, PERMANOVA, LefSe, and ANCOM-BC analyses, respectively.

Conclusion: Alarmin- and endotoxin-induced intra-amniotic inflammation led to cervical shortening, and this was not associated with an acute alteration of the cervicovaginal microbiome.