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First Trimester Vaginal Microbiome as Pregnancy Outcome Predictor

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Background

• The human microbiome can play a protective or harmful role during a woman’s pregnancy.
• The non-gravid vaginal microbiome fluctuates in diversity depending on hormonal changes, menses, contraception, etc., but the vaginal microbiome during pregnancy is more stable and dominated by fewer organisms.
• Lactobacillus spp. are the predominant species in the gravid vaginal microbiome and inhibit colonization of pathogenic species such as Gardnerella vaginalis, N. gonorrhoeae, "Lachnospiraceae BVAB1," and Snethia spp. The prevalence of these pathogenic microorganisms increases the susceptibility to infections such as bacterial vaginosis, which has been linked to premature rupture of membranes (PROM) and preterm birth.
• Previous studies have attempted to link certain organisms and microbiome patterns to clinical outcomes. Furthermore, most studies have been observational rather than investigating how these microbiome characterizations can be used as a potential screening tool for early intervention.
• We will adopt the opposite approach, starting with clinical outcomes and then examining the microbiomes for patterns. By comparing microbiomes at different trimesters in women with uncomplicated, healthy pregnancies and those who had adverse outcomes, we are looking to identify a microbial signature associated with complications such as preterm premature rupture of membranes (PPROM), premature rupture of membranes (PROM), gestational diabetes (GDM), gestational hypertension (GHTN), pre-eclampsia, and chorioamnionitis.

Methods

1. Subjects were pregnant women enrolled in VCU’s Vaginal Human Microbiome Project (VaHMP) and delivered at VCU. Vaginal swabs were obtained during an antenatal visit and microbiome analysis by 16s gene rRNA was performed. Clinical outcomes were abstracted from medical records.
2. Exclusion criteria included: multipara pregnancies (twins, etc.), immunosuppression (HIV, etc.), fetal demise (miscarriage, intrauterine fetal demise, etc.)
3. Complicated pregnancies were defined as: preterm delivery (<37 weeks), PPROM, PROM, GHTN, CHTN, pre-eclampsia, chorioamnionitis. Healthy pregnancies were defined as: term delivery (≥37 weeks), without any pregnancy or labor complications
4. Healthy vs. complicated pregnancies were case-control matched based on demographics and gestational age at sampling and the microbiome taxa were compared by LEfSe linear discrimination analysis (LDA).

Results

Table 1: Demographics of subjects in study

Table 2: Pregnancy Clinical Outcomes based on trimester sampled

Figure 2: First Trimester Vagitypes

Vagitypes of subjects sampled in first trimester. Vagitype is defined by the microorganism that was ≥30% predominance in the vaginal sample. Controls = healthy pregnancies sampled in first trimester

Figure 3: Significant microorganisms associated with PPROM

These LEfSe plots reveal microorganisms from A) first trimester samples and B) all samples overall that are significantly associated with pregnancies that ended in PPROM. An LDA score ≥2 is significant.

Future Study

• Little is known about “Candidatus Mycoplasma girerdii,” and data from this study suggests further investigation is necessary. Perhaps treating this microorganism early on in the pregnancy could prevent outcomes such as preterm delivery and PPROM.
• We hope to use this approach to further analyze other clinical outcomes for possible vaginal microbiome signatures.

Conclusion

• We have developed clinical definitions of healthy and complicated pregnancies based on pathologies that will be used in future VaHMP studies.
• Although one study7 found dysbiotic vagitypes in all three semesters of women who had PPROM, none of our PPROM subjects had a BVAB1 vagitype, and there were equal Gardnerella vaginalis vagitypes in both the controls and subjects who had PPROM (Fig. 2).
• While there were more PPROM subjects with Lactobacillus iners vagitypes, this Lactobacillus is less protective as it can coexist with pathogenic anaerobic bacteria.

Resources