## O-029   The Vaginal Microbial Predictors of the Endometrial Microbiota

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**Study question:** Can we find specific biomarkers in vaginal microbiota predicting the state of endometrial microbiota?

**Summary answer:** The higher levels of *Eubacterium spp.* in the vagina could serve as a predictor of the non-*Lactobacillus*-dominated microbial community in the uterus.

**What is known already:** The absence of microorganisms or the *Lactobacillus*-dominated community in the uterus cavity is considered more favorable than the non-*Lactobacillus*-dominated community. The latter is associated with poor pregnancy outcomes in women undergoing in vitro fertilization. However, endometrial microbiota analysis is challenging due to the possibility of contaminating the samples with vaginal microbiota during transvaginal sampling. Also, there is always a risk of upper genital tract inflammation after the sampling. For these reasons, the idea of finding markers predicting the state of endometrial microbiota is promising.

**Study design, size, duration:** It is a cross-sectional study of the vaginal and endometrial microbiota in 61 reproductive-age women with the normal histological pattern of endometrial samples. Endometrial and vaginal samples were collected simultaneously on days 7–10 of the menstrual cycle. Depending on the type of endometrial microbiota, the women were divided into two groups: Group 1 – the *Lactobacillus*-dominated microbiota or no microbiota (n = 43), Group 2 – the non-*Lactobacillus*-dominated microbiota (n = 18).

**Participants/materials, setting, methods:** All women came to the "Garmonia" Medical Center (Yekaterinburg, Russia) seeking infertility treatment from 2019 to 2021. Vaginal and endometrial microbiota was analyzed using Femoflor and Androflor real-time PCR kits (DNA-Technology, Russia). For the vaginal samples, the quantities and proportions of 22 microorganism groups were compared in Group 1 and Group 2 using Mann-Whitney test. For the variables with significant differences, ROC curves were constructed to assess the diagnostic value of the tests.

**Main results and the role of chance:** When comparing vaginal microbiota in Groups 1 and 2, we registered the statistically significant differences for 6 out of 44 variables (quantities and proportions of 22 microorganism groups). These variables were the quantities of *Eubacterium spp.* ($10^\circ$ vs. $10^{4.7}$, p = 0.002) and *Gardnerella vaginalis* ($10^\circ$ vs. $10^{4.0}$, p = 0.033), the proportions of obligate anaerobes (0% vs. 6.0%, p = 0.010), *Peptostreptococcus spp./Parvimonas spp.* (0% vs. 0%, p = 0.011), *G. vaginalis* (0% vs. 0.2%, p = 0.012), *Eubacterium spp.* (0% vs. 0.6%, p = 0.033). "Eubacterium spp.' quantity" variable demonstrated the highest discriminatory power (the area under the ROC curve value — 0.737 [CI 0.593-0.882], p = 0.004). The AUC value was considered as acceptable to divide patients into Group 1 and Group 2. The cutoff value of *Eubacterium spp.* $10^{3.15}$ genome-equivalent/ml (GE/ml)) allowed to predict the non-*Lactobacillus*-dominated microbiota in the uterus cavity with 77.8% sensitivity and 62.8% specificity.

**Limitations, reasons for caution:** The results were obtained on a small population group of women with the normal histological pattern of endometrial samples. It may be different if the larger pool of samples is investigated. It is also possible, that the results will not apply to the patients with endometrial abnormalities.

**Wider implications of the findings:** Further research should determine the diagnostic value of *Eubacterium spp.* identified in vaginal samples as the predictor for the endometrial microbiota composition in women with endometrial abnormalities. The next step is research dedicated to the link between different signatures in vaginal microbiota and endometrial abnormalities.

**Trial registration number:** Protocol № 7 dated September 20, 2019