O-143 Characterization of vaginal and endometrial microbiome in patients with chronic endometritis (CE).

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Study question: Could vaginal and endometrial microbiome by sequencing 16S rRNA be comparable to classic diagnostic methods or immunohistochemistry CD138 for diagnosis of chronic endometritis?

Summary answer: A characteristic endometrial and vaginal microbiome is present in patients with chronic endometritis. An abnormal vaginal microbiome correlates with the presence of chronic endometritis.

What is known already: Chronic endometritis is a disease characterized by persistent inflammation of the endometrial lining. Currently, histopathological evaluation by immunohistochemistry CD138 marker is most common diagnostic method for CE. Microbiome analysis based on subunit 16S rRNA sequencing is a fast tool that can enable the identification of pathogenic microorganisms associated with CE. The main bacteria at vaginal and endometrial level belong to genus *Lactobacillus*, producers of lactic acid that allows maintaining acidic pH of vagina and acts as barrier against pathogens. Investigations on the effect of an abnormal endometrial and vaginal microbiome could improve assisted reproductive technologies.

Study design, size, duration: This is a observational pilot study (60 patients and 120 samples). The study population consists of patients attending to our fertility clinic for frozen euploid embryo transfer (FET) from May 2017 to May 2019. Preimplantation Genetic Testing of aneuploidy (PGT-A) was performed at blastocyst stage using Veriseq (Illumina). The inclusion criteria to be meet by patients were: age between 18 and 50 years, own or donated oocytes and use of ICSI.

Participants/materials, setting, methods: Cohort study with sixty patients undergoing assisted reproductive treatment (TRA) with their own or donated gametes and PGT-A Vaginal and endometrial samples were taken in the cycle prior to embryo transfer. The vaginal and endometrial microbiome was analyzed by mass sequencing of the V3V4 region of 16S rRNA. Bioinformatics analysis was performed using QIIME2 and MicrobiomeAnalyst packages. Alpha, beta diversity and taxonomic characterization were compared with positive and negative CD138 groups for chronic endometritis (CE).

Main results and the role of chance: Different bacterial communities were detected when vaginal and endometrial samples were analyzed in patients with and without endometritis diagnosed with CD138 immunohistochemistry. In patients with endometritis, a higher alpha diversity index tendency was found in vaginal samples (p=0.15 for the Shannon index) and significant differences in endometrial samples (p=0.01 for the Shannon index). In the beta diversity analysis, no significant differences were observed between the groups established as per the diagnosis of endometritis. Vaginal and endometrial samples from women with endometritis showed a microbiome pattern not dominated by *Lactobacillus* spp. Relative abundance analysis identified the genera *Ralstonia* and *Gardnerella* in endometrial sample, and the genera *Streptococcus* and *Ureaplasma* in vaginal sample of patients diagnosed with CD138 for endometritis. Comparing endometrial and vaginal samples CD138 positive diagnosed for endometritis, alpha diversity (p=0.06 for the Shannon index and p=0.08 for the Simpson index) and beta diversity (p<0.0001) showed significant differences. Relative abundance identified the genera *Lactobacillus* (p=3.76E-4), *Ralstonia* (p=8.19E-4), *Delftia* (p=0.004) and *Anaerobacillus* (p=0.004) in these sample groups.

Limitations, reasons for caution: The main limitation of this study is the small sample size. Larger studies including a higher number of samples are needed to confirm the different microbiome pattern observed at the vaginal and endometrial levels in correlation with chronic endometritis. The microbiome pattern has not been analyzed after treatment of CE.

Wider implications of the findings: Our findings suggest the existence of a characteristic vaginal and endometrial microbiota in patients with chronic endometritis. Different genera and species were identified in patients with and without endometritis depending on whether the sample was endometrial or vaginal. An abnormal vaginal microbiome appears to be strongly correlated with chronic endometritis.

Trial registration number: Not Applicable