

Differential composition of vaginal microbiome is associated with successful intrauterine insemination (IUI) in couples with idiopathic infertility: a prospective observational study.

Virginia Amato ^{1*}, Enrico Papaleo ⁴, Renée Pasciuta ², Paola Viganò ⁶, Roberto Ferrarese ⁵, Nicola Clementi ¹, Ana Maria Sanchez ⁶, Lavinia Quaranta ⁴, Roberto Burioni ¹, Alessandro Ambrosi ⁶, Andrea Salonia ⁷, Massimo Clementi ^{1,2}, Massimo Candiani ^{4,5}, Nicasio Mancini ^{1,2}

* (lead presenter) amato.virginia@hsr.it

¹ Microbiology and Virology Unit, “Vita-Salute” San Raffaele University, Milan, Italy.

² Microbiology and Virology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy.

³ Faculty of Medicine and Surgery, “Vita-Salute” San Raffaele University, Milan, Italy

⁴ Obstetrics and Gynaecology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy

⁵ Department of Obstetrics and Gynecology, “Vita-Salute” San Raffaele University School of Medicine, IRCCS, Ospedale San Raffaele, Milan, Italy

⁶ Reproductive Sciences Laboratory, Division of Genetics and Cell Biology, IRCCS San Raffaele Scientific Institute, Milan, Italy.

⁷ Division of Experimental Oncology/Unit of Urology, URI, IRCCS Ospedale San Raffaele, Milan, Italy.

Keywords (maximum 8): vaginal microbiota; idiopathic infertility; intrauterine insemination; lactobacillus crispatus

Background. Vaginal and seminal microbiome have gained increasing interest for their involvement in reproductive health and fertility. However, their role in reproductive outcome is not fully ascertained yet. In this study, we aimed to characterize vaginal and seminal microbiome in 23 couples with idiopathic infertility undergoing intrauterine insemination (IUI) treatment, correlating it to the clinical pregnancy rate after IUI.

Methods. Vaginal swabs and seminal fluids were collected on the day of IUI procedure and analyzed through PCR amplification of variable regions 3 and 4 (V3–V4) of 16S rRNA genes and Illumina MiSeq sequencing. The taxonomic data were then correlated to IUI success, together with a panel of clinical and laboratory variables.

Results. We observed a differential composition of vaginal microbiome in our cohort of women with different IUI outcome. In particular, women experiencing IUI success showed a clear domination by *L. crispatus*, marker of a healthy vaginal ecosystem, while women experiencing IUI failure featured a more diverse pattern, even with non-*Lactobacillus* species. Importantly, considering all investigated variables, vaginal *L. crispatus* domination was the only factor strongly correlated to IUI success (p-value = 0,0002).

Discussion. Our results strengthen the potential role of *L. crispatus* in promoting a favorable environment for pregnancy and suggest that microbiome characterization could be useful, together with standard clinical and laboratory assessments, in the pre-IUI evaluation of infertile couples.