EXPLORING ASSOCIATIONS OF THE VAGINAL MICROBIOME AND STI CO-INFECTIONS WITH SPONTANEOUS CLEARANCE OF UROGENITAL *CHLAMYDIA TRACHOMATIS*

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Background:
Urogenital *Chlamydia trachomatis* (CT) spontaneously clears (without antibiotics) in up to 44% of women between screening and treatment initiation; underlying mechanisms are poorly understood. We investigated relationships of clinical and microbiome characteristics with CT persistence versus spontaneous clearance.

Methods:
From 1999-2003, the Longitudinal Study of Vaginal Flora followed reproductive-age women every three months for one year. CT screening for asymptomatic participants started after ligase chain reaction became available mid-study; unscreened endocervical swabs were tested after study completion. We identified CT persistence and clearance events between consecutive visits without CT-active antibiotic use, and we characterized the vaginal microbiome by metagenome sequencing at CT-positive index visits in these events. We used mixed-effects logistic regression to estimate associations between exposures at CT-positive visits and CT persistence versus clearance at subsequent visits.

Results:
This analysis includes 310 persistence and 301 spontaneous clearance events from 425 participants. In univariable models, CT persistence at the following visit was associated with Black race, age $\leq$25, bacterial vaginosis (Nugent score $\geq$7), prescription of metronidazole/clindamycin, and *Mycoplasma genitalium* co-infection (all $p<0.05$). CT persistence was also associated with *Candidatus* Lachnocurva vaginae-dominated and *Gardnerella*-dominated vaginal microbiomes, compared to *Lactobacillus crispatus*, *gasseri*, and *jensenii*-dominated microbiomes (all $p<0.05$). *M. genitalium* co-infection remained significantly associated with persistence when adjusting for race, bacterial vaginosis, and metronidazole/clindamycin prescription (OR=1.72, 95% CI: 1.04-2.82). *Ca*. L. vaginae dominance (OR=4.86, 95% CI: 2.04-11.57) and *Gardnerella* dominance (OR=2.65, 95% CI: 1.32-5.33) remained significantly associated with persistence when adjusting for age, race, and metronidazole/clindamycin prescription. Hormonal contraception, smoking, douching, baseline CT history, and *Neisseria gonorrhoeae* and *Trichomonas vaginalis* co-infections were not associated with CT persistence versus clearance.

Conclusion:

An optimal vaginal microbiome during CT infection may reduce CT persistence. The association between *M. genitalium* co-infection and CT persistence should be interrogated further as co-infection may uniquely contribute to adverse sequelae.

Disclosure of Interest Statement:
ST has been a consultant for Biofire Diagnostics, Roche Molecular Diagnostics, and Luca Biologics; receives royalties from UPTODATE; has received speaker honoraria from Roche Molecular Diagnostics and Medscape; and has received in-kind donation of sexually transmitted infection (STI) test kits to her institution through Hologic. JR is a cofounder of LUCA Biologics, a biotechnology company focusing on translating microbiome research into live biotherapeutic drugs for women's health. RMB has received in-kind donation of STI test kits to her institution through Hologic. All other authors report no potential conflicts.