TITLE: Microbial diversity in the vaginal ecosystem of women with human papillomavirus-associated cervical lesions

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ABSTRACT:

Vaginal microbiota is a complex ecosystem. Factors such as immunity and hormonal variations may lead to disruptions resulting in proliferation of opportunistic pathogens. Bacterial vaginosis (BV) is a polymicrobial syndrome, which may happen associated to other infections such as by Human Papillomavirus (HPV). HPV is highly prevalent in sexually active women, and is considered a risk factor for cervical cancer. As long as few data is available on vaginal microbiota of women with HPV-associated cervical lesions, our objectives were to evaluate the diversity in vaginal ecosystem in these women. To all patients, clinical and socio-demographic data were collected after gynecological examination. Vaginal secretion and cervical scraping were collected. Gram-stained smears were evaluated to establish Nugent score for BV determination. Viral and bacterial DNA obtained was used as template for HPV genotyping (PCR) and bacterial fingerprint (REP-PCR). In total 31 patients were included (mean age 35 and 93.6% sexually active). The Nugent score showed that 38.7% were BV. From the medical records, Pap smear tests showed that 32.3% had low grade squamous epithelial lesion (LSIL), 29% had high grade squamous epithelial lesion (HSIL), 25.8% had atypical squamous cells of undetermined significance (ASC-US) and 12.9% with atypical squamous cells that would not exclude high-grade lesion (ASC-H). All participants were HPV^{+}. HPV-16 was the most frequent (87.1%), followed by HPV-18 (61.3%). HPV-31, HPV-52 and HPV-58 were also detected. Coinfection HPV-16/HPV-18 was observed in 75%. In the 18-30 age group, HPV-16 was detected in 40%, and HPV-16/HPV-18 coinfection in 35%. HPV-16 was associated to 30% of ASC-H and 20% of HSIL patients. BV was observed in 50% of $HPV\text{-}16^{+}$ participants and in 45% of $HPV\text{-}16/HPV\text{-}18^{+}$. Fingerprints of bacterial communities showed clusters with low similarity suggesting high heterogeneity in vaginal microbiota within the sampled group. Overall the data is worrisome once cervical-cancer highly risk-associated HPV-types were identified. The high microbial diversity observed may be related to the different levels of cellular lesions, and different physiological conditions of the participants (age, social behavior, education). Further prospective studies are needed to better address correlations and BV and microbial imbalance in vaginal ecosystems which would be related to the different cellular lesions in women with HPV infections.

Keywords: Human papilomavirus; bacterial vaginosis; cervical intraepithelial lesions; cervical cancer

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