Associations Between Vaginal Infections and Potential High-risk and High-risk Human Papillomavirus Genotypes in Female Sex Workers in Western Kenya

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ABSTRACT

Purpose: Infection with and persistence of high-risk human papillomavirus (HR HPV) are the strongest risk factors for cervical cancer. Little is known about the prevalence and role of concurrent sexually transmitted infections (STIs) found in HPV-infected female sex workers (FSW) in Africa. This study purports to test our a priori hypotheses that STIs are associated with genotypes pertaining to the α-group species 9. The objectives were to determine the prevalence of bacterial vaginosis (BV), *Trichomonas vaginalis*, and *Candida* spp in FSW, the association between these STIs and the prevalence of any potential HR and HR HPV genotypes in FSWs.

Methods: A cross-sectional study design of 616 FSW from Western Kenya aged between 18 and 61 years during 2009–2015 using a peer recruitment sampling strategy. Inclusion criteria for the study entailed female sex and >18 years of age and having engaged in transactional sex in exchange for money, goods, services, or drugs in the last 3 months. Women were excluded if they were pregnant, <18 years of age, had a history of cervical dysplasia or cancer, had current abnormal bleeding, or had a hysterectomy.

Findings: Of the FSW, 33.3% had HIV and 57.7% harbored a potential HR and HR HPV genotype. The 2 most prevalent potential HR and HR genotypes were HPV 16 (16.10%) and HPV 59 (12.20%). BV was the most common infection (48.3%), followed by *Trichomonas vaginalis* (31.4%) and *Candida* spp (19.9%). A multivariate regression revealed significant associations with both α-group 9 and 6; BV and HPV 58 (adjusted odds ratio [aOR] = 2.3; 95% CI, 1.0–5.2; $P = 0.05$), *Trichomonas vaginalis* and HPV 31 and HPV 35 (aOR = 2.0; 95% CI, 1.0–3.8; $P = 0.04$ and aOR = 1.8; 95% CI, 1.0–3.3, $P = 0.05$ respectively); and between *Candida* spp and HPV 53 (aOR = 2.0; 95% CI, 1.1–4.0; $P = 0.03$) and 16 (aOR = 1.9; 95% CI, 1.1–3.3; $P = 0.03$).

Implications: Snowball sampling may have inadvertently excluded FSW less likely to benefit from a social network. Significant associations between BV and HPV 58 and between *Candida* spp and HPV 16 and 53 suggest the need for sexually transmitted disease management within a cervical cancer prevention program. The probable synergistic effects of the vaginal microbiota should be elucidated, especially within this vulnerable population. Given the potential for FSW to transmit STIs, robust epidemiologic sampling methods are urgently required that account for the heterogeneity of the FSW population. (*Clin Ther*. 2016;38:2567–2577)

Key words: bacterial vaginosis, *Candida* spp, female sex workers, HIV, potential-high-risk and high-risk HPV, *Trichomonas vaginalis*.

INTRODUCTION

Human papillomavirus (HPV) is a sexually transmitted infection and high-risk (HR) HPV DNA has been found

Accepted for publication October 10, 2016.
http://dx.doi.org/10.1016/j.clinthera.2016.10.005
0149-2918/$ - see front matter

to be present in 99.7% of cervical cancers worldwide.[1] More than 200 HPV genotypes have been identified and are divided into high- and low-risk carcinogens, depending on their capacity to induce cervical intraepithelial neoplasia and invasive cervical cancer. HR HPV types include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59. Others HPV types are classified only as potential high risk (pHR) (types 53, 66, 68, 70, 73, and 82). HPV 16 and HPV 18 are the most virulent HR HPV genotypes, causing about 70% of all invasive cervical cancers in the world.[2] The 15 HR oncologic viral strains can be disaggregated into the HPV 16 group (α-9) of the α-papillomavirus genus (HPV 31, HPV 33, HPV 35, HPV 52, and HPV 58) and the HPV 18 group (α-7; HPV 39, HPV 45, HPV 59, and HPV 68) and HPV 53, HPV 30, and HPV 56 from the α-6 type species.[3,4]

In Kenya, the Ministry of Public Health and Sanitation has conceived a comprehensive cervical cancer prevention strategy that includes plans for administrating quadrivalent vaccine, including HPV 16, 18, 6, and 11 to preteen girls in the near future. Currently, the Gavi-supported HPV vaccine pilot program is being implemented in Kitui County in Eastern Kenya, and is currently awaiting approval for nationwide rollout and successful global funding.[5] In 2014, a nonavalent vaccine containing additional HPV types (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58 antigens) was licensed by the US Food and Drug Administration,[6] which represents a milestone in the global cervical cancer prevention landscape, as it is expected to prevent 90% of invasive cervical cancer cases worldwide.

However, despite these strides in the cervical cancer prevention landscape, concomitant sexually transmitted diseases in HPV-infected women may hamper cervical cancer prevention by resulting in prolonged HPV infection and further increasing the risk of cervical intraepithelial neoplasia.[7–10]

African women have the highest prevalence of bacterial vaginosis (BV) in the world, which is characterized by an overgrowth of vaginal anaerobic flora and reduction of H_2O_2-producing lactobacilli.[11] A recent longitudinal study conducted in Kenya, Rwanda, and South Africa, revealed a BV prevalence of 38% in HIV-negative women[12] in Kenya. It is posited that BV increases the risk for HR HPV infection due to its association with high levels of anaerobic micro-organisms and their by-products, which in turn can disrupt the vaginal epithelium, degrade cervical mucus, and cleave immunoglobulin A.[13–15] A recent meta-analysis of available literature reported a positive association between BV and HPV infection,[16] and a recent HIV Epidemiology Research study in Tanzania found increased odds for incident of HPV, as well as delayed clearance among women with BV.[17]

Trichomonas vaginalis (TV) is the second most common cause of lower genital tract infection worldwide, and a multiplicity of studies have reported an association with previous and current TV infection and cervical dysplasia and HR HPV.[18–21] Similarly to mechanisms implicated in BV, TV produces microtrauma in the cervical epithelium that may increase the risk for HR HPV infection.[22]

While *Candida albicans* is the most prevalent species in asymptomatic vulvovaginal candidiasis, certain species of *Candida* are more pathogenic and capable of inducing hyphal and pseudo-hyphal formation, enhancing proteolytic activity and antigen modulation.[23] This would theoretically enable *Candida* to penetrate the mucosal surface and induce mucosal swelling, erythema, and exfoliation of cells[24] and, consequently, increase the risk for HPV.[25]

In Kenya, as in many parts of sub-Saharan Africa, FSW bear the greatest burden of HIV infection and, as early as 1985, a study reported that HIV prevalence was as high as 61% among a group of FSW in Nairobi.[26] In Kenya, where the penal code specifically punishes prostitution,[27] a recent study estimated that 5% of the urban female population of reproductive age could be sex workers.[28]

This analysis attempts to test our a priori hypotheses that sexually transmitted infections (STIs) are associated with genotypes pertaining to the α-group 9. The objectives of this study are to assess the prevalence of pHR and HR HPV genotypes, BV, TV, and *Candida*, the most important STIs in FSW women undergoing cervical cancer screening in a private clinic in Western Kenya, and explore associations between HR HPV genotypes and these vaginal microbiota.

METHODS

Study Design

A cross-sectional design was used to explore associations between BV, TV, and *Candida* and different pHR and HR HPV genotypes. This cross-sectional study based on record reviews adhered to