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Prevalence, genotyping, and correlates of anogenital HPV infection in a population-based sample of women in Puerto Rico

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ABSTRACT

Background: Oncogenic HPV infection is associated to anogenital cancer. We estimate the prevalence and correlates of anogenital HPV infection among a population-based sample of women aged 16–64 years living in the metropolitan area of Puerto Rico.
Methods: 564 women completed face-to-face and computer assisted interviews and self-collected anal and cervical specimens. HPV DNA testing used MY09/MY11 consensus HPV L1 primers and beta-globin as an internal control for sample amplification. Positive specimens were typed by dot-blot hybridization.
Results: Weighted prevalence of cervical, anal, and cervical/anal co-infection was 29.4%, 38.6%, and 17.1%, respectively. The commonest oncogenic HPV types detected in the cervix and anus were: 68 (8% vs. 7%) and 16 (5.5% vs. 5.1%), correspondingly. Having ≥ 3 lifetime sexual partners (OR: 2.3; 95% CI: 1.5–3.5) and last year anal intercourse (OR: 1.6; 95% CI: 1.1–2.5) increased the odds of anogenital HPV infection. Cervical infection was independently associated to anal infection (OR: 3.0; 95% CI: 2.0–4.6).
Conclusions: Similar to others, our results confirm the burden of anogenital HPV infection in women and its relationship with sexual behavior. As vaccination increases, future studies should monitor changing trends in HPV infection in this population, and the relationship between anal and cervical HPV-related disease.

1. Background

Human papillomavirus (HPV) is mainly transmitted through sexual contact and it is common among the general population [1]. HPV genotypes are classified as High Risk (HR) or Low Risk (LR) types depending on their oncogenic potential, HR infections cause cervical and anal cancers [1–3]. The cervix and anus possess a transformation zone characterized by a metaplastic epithelial site, which make them susceptible for HPV infection [3]. HPV prevalence differs across geographical regions and depends on age distribution and sexual practices of the populations [4,5]. Despite the burden of HPV infection and its causal relationship with various cancers [1–3], there is no routine surveillance system for HPV.

Although HPV-16 is the most common HPV genotype at the time of cervical diagnosis of squamous cell carcinoma (SCC), HPV-18 is the type most strongly associated with adenocarcinoma [2]. Three vaccines have been licensed for the prevention of HPV infection and its related malignancies [6]. In order to assess the impact of HPV vaccination programs, it is essential to establish baseline estimates of the type-specific HPV prevalence in the general population [7–9].

Our group has documented a high burden of HPV-related cancers in Puerto Rico [10–13], as well as an elevated prevalence of high-risk sexual practices [14]. Having baseline information on the burden of cervical and anal HPV infections is important in order to measure the impact in the prevention and control of HPV infection and related malignancies in this population, which still has low vaccine uptake [15]. This study described the prevalence and correlates of cervical and anal HPV infections in a population-based sample of women living in the San Juan Metropolitan area (SJMA) of Puerto Rico.

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2. Methods

2.1. Study population

A detailed description of the design and methods of this study has been described elsewhere [16]. Briefly, 566 non-institutionalized women aged 16–64 years living in the SJMA of Puerto Rico participated in the study from August 2010 to May 2013. Participants were identified through a four-stage probability sample design of households in the SJMA: stage-1) systematic random selection of 50 census blocks groups; stage-2) random selection of one block from each census block group; stage-3) random selection of one segment of about 12–16 households on each census block was randomly selected; and stage-4) selection of one eligible woman per household. If more than one woman were eligible, selection was performed by simple random sampling. Women were not eligible to participate if they were HIV positive, pregnant, and/or were cognitive or physically impaired. All 566 participants signed the informed consent and completed study procedures. Of these, 564 provided adequate cervical and anal samples for HPV testing. All cervical specimens (100%) and 95% of anal specimens ($n=536$) were positive for the human β-globin, and thus suitable for HPV typing [16]. This study was approved by the Institutional Review Board of the Medical Sciences Campus, University of Puerto Rico.

2.2. Data collection procedures

After signing the informed consent, women completed a face-to-face interview and a self-administered questionnaire using an Audio Computer Assisted Self-Interview (ACASI) system. The face-to-face interview collected information on risk factors for anogenital HPV infection, including demographic and behavioral characteristics and reproductive and health history. The ACASI system was used to collect sensitive information on sexual practices, condom utilization, and drug use.

2.3. Biological specimens' collection

Anal and cervical specimens were self-collected. Each participant received a collection kit that included the necessary materials for self-collection. Additionally, staff personnel provided a verbal explanation and written instructions including diagrams, comparable to those used in past studies [17,18], to each participant. Upon completion of the study procedures, samples were stored at −70 °C and shipped on dry ice to the University of California, San Francisco for HPV typing. After completing the study procedures, participants received educational material on HPV and HPV vaccine, and a monetary compensation for their time and effort.

2.4. Analysis of cervical and anal biological specimens

HPV DNA was purified from samples. HPV typing was performed using L1 consensus primer polymerase chain reaction (PCR) with MY09/MY11 primers sets and β-globin as an internal control for sample amplification. PCR products from positive samples were typed by dot-blot hybridization using 40 individual type-specific probes, including oncogenic HR HPV types as defined by the International Agency of Research on Cancer (IARC) (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) and non-oncogenic types LR (6/11, 26/69, 30, 32/42, 34, 53, 54, 57/2/27, 61, 62, 66, 67, 70, 71, 72, 73, 81, 82, 83, 84, 85, 86/87, 90/106, 97, 102/108, as well as 2 separate mixtures, mix1 contains 7/13/40/43/44/55/74/91, and mix2 contains 3/10/28/29/77/78/94 plus all those HPV types that hybridized only with the consensus probe). Samples that were positive for the consensus probe on the Linear Array (LA) HPV strip were considered HPV positive and those that were negative for the consensus probe were considered HPV negative. Specimens with β-globin undetected were considered inadequate and were excluded from the analysis.

2.5. Statistical analysis

The variables cervical infection (yes/no) and anal infection (yes/no) were defined independently. In addition, participants were classified into one of four groups according to their cervical–anal HPV infection status: (1) no HPV infection in either site (Cervix−/Anus−), (2) HPV infection only in the anus (Cervix−/Anus+), (3) HPV infection only in the cervix (Cervix+/Anus−), and (4) HPV concurrent cervical/anal infection or co-infection (Cervix+/Anus+). The overall and type-specific HPV prevalence, for each group above, was estimated with 95% confidence intervals (95% CI) using a logistic regression model. In order to control for the effect of the sampling design on the prevalence estimation, a normalized weighting factor was considered in this model using the inverse probability of selection for each participant and the inverse probability of participation [16] as follows:

$$w_i = \frac{1/(f_1 \times f_2)}{\bar{w}}$$

where f_1 indicates the selection probability for each participant, f_2 is the rate of participation in each block, and $\bar{w}$ is the mean final weight of the entire sample.

Meanwhile, the Kappa statistic was used to assess the concordance of the HPV types observed in the cervical and anal samples among women with co-infection. The chi-square statistic was used to assess differences in covariates across the four groups and an age-adjusted polytomous logistic regression model was used to quantify the magnitude of the association between cervical–anal HPV infection categories and covariates. Given the small sample size in each category, and thus limited statistical power for detecting differences in the groups HPV positive in different anatomical sites, a multivariate logistic regression model (MLRM) was also used to describe factors associated to any anogenital HPV infection, using those cervix−/anus− as the reference group. Furthermore, in order to assess the association between anal and cervical infection, another multivariate logistic regression model, adjusted by covariates significantly associated in the bivariate analysis to anal and cervical infection, was used. Variables that were significant ($p < 0.05$) in the bivariate analyses to the outcome variables for each case and those considered relevant based on the previous literature were included in the polytomous and MLRMs models to estimate the adjusted odds ratio (OR). The MLRMs were fitted using an estimable generalized equations approach for controlling the correlation between the measurements of women living in the same households block. Evaluation of interaction terms in these models was performed using the likelihood ratio test. The statistical package Stata (Version 13.0, College Station, TX, USA) was used to perform data management and all statistical analyses.

3. Results

3.1. Weighted HPV prevalence by anatomic site

The prevalence of cervical HPV infection (29.4%, 95% CI: 23.2–36.4%) was lower than anal HPV infection (38.6%, 95% CI: 30.1–47.9%). The prevalence of HR types in the cervix (8.4%, 95% CI: 5.6–12.6%) was lower than LR types (17.4%, 95% CI: 13.0–23.0%), while anal prevalence for HR and LR types was similar (12.5%, 95% CI: 8.4–18.3% and 12.3%, 95% CI: 8.7–17.3%, respectively). Meanwhile,