Prevalence of Cervical and Oral Human Papillomavirus Infections Among US Women

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Data from the National Health and Nutrition Examination Survey, 2009–2010, indicated that the prevalence of human papillomavirus (HPV) infection among women was 42.7% in the cervix and 3.8% in the oral cavity. The prevalence of oral HPV infection was 5-fold higher among women with than among those without cervical HPV infection (7.0% vs 1.4%; prevalence ratio, 4.9 [95% confidence interval, 2.7–8.7]). Among the 3% of women with HPV detected at both sites, complete type concordance was detected in 6.6%, and partial agreement was detected in 37.7%. These data suggest that HPV infections at these 2 sites are not independent, although type-specific concordance is low.

Keywords: human papillomavirus; cervix; oral cavity; HPV prevalence; NHANES

The causal role of human papillomavirus (HPV) in cervical and other anogenital malignancies is well established. The presence of HPV in the cervicovaginal region of US females has therefore been monitored through the National Health and Nutrition Examination Survey (NHANES) since 2002. Data collected between 2003 and 2006, before HPV vaccine introduction, showed an overall prevalence of 43% among 14–59-year-old females [1]. The association of HPV with a subset of head and neck cancers [2] has stimulated interest in investigating the prevalence of HPV infection in the oral cavity. A disproportional increase in HPV-attributable oropharyngeal cancers in some demographic groups, most notably non-Hispanic white males, has further increased attention [3]. Oral rinse and gurgle specimens for determining the prevalence of HPV infection in the entire oral cavity, including the tongue and tonsils, have been collected through the NHANES since 2009, with an overall prevalence of 7% among 14–59-year-old males and females in 2009–2010 [4].

Limited information is available about the relationship between cervical and oral infections in the U.S. Studies in which HPV typing was performed at both anatomic sites assessed convenience samples [5, 6] were restricted to particular high-risk groups [7, 8] and/or focused on prevalence differences between sub-groups or time-points [9, 10]. Available data indicate that concurrent oral-cervical HPV coinfections are relatively rare and that type-specific concordance detected at both sites is low. However, the prevalence of HPV in the oral cavity varies depending on demographic and geographic factors. Concordance of genotype specific oral and cervical HPV infections have not been determined in the general U.S. population. This report reviews HPV typing data among simultaneously collected cervical and oral specimens from women who participated in the NHANES between 2009 and 2010.

MATERIALS AND METHODS

Study Design and HPV Genotyping

The NHANES is an ongoing series of cross-sectional surveys conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. The surveys are designed to be nationally representative of the civilian, noninstitutionalized US population. We used data from NHANES 2009–2010 for this analysis. Self-collected cervicovaginal swabs and oral rinse samples from females aged 18–59 years were obtained at mobile examination centers and processed as previously described [4, 11]. DNA extracts from both specimen types were tested with the Linear Array HPV genotyping assay (Roche Diagnostics, Indianapolis, IN) to determine the presence of 14 high-risk HPV genotypes (ie, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 64 and 68) and 23 low-risk HPV genotypes (ie, 6, 11, 40, 42, 53, 54, 55, 56, 61, 62, 66, 67, 69, 70, 71, 72, 73, 81, 82, 83, 84, 18, 39, and 89), albeit in different laboratories and by use of different extraction methods. In cases where the activity of the cross-hybridizing XR probe could not be interpreted unambiguously, the status of HPV-52 was confirmed by real-time polymerase chain reaction.
Demographic information was ascertained during the household interview. Sexual history information was determined by self-report using an audio computer-assisted self-interview.

Statistical Analysis

All estimates were weighted to account for the unequal probabilities of selection and adjustment for nonresponse [12]. Prevalence values were estimated and reported as percentages with 95% confidence intervals (CIs). Estimates with a relative standard error of >30% are noted; these are considered unstable and should be interpreted with caution. Bivariate associations with selected demographic and sexual behavior characteristics were examined using the Wald F test, with adjustment for survey design. All analyses were conducted using SAS (version 9.3, SAS Institute, Cary, NC) and SAS-callable SUDAAN (version 11.0, RTI, Cary), with adjustment for survey design. All analyses were conducted using SAS-callable SUDAAN (version 11.0, RTI, Cary). Differences with \( P \) values of <.05 were considered statistically significant. Concordance was defined as detection of the same HPV types at oral and cervical sites in the same woman and was considered to be complete if all of the same types were detected at both sites or to be partial if at least 1 but not all types were detected at both sites.

RESULTS

HPV DNA typing results for both oral and cervical specimens were available for 1812 participants (Table 1). The weighted prevalence of cervical infection with any HPV type was 42.7% (95% CI, 39.3–46.3) overall and 39.8% (36.4–43.2) among women without concurrent HPV in the oral cavity. The prevalence of oral HPV infection was 3.8% (95% CI, 2.7–4.4) overall; only 0.8% (95% CI, 0.4–1.5) of women had oral HPV infection without concurrent cervical HPV infection. Among women with oral HPV infection, 78.4% (95% CI, 86.4–87.0) were also positive for cervical HPV infection.

At least 1 HPV type was detected in both cervical and oral samples in 3.0% (95% CI, 2.1–4.3) of women. In the cervix, 37 different genotypes were found, while 27 different types were detected in the oral cavity. Types that were present in cervical and oral samples from the same women included high-risk HPV types 16, 18, 45, 51, 58, 59, 66, and 68 and low-risk HPV types 6, 53, 54, 61, 62, 81, 83, 84, and 89 (Figure 1).
We found that non-Hispanic blacks had a significantly higher prevalence of cervical HPV infection, compared with individuals of other races, but there were no statistically significant differences by race for the oral HPV infection prevalence. The cervical HPV infection prevalence was significantly higher among women with a lifetime history of ≥3 sex partners. The prevalence of oral HPV infection (with or without cervical HPV infection) was also higher among women with a lifetime history of ≥3 sex partners, but the difference did not reach statistical significance. The prevalence of oral and cervical HPV infection by age was notably different (Table 1). Cervical infections decreased with increasing age, but this was not the case for oral infections or oral-cervical coinfections (Supplementary Figure 1).

The prevalence of oral HPV infection was higher among women with cervical infection (7.0% [95% CI, 4.9–10.0]) than among those without cervical HPV infection (1.4% [95% CI, .8–2.7]; P < .001), with an unadjusted prevalence ratio of 4.9 (95% CI, 2.7–8.7). The prevalence of any vaccine-associated HPV type (ie, 6, 11, 16, or 18) in oral samples was also higher among women positive for a vaccine type in cervical samples (4.7% [95% CI, 1.5–13.5]) than among those with no vaccine types in cervical samples (0.27% [95% CI, .08–.89]; P < .0001); the unadjusted prevalence ratio was 17.2 (95% CI, 7.9–37).

Figure 1. Shown is the frequency of individual human papillomavirus (HPV) types detected in oral and cervical specimens from women aged 18–59 years who participated in the National Health and Nutrition Examination Survey, 2009–2010. HPV types were detected by the Linear Array assay. Graphs present the total prevalence of HPV infection, by type, in the cervix (A) and oral cavity (B) and the prevalence of infection in both the cervix and oral cavity (C). The asterisks denote prevalence values with a relative standard error of >30%.
Among women positive for HPV at both anatomic sites, 43.2% (95% CI, 28.3–59.5) were concordant for at least 1 type, 50.4% (95% CI, 34.3–66.4) had complete type discordance (ie, no types in common), and only 6.4% (95% CI, 2.3–16.8) had the same HPV type at both sites. No specimen pairs were identical for more than one type.

**DISCUSSION**

We described the HPV prevalence in oral and cervicovaginal specimens in a nationally representative US population and observed oral HPV infection to be 5-fold greater among women with a cervical infection, compared with those without cervical infection.

Although a majority (79%) of oral HPV infections occurred in conjunction with cervical HPV infection, type-specific concordance at the 2 sites was low. These findings are consistent with other reports, particularly in US studies [13]. The biological relationship between the 2 sites might be complex, but the higher prevalence in oral samples among women positive for cervical HPV indicates that such infections are unlikely to be independent of one another. The high type-specific discordance we observed suggests either separate exposure events or differences in the natural history of infection at the 2 sites. Sexual activity likely plays a role in the observed coincidences, but it is also possible that one infection site provides a reservoir that can increase the risk of autoinoculation at anatomically distant locations. The significance of this correlation is somewhat supported by a Swedish cancer registry study that found slightly elevated risks for aerodigestive tract cancers among women with a previous diagnosis of in situ cervical cancer and even greater risks among those with invasive cancer [14]. However, this association did not reach significance for cancers in other anatomic sites linked to HPV (ie, the tonsils and the base of the tongue).

In support of this hypothesis is the observed difference in the HPV infection prevalence by age. Cervical HPV infection was negatively associated with age, but this was not observed for oral HPV infection. Alternatively, other ongoing modes of transmission (eg, through saliva exposure) could account for continued oral exposure with age.

There are several limitations to our study. The cross-sectional nature of the survey prevented examination of temporal associations with demographic and sexual behavior characteristics. Additionally, self-reported sexual behaviors may not be accurate. Importantly, the low prevalence of oral HPV infection led to unstable estimates when assessing type-specific HPV infection. Furthermore, we might not have been able to detect differences with respect to demographic or behavioral variables that would be apparent with larger numbers; additional years of data will be needed for further analyses.

Although the prevalence of oral HPV infection was low in this population, our data suggest an association between infections at the cervix and oral cavity among women. Additional years of NHANES data and findings from other studies may allow a more detailed examination of type-specific concordance, further assessment of risk factors and possible modes of acquisition. Continued analysis of NHANES data may also allow evaluation of whether prevalence of vaccine-targeted types in the oral cavity will follow trends similar to those in the cervix [15].

**Supplementary Data**

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

**Notes**

**Disclaimer.** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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**Potential conflicts of interest.** All authors: No reported conflicts.

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