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ORIGINAL RESEARCH

Sexual behavior and infection with cervical human papillomavirus types 16 and 18

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Objective: This study assessed whether sexual behavior, including engaging in early sexual intercourse and having had multiple sexual partners, can predict the risk of infection with cervical human papillomavirus (HPV) types 16 and 18.

Methods: Records were reviewed of women who underwent cervical cancer screening and were found to be infected with high-risk HPV. The genotypes of high-risk HPV were categorized as HPV 16, HPV 18, and other than 16 or 18. Early sexual intercourse was defined as first sexual intercourse at the age of 19 years or younger. Multiple sexual partners was defined as having more than three lifetime sexual partners. Associations between sexual behavior and HPV 16/18 infection were presented as odds ratios (ORs) and 95% confidence intervals (CIs).

Results: Of the 349 women included in the study, 72 (20.6%) and 30 (8.6%) were infected by HPV 16 and 18, respectively. Eighty-two women (26.0%) reported having engaged in early sexual intercourse, and 33 (10.4%) reported having had multiple sexual partners. After adjustment for age, parity, and smoking habits, we found that women who had engaged in early sexual intercourse tended to have a higher risk of HPV 16 (OR 1.74; 95% CI 0.93–3.29), and those who had had multiple sexual partners were found to be at a significantly higher risk for HPV 18 (OR 4.58; 95% CI 1.44–14.58).

Conclusion: Sexual behavior was associated with an increased risk of HPV 16/18 infection. Engaging in early sexual intercourse increased the risk of HPV 16 infection, and having had multiple sexual partners increased that of HPV 18.

Keywords: sexual behavior, human papillomavirus, cervical neoplasia, sexual partner

Introduction

Human papillomavirus (HPV) infection is the most common sexually transmitted infection worldwide.[1] Currently, at least 14 types of HPV are known to cause cancer and are, thus, classified as "high-risk types".[1] Cervical cancer is the most common HPV-related disease.[1] Almost all cases of cervical cancer can be attributed to infection with high-risk HPV.[1,2] The risk of developing cervical precancerous lesion or cervical cancer, however, varies widely by HPV type, with types16 and 18 being associated with by far the highest risk.[2–6]

HPV types 16 and 18 cause approximately 70% of cervical cancers and pre-cancerous cervical lesions.[5] The 3-year cumulative risk of cervical intraepithelial neoplasia (CIN) 3 (known to be an immediate precursor of cervical cancer) among women with HPV 16 and HPV 18 infection is 10.6% and 5.9%, respectively, while women who are negative for HPV 16 and 18 carry a much lower risk of 2.0–2.4%, respectively.[7] A recent systematic review and meta-analysis also indicated a significantly higher risk of CIN 2 or

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worse among women who are positive for HPV types 16/18.[8] Because of the aggressive natural course of HPV 16/18, women found positive for these types should undergo immediate colposcopy to ensure there is no underlying significant cervical lesion.[9]

Determining the risk factors for various types of HPV infection is the basis for both understanding the natural courses of different HPV types and designing comprehensive strategies against cervical cancer. We hypothesize that women who engage in risky sexual behavior may have a greater risk of contracting HPV types 16 and 18. Accordingly, this study was undertaken to assess sexual behavior among women infected with HPV 16/18 compared to those infected with other high-risk types.

Methods

This was a retrospective study, and the target population was women who underwent cervical cancer screening and were found to be infected with high-risk HPV. Data were retrieved from the records of women who were referred to Colposcopy Clinic at Khon Kaen University's Srinagarind Hospital from October 2013 to October 2018. The study was approved by the Research Ethics Committee of Khon Kaen University. Because it was a retrospective study and the data were analyzed anonymously, the need for informed consent was waived by the committee.

Based on a relatively high incidence of underlying significant cervical lesions, including invasive disease, in Thai women who have abnormal cervical screening results,[10,11] it is our policy to recommend colposcopy for all women who are positive for high-risk HPV irrespective of genotype.

Abstracted data included baseline characteristics of patients, underlying disease, HPV genotype and engagement in risky sexual behavior. High-risk HPV genotypes were categorized as HPV 16, HPV 18 and high-risk HPV other than 16/18. Sexual behavior was assessed based on age at first experience with sexual intercourse and number of sexual partners. Early sexual intercourse was defined as first sexual intercourse at the age of 19 years or younger. Multiple sexual partners was defined as having more than three more lifetime sexual partners. We excluded women with high-risk HPV infection who had no further HPV genotyping results.

Demographic characteristics of the patients were summarized as number (percentage) or mean ± standard deviation (SD) as appropriate. Binary logistic regression and multinomial logistic regression were used to determine the association between sexual behavior and HPV 16/18 infection. Covariates to be adjusted in the regression model were derived from a literature review and consisted of patients' age, parity status and history of smoking.[12–14] Associations were presented as adjusted odds ratios (ORs) and 95% confidence intervals (CIs). A 95% CI that did not include unity was considered statistically significant. Statistical analysis was carried out via STATA.

Results

Demographic characteristics are shown in Table 1. One hundred and three women in the study were postmenopausal, and 93 were nulliparous. Most of the women (90.0%) had no symptoms at the time of cervical cancer screening.

All HPV tests in this study were performed as a part of co-testing. Of the 349 women included, 72 (20.6%) and 30 (8.6%) were infected by HPV 16 and HPV 18, respectively, making the overall rate of HPV 16/18 infection 29.2% (95% CI 24.4–34.0%). Two hundred twenty-one women had normal cervical cytology results. The remaining 128 had (36.7%) atypical squamous cells of undetermined significance (36), atypical squamous cells cannot exclude high-grade lesion (8), low-grade squamous intraepithelial lesions (47), high-grade squamous intraepithelial lesions (24), squamous cell carcinoma (1), atypical glandular cells (3), adenocarcinoma in situ (1) and unknown conditions (8).

Early sexual intercourse was reported in 82 (26.0%) women, and 33 (10.4%) reported having had more than three sexual partners. Table 2 displays the impact of risky sexual behavior on the risk of HPV 16/18 infection. Women with HPV 16 infection were more likely to report having engaged in early sexual intercourse compared to other groups. Women who were infected with HPV 18 were more likely to have multiple sexual partners than those who were infected with other HPV types (Table 1).

Table 2 displays the results of binary logistic regression analysis to determine the effect of sexual behavior on the risk of HPV 16/18 infection. Women who engaged in sexual intercourse at a younger age tended to have a higher risk of harboring HPV 16/18 infection (unadjusted OR 1.53; 95% CI 0.90–2.61), and women who had had multiple sexual partners had a significantly higher risk of HPV 16/18 infection (OR 2.15; 95% CI 1.03–4.48).

Table 3 shows the association between sexual behavior and HPV 16 or HPV 18 infection using multinomial logistic regression. Women who reported having first engaged in sexual intercourse at 19 years of age or younger tended to have a higher risk of acquiring HPV 16 infection

Table 1 Clinical and demographic data stratified by HPV type

Variables	Total (n=349)		Type 16 (n=72)		Type 18 (n=30)		Other type (n=247)	
Age (mean ± SD)	44.52±9.8		42.7±9.9		46.2±8.3		44.9±9.9	
24–29 years	16	(4.6)	6	(8.3)	1	(3.3)	9	(3.6)
30–54 years	271	(77.7)	55	(76.4)	25	(83.3)	191	(77.3)
≥55 years	62	(17.8)	11	(15.3)	4	(13.3)	47	(19.0)
Missing data	0							
Education								
Primary school	11	(4.5)	1	(2.0)	1	(4.0)	9	(5.4)
Secondary school	60	(24.6)	11	(21.6)	3	(12.0)	46	(27.4)
Bachelor	148	(60.7)	35	(68.6)	17	(68.0)	96	(57.1)
Bachelor's degree and higher	25	(10.3)	4	(7.8)	4	(16.0)	17	(10.1)
Missing data	105							
Parity								
0	93	(26.7)	17	(23.6)	9	(30.0)	67	(27.1)
≥1	256	(73.3)	55	(76.4)	21	(70.0)	180	(72.9)
Missing data	0							
Menopausal status								
Premenopausal	246	(70.5)	53	(73.6)	20	(66.7)	173	(70.0)
Postmenopausal	103	(29.5)	19	(26.4)	10	(33.3)	74	(30.0)
Missing data	0							
Smoking status								
None	279	(88.0)	59	(86.8)	25	(92.6)	195	(87.8)
Smoker	6	(1.9)	1	(1.5)	0	(0.0)	5	(2.3)
Passive smoker	32	(10.1)	8	(11.8)	2	(7.4)	22	(9.9)
Missing data	32							
Age of first sexual intercourse								
≥30 years	31	(9.8)	7	(10.3)	3	(11.5)	21	(9.5)
20–29 years	203	(64.2)	37	(54.4)	17	(65.4)	149	(67.1)
≤19 years	82	(26.0)	24	(35.3)	6	(23.1)	52	(23.4)
Missing data	33							
Number of sexual partners								
≤3 partners	283	(89.6)	59	(86.8)	20	(76.9)	204	(91.9)
>3 partners	33	(10.4)	9	(13.2)	6	(23.1)	18	(8.1)
Missing data	33							

Note: Data are present as number (percentage) unless stated otherwise.
Abbreviations: HPV, human papillomavirus; SD, standard deviation.

(adjusted OR 1.74; 95% CI 0.93–3.29). The risk of HPV 18 infection was significantly higher among women who reported having had multiple sexual partners (adjusted OR 4.58; 95% CI 1.44–14.58).

Discussion

In the present study, infection with HPV 16/18 was noted in 29.2% of women whose co-testing results for HPV were positive. Sexual behavior was associated with an increased risk of HPV 16/18 infection. Women who had first engaged in sexual intercourse at a younger age tended to have a higher risk of HPV 16 infection, and having had multiple sexual partners increased the risk of HPV 18 infection.

Although there is evidence supporting a direct association between the number of lifetime sexual partners and

Table 2 Sexual behavior and risk of HPV16/18 infection

Variables	OR[a] (95% CI)
Age of first sexual intercourse	
>19 years	1.00
≤19 years	1.53 (0.90–2.61)
Number of sexual partners	
≤3 partners	1.00
>3 partners	2.15 (1.03–4.48)

Note: [a]The multivariable binary logistic regression analysis was adjusted for age, parity and smoking.
Abbreviations: HPV, human papillomavirus; OR, odds ratio; CI, confidence interval.

high-risk HPV infection,[15–17] there is little information on this with regard to particular types of high-risk HPV. A previous study conducted in Costa Rica noted a significantly higher risk of HPV 16/18 infection among women who had more than one lifetime sexual partner, with adjusted ORs ranging from 1.39 to 2.19 depending on the reported number of sexual partners.[18] A study conducted among young Norwegian women confirmed a higher risk of HPV 16/18 infection among women who had had multiple sexual partners. Women who reported having had 3–4, 5–9 and more than 10 sexual partners were more likely to be infected with HPV 16 by 1.78 times (95% CI 1.09–2.91), 2.70 times (95% CI 1.71–4.25) and 5.71 times (95% CI 3.40–9.57), respectively. The same study also noted that there was a significantly higher risk of HPV 18 infection among women who had had multiple sexual partners. There were 2.44-fold (95% CI 1.14–5.22), 4.08-fold (95% CI 2.03–8.18) and 7.31-fold (95% CI 3.52–15.18) increases in the risk of HPV 18 infection among women who reported having had 3–4, 5–9 and more than 10 sexual partners, respectively.[19] Our finding is consistent with those reported in the literature, in that women who had had three or more sexual partners were approximately twice as likely to harbor HPV 16/18 infection (95% CI 1.03–4.48; Table 2) compared to those who had had fewer sexual partners, particularly for HPV 18 infection (adjusted OR 4.58; 95% CI 1.44–14.58; Table 3).

Previous studies have consistently noted a higher risk of high-risk HPV infection and significant cervical pathology among women who first engaged in sexual intercourse at a young age.[19–21] A study conducted by Kim et al[19] noted that early sexual intercourse significantly increased the risk of HPV 16 infection. Women who had engaged in sexual intercourse at younger 16 years of age were approximately twice as likely to have HPV 16 (adjusted OR 1.99; 95% CI 1.30–3.06) than those who first engaged in sexual intercourse at an older age. The risk of HPV 18 infection among women experiencing early sexual intercourse appeared to be similar to those who have first sexual intercourse at a later age (adjusted OR 1.51; 95% CI 0.84–2.71).[19] In a study conducted by Burger et al[22] to determine the age at which women with cervical cancer were infected with HPV noted that causal HPV16 infection was acquired at a younger age relative to other types of high-risk HPV infection. In our study, women who reported first engaging in sexual intercourse at 19 years of age or younger were more likely to have HPV 16/18 infection (unadjusted OR 0.90; 95% CI 0.90–2.61). When stratified by type of HPV, women who had engaged in early sexual intercourse were more likely to be infected with HPV 16 with an adjusted OR of 1.74 (95% CI 0.93–3.29). However, younger age at first experience with sexual intercourse did not increase the risk of acquiring HPV 18 infection (adjusted OR 0.61; 95% CI 0.20–1.85; Table 3).

Table 3 Sexual behavior and risks of infection with HPV16 and HPV 18

Variables	Type 16 versus other types*				Type 18 versus other types*			
	OR	(95% CI)	aOR[a]	(95% CI)	OR	(95% CI)	aOR[a]	(95% CI)
Age of first sexual intercourse								
>19 years	1.00		1.00		1.00		1.00	
≤19 years	1.78	(0.99–3.21)	1.74	(0.93–3.29)	0.98	(0.37–2.57)	0.61	(0.20–1.85)
Number of sexual partners								
≤3 partners	1.00		1.00		1.00		1.00	
>3 partners	1.73	(0.74–4.05)	1.32	(0.53–3.28)	3.40	(1.21–9.54)	4.58	(1.44–14.58)

Notes: [a]The multivariable multinomial logistic regression analyses for HPV type 16 and 18 infection were adjusted for age, parity and smoking. *The category "Other types" was treated as a reference.
Abbreviations: HPV, human papillomavirus; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval.

The previously reported prevalence of HPV 16/18 infection among women with high-risk HPV-positive varied widely, ranging from 20% to 40%.[11,12,23–25] This remark emphasizes the differences in the background risk of acquiring HPV 16/18 infection across the population. In the present study, prevalence of HPV 16/18 infection among women with high-risk HPV-positive was 29% which was congruent with the previously reported prevalence in Asian women.[11,12,23,24] However, it appears to be lower than the reported prevalence of 40% in European country.[25]

The strength of this study is that we accounted for potential confounding factors by adjusting for age, parity and smoking in order to assess the significant independent impact of risky sexual behavior on the risk of HPV 16/18 infection. One important limitation of this study was the cross-sectional nature of the analysis, which means that we had no information on the duration of HPV infection. The pragmatic nature of the cross-sectional study model also prevented us from assessing the causal relationships between risky sexual behaviors and infection. Thus, we were unable to determine the biological role that risky sexual behaviors play in HPV 16/18 infection. We did not have information on the smoking habits and sexual behavior of the partners of the women included in this study, which are factors that may have influenced the study outcomes.[26] In addition, some clinically important information such as history of other sexually transmitted diseases and socioeconomic status which might influence to the findings of this study was not available.

Conclusion

In summary, risky sexual behavior was associated with a higher probability of acquiring HPV 16/18 infection. Early sexual intercourse increased the risk of HPV 16 infection, and HPV 18 infection was more prevalent among women who reported having had multiple sexual partners.

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Disclosure

The authors report no conflicts of interest in this work.

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