RESEARCH COMMUNICATION

Prevalence and Determinants of High-risk Human Papillomavirus Infection in Women with High Socioeconomic Status in Seoul, Republic of Korea

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Abstract

We aimed to estimate the prevalence of high-risk human papillomavirus (HPV) infections in women of high socioeconomic status (SES) in Seoul, Republic of Korea and to identify risk factors. This study included 13,386 women visiting a prestigious healthcare center located in Seoul between 2003 and 2008. High-risk HPV infections were detected in 994 (7%) and the age-standardized prevalence was 8%. Abnormal Pap smear results ≥ atypical squamous cells of unknown significance (ASCUS) were observed in 280 of 12,080 women (2%). Based on univariate analysis, age, level of education and number of children were associated with high-risk HPV infections. Based on multivariate analysis, age and high-risk HPV infections had an inverse relationship. In women with high SES in Seoul, the prevalence of high-risk HPV infection was 7% and the age-standardized prevalence was 8%. Age was a strong determinant of high-risk HPV infection.

Key words: Human papillomavirus - papillomavirus infection - prevalence - social class - age factor - Korea

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Introduction

Cervical cancer is one of the most common malignancies and the leading cause of cancer-related deaths in females worldwide (Kim, 2009). For example, there were 529,800 new cervical cancer cases and 275,100 deaths due to cervical cancer worldwide in 2008 (Jemal et al., 2011). Human papillomavirus (HPV) is the primary cause of cervical cancer and > 100 types of HPV have been identified (Kim, 2009). HPVs are classified as high- or low-risk types based on oncogenicity (de Villiers et al., 2004), and numerous studies have shown that high-risk HPV infections are an independent risk factor for cervical cancer (Bosch et al., 1995).

Recently, HPV vaccines were developed and showed promising efficacy in preventing high-risk HPV infections and cervical pre-cancerous diseases [1]. To estimate the cost and benefit of implementation of HPV vaccines, knowledge of the prevalence and risk factors for high-risk HPV infections is critical. Previous studies have demonstrated that the prevalence of HPV varies according to region and socioeconomic status (SES) (Clifford et al., 2003; 2005; Kahn et al., 2007; Bao et al., 2008; Silva et al., 2009). Therefore, the prevalence of HPV according to region and SES are necessary to estimate the impact of implementation of HPV vaccines.

The prevalence of HPV in Korean women has been investigated in several studies (Bae et al., 2008; Kim, 2009). However, most studies have not specified the region involved, and studies including women in Seoul are still insufficient, considering the population size of Seoul over ten million. Furthermore, there are no studies investigating the prevalence of HPV in women with low or high SES.

The aims of this study were to estimate the prevalence of high-risk HPV infections in women with high SES who underwent a health check-up at a prestigious healthcare center in Seoul and to identify risk factors for high-risk HPV infections.

Materials and Methods

The Population

This study included women visiting a healthcare center located in the Gangnam area of Seoul, Republic of Korea between 2003 and 2008. The healthcare center is a branch of a university hospital and performs approximately 50000 health evaluations per year.

After acquiring the approval of the Institutional Review Board (B-1104-125-110), all women visiting the healthcare center between 2003 and 2008 were identified. Women who did not undergo a HPV test (Hybrid Capture

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2; Digene Corporation, Inc., Gaithersburg, Maryland, USA) or did not have an intact cervix were excluded. Women who had other HPV tests, such as the DNA chip test, were also excluded.

Health evaluation

Two or three weeks before a health evaluation, a structured questionnaire was sent to the women who had made an appointment. The questionnaire included questions regarding demographic and socioeconomic variables, medical history, and current symptoms. Return of the self-completed questionnaire was requested before the health evaluation and the contents of the questionnaire were input into a database by data managers.

At the health evaluation, a gynecologist performed a pelvic examination and obtained a specimen for the HPV test from the cervix using a cervical sampler. On the day of collection, the specimens were sent to the Department of Laboratory Medicine in the healthcare center and analyzed. In most cases, a Papanicolau (Pap) smear was also performed before the HPV test because most of the health evaluation programs included both tests.

HPV test

To detect high-risk HPV infections, the Hybrid Capture 2 (HC2) test was performed according to the manufacturer's instructions. The specific procedures of the HC2 test have been described in numerous studies (Nam et al., 2009). The results of the HC2 test were reported as positive or negative for high-risk HPV infections (HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68).

Variables

The HPV test results, age, Pap smear results, smoking history, level of education, monthly income, number of children, and age at first delivery were extracted from the healthcare center database. In women who had the HPV test more than once during the study period, the data at the time of the first HPV test were obtained. The unit of monthly income was converted from Korean won to US dollars using an exchange rate of 1$ = 1100 won.

Statistical analysis

The age-standardized prevalence of high-risk HPV infections was calculated using the age distribution of Korean women in 2000. To estimate the association of variables with high-risk HPV infections, the values of each variable were categorized appropriately or using quantile values. The prevalence and odds ratio (OR) with 95% confidence interval (CI) for high-risk HPV infections according to categorized variables were calculated using unadjusted logistic regression analysis. In addition, for ordinal variables, trend analyses were performed using a chi-square test or linear-by-linear association method.

Variables which were associated with high-risk HPV infections in univariate analysis were dichotomized appropriately or using median values. The dichotomized variables were included in the binary logistic regression analysis to identify the independent risk factors for high-risk HPV infection. SPSS version 18.0 (IBM Corporation, Somers, NY, USA) and P value < 0.05 was used to determine the statistical significance.

Table 1. Association of Age with High-risk HPV Infection

Age	HPV-	HPV+	% of HPV+	OR	(95% CI)	P for trend
≤ 29	211	25	11	1		<0.01
30 - 39	2142	214	9	0.8	(0.5 - 1.3)	
40 - 49	4329	418	9	0.8	(0.5 - 1.2)	
50 - 59	4060	247	6	0.5	(0.3 - 0.8)	
60 - 69	1477	83	5	0.5	(0.3 - 0.8)	
≥ 70	173	7	4	0.3	(0.1 - 0.8)	

Table 2. Association of Pap Smear Results with High-risk HPV Infections

Pap	HPV-	HPV+	% of HPV+	OR	(95% CI)
Normal	11070	730	6	1	
ASCUS	60	59	50	14.9	(10.3 - 21.5)
AGC-NOS	5	2	29	6.1	(1.2 - 31.3)
LSIL	26	74	74	43.2	(27.4 - 67-9)
ASC-H	6	10	63	25.3	(9.2 - 69.7)
HSIL	4	27	87	102.4	(35.7 - 293.3)
AGC-N	1	1	50	15.2	(0.9 - 242.7)
Cancer	1	4	80	60.7	(6.8 - 543.4)

ASCUS, atypical squamous cells of unknown significance; AGC-NOS, atypical glandular cells not otherwise specified; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells cannot exclude HSIL; HSIL, high-grade squamous intraepithelial lesion; AGC-N, atypical glandular cells favor neoplastic

Table 3. Association of smoking-related Variables with High-risk HPV Infections

Age	HPV-	HPV+	% of HPV+	OR	(95% CI)	P for trend
Smoking						-
Never	8597	689	7	1		
Ever	956	91	9	1.2	(0.9 - 1.5)	
Former	418	42	9	1.3	(0.9 - 1.7)	
Current	538	49	8	1.1	(0.8 - 1.5)	
Age of smoking onset, year						NS
≤ 20	83	11	12	1		
21 - 25	89	8	8	0.7	(0.3 - 1.8)	
≥ 26	80	6	7	0.6	(0.2 - 1.6)	
Pack-years						NS
≤ 1.0	183	22	11	1		
1.1 - 3.6	170	19	10	0.9	(0.5 - 1.8)	
3.7 - 7.5	194	17	8	0.7	(0.4 - 1.4)	
≥ 7.6	177	21	11	1	(0.5 - 1.9)	

Results

HPV prevalence and baseline characteristics

A total of 13,386 women were included in this study

Table 4. Association of Socioeconomic Variables with High-risk HPV Infections

Age	HPV-	HPV+	% of HPV+	OR	(95% CI)	P for trend
Level of education						0.01
Primary school	902	50	5	1		
Middle school	352	25	7	1.3	(0.8 - 2.1)	
High school	2637	221	8	1.5	(1.1 - 2.1)	
College or university	4834	396	8	1.5	(1.1 - 2.0)	
Graduate school	1387	125	8	1.6	(1.2 - 2.3)	
Monthly income, USD						NS
< 2727	1060	66	6	1		
2727 – 4545	1846	154	8	1.3	(1.0 - 1.8)	
4545 - 7273	1968	170	8	1.4	(1.0 - 1.9)	
7273 - 9091	1290	109	8	1.4	(1.0 - 1.9)	
9191 - 13636	1245	100	7	1.3	(0.9 - 1.8)	
13636 - 18182	462	37	7	1.3	(0.8 - 2.0)	
> 18182	897	83	9	1.5	(1.1 - 2.1)	

Table 5. Association between Obstetric Variables and High-risk HPV Infections

Age	HPV-	HPV+	% of HPV+	OR	(95% CI)	P for trend
No. of children						<0.01
0	815	92	10	1		
1	1190	104	8	0.8	(0.6 - 1.0)	
2	5356	419	7	0.7	(0.5 - 0.9)	
3	1967	160	8	0.7	(0.6 - 0.9)	
> 3	719	36	5	0.4	(0.3 - 0.7)	
Age at first delivery, years						NS
≤ 24	2322	186	7	1		
25 - 26	2625	196	7	0.9	(0.8 - 1.1)	
27 - 28	2169	161	7	0.9	(0.7 - 1.2)	
≥ 29	1968	161	8	1	(0.8 - 1.3)	

Table 6. Association between Variables and High-Risk HPV Infections based on Multivariate Analysis

Variable		P	OR	(95% CI)
Age	≤ 48 vs. > 48	<0.01	0.5	(0.5 - 0.6)
Level of education	≤ High school vs. > High school	NS	0.9	(0.8 - 1.1)
No. of children	≤ 2 vs. > 2	NS	1.1	(0.9 - 1.3)

and high-risk HPV infection was detected in 994 women (7%). The age-standardized prevalence of high-risk HPV infection was 8%.

The median age was 48 years. Abnormal Pap smear results (atypical squamous cells of unknown significance [ASCUS] or more severe cytologic changes) were observed in 280 of 12080 women (2%) who had Pap smears. Ever-smoking was reported in 956 of 9553 women (10%) who responded. The median age when women started smoking was 23 years and the median number of pack-years was four. Education beyond high school was reported in 6221 of 10112 women (62%) who responded. The median monthly income was 4545 - 7273 USD. The median number of children was two, and the median age at the time of the first delivery was 26 years.

Association of variables with high-risk HPV infections

Age and high-risk HPV infections had an inverse relationship. For example, women > 50 had a significantly lower prevalence of high-risk HPV infections than women < 30 years of age (Table 1). Women with abnormal Pap smear results had a higher prevalence of high-risk HPV infections than women with normal Pap smear results (Table 2). Ever-smoking, age of smoking onset, and pack-years of smoking was not associated with high-risk HPV infections (Table 3). The level of education had a positive relationship with high-risk HPV infections. For example, women who graduated from high school or more had a higher prevalence of high-risk HPV infection than women who only completed primary school (Table 4). The monthly income was not associated with high-risk HPV infections (Table 4). The number of children and high-risk HPV infections had an inverse relationship. To explain further, women who had two or more children had a lower prevalence of high-risk HPV infection than women without a child (Table 5). However, the age at the time of first delivery was not associated with high-risk HPV infections (Table 5).

Based on multivariate analysis, age was associated with high-risk HPV infections, but neither the level of education nor the number of children was associated with high-risk HPV infections (Table 6).

Discussion

The women in the current study were older, more educated, and had higher monthly income than the "average" woman in Seoul or Korea. Specifically, the median age of women included in this study was 48 years, but the median age of all women in Seoul was 35 years in 2005 (Korea Statistical Information Service, 2011). The percentage of women who had abnormal Pap smear results (ASCUS or more severe cytologic features) in the current study (2%) was similar to other studies involving Korean women. For example, a study including 3091 women visiting a healthcare center in Seoul reported abnormal Pap smear results in 2% of women (Joo et al, 2004). Another study including 4595 women participating in the National Cervical Cancer Screening Program in Busan and Suwon showed a 3% abnormal Pap smear rate (Oh et al., 2009). The rate of current-smoking (6%) in the present study was similar with the rate reported in Korean women (5% at 2007) (Korea Statistical Information Service, 2011). In the current study, the percentage of women who graduated post-graduate school was 14%, which is much higher than the reported 4% of all Korean women (Korea

Statistical Information Service, 2011). In addition, the level of monthly income of women in the current study (median, 4545 - 7273 USD) was higher than the average monthly income of a Korean family (approximately 3000 USD) . To remove the effect of age on monthly income, we compared the monthly income of women < 40 years of age with the average monthly income of a Korean family. The level of monthly income of women in the current study was higher than the average monthly income of a Korean family (data not shown). The number of children of women in the current study (median number of children, two) was similar to women in Seoul considering the median size of the family, including women, in Seoul was four people. The age at the first delivery of women in the current study was similar to that of women in Seoul. To explain further, the median age of women in the current study was 48 years and the median age at the time of first delivery was 26 years. Because the age at the time of first delivery increased with time, the median age at the time of first delivery for women in the current study was compared with that of women in Seoul in 1983 when the women in the current study had the first delivery. The mean age at the time of first delivery for women in Seoul in 1993 was 27 years, and the age at the time of first delivery in 1983 was < 27 years (Korea Statistical Information Service, 2011).

The HPV prevalence in Korean women has been reported to be between 10% and 40% (Kim, 2009). The comparison of HPV prevalence between studies is difficult to perform because the age distribution and type of HPV tests were different. Therefore, we selected studies providing age-standardized prevalence and using HC2 as HPV tests. The prevalence of high-risk HPV infections in the current study was markedly lower than the rates in previous studies, including Korean women. The current study showed that the prevalence of high-risk HPV infections was 7% and the age-standardized prevalence was 8%. However, a study involving 3091 women in Seoul reported that the prevalence of high-risk HPV infections was 13% and the age-standardized prevalence was 16% (Joo et al, 2004). In another study involving 4595 women in Busan and Suwon, the prevalence of high-risk HPV infections was 8% and the age-standardized prevalence was 10% (Oh et al., 2009). The low prevalence of high-risk HPV infection in the current study could be due to the characteristics of the study population, such as high SES.

Previous studies have examined the association between variables and HPV infections, and identified age, smoking, number of lifetime sex partners, alcohol consumption, age at menarche, seropositivity for herpes simplex virus type 2, extramarital affairs (husband), and vasectomy (husband) as risk factors for HPV infections (Shin et al., 2003; 2004; Joo et al., 2004; Oh et al., 2009).

The current study showed that age is an important risk factor for high-risk HPV infections and has the inverse relationship with high-risk HPV infections. Similar findings were observed in many studies, including women in the highest-income countries (Franceschi et al., 2006). The level of education and number of children were thought to be surrogate variables of age because the statistical significance of those variables on univariate analysis disappeared on multivariate analysis. In contrast to the results of previous studies (Shin et al., 2003; 2004), smoking was not associated with high-risk HPV infections in the current study.

The current study had several limitations. First, this was a single center study and the study population was not randomly selected. Therefore, the extrapolation of the results of the current study was limited. Second, variables regarding sexual behavior which were associated with HPV infections in other studies were not analyzed because those data could not be obtained. Third, the detailed disease history was not available and there was the possibility that few women with a history of cervical cancer or cervical intraepithelial neoplasia were included. However, we reasoned that the large size of the current study would make the effect of those women negligible.

In women with high SES in Seoul, the prevalence of high-risk HPV infections was 7% and the age-standardized prevalence was 8%. Age was a strong determinant of high-risk HPV infections. The low prevalence of high-risk HPV infections in women with high SES suggested that the public support for HPV vaccination should be focused on women with low SES. The high prevalence of high-risk HPV infections in young women supported the importance of HPV vaccination in young women.

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