RESEARCH COMMUNICATION

Co-Risk Factors for HPV Infection in Northeastern Thai Women with Cervical Carcinoma

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Abstract

HPV infection is the main cause of cervical cancer; however, factors that promote and maintain HPV infection are still unclear. This study was designed to search for factors responsible for the HPV infection in Northeastern Thai women. A total of 190 volunteers with a normal histopathologic appearance of cervix as controls (n=100) and with squamous cell cervical carcinoma (SCCA) (n=90) were the subjects. Variables of risk factors including sexual behaviors, history of reproduction, history of sexually transmitted diseases and smoking were conducted with self-report and direct interview. Number of sexual partners and smoking history increased the likelihood of high-risk HPV infection. Multiple sexual partners showed significantly higher 3.94-fold risk for HPV infection (95% CI = 1.82-8.82, *p-value*<0.001). Smoking history of partner increased the risk for HPV infection 3.03-fold (95%CI=1.42-6.58, *p-value*< 0.002). After OR were adjusted, significant difference was still observed in the number of sexual partners (*p-value* <0.0001) and smoking history of the partner (*p-value*<0.005). To decrease the incidence of cervical cancer, we should prevent HPV dissemination and be on the alert for having multiple sexual partners and a partner' s smoking habit, which must be included in our public health planning.

Key Words: Risk factors - HPV infection - Northeastern Thai - cervical carcinoma

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Introduction

Cervical cancer is still the most common cancer of Northeastern Thai women (Sriamporn et al., 1999; Cancer Unit, Khon Kaen University, 2003). Epidemiological evidence has indicated that not a single factor can explain development of the disease. Although human papillomavirus (HPV) infection is a major cause, in particular for squamous cell cervical carcinoma, most infected women do not develop invasive lesions. This means that HPV infection in itself is not a sufficient factor, and co-factors must therefore play roles (Moore et al., 2003) . Our previous studies on cervical cancer in Northeast Thailand have confirmed that HPV infection is a critical risk and other risk factors such as sexual behavior and smoking contribute to cancer development (Settheetham-Ishida et al., 2004; Settheetham-Ishida et al., submitted).

Factors that promote and maintain HPV infection are still unclear but they may correspond to the risks for cervical cancer. Since several risk factors for cervical cancer were nominated in our previous study, this study was thus designed to search for the co-factors responsible for the HPV infection resulting in developing cervical cancer in Northeastern Thai women.

Subjects and Methods

Study Population

A total of 190 volunteers with normal histopathologic appearance of cervix as controls (n=100) and with squamous cell cervical carcinoma (SCCA) (n=90) at Out Patients Department (OPD) of Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand were the subjects. They were informed about the experimental procedures and the purpose of this study and written informed consent was obtained from each. This study was approved by the Ethics Committee of Khon Kaen University.

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Data Sources

Information on variables including sexual behavior, history of reproduction, history of sexually transmitted disease (STD: gonorrhea, syphilis, genital wart, and herpes) and smoking was obtained from self-reporting and direct interview (Settheetham-Ishida et al 2004).

The genotype for the *p53* codon 72 polymorphism and HPV infection status of each subject were investigated previously (Settheetham-Ishida et al 2004; Settheetham-Ishida et al., submitted).

Statistical Analysis

The χ^2 test was performed to examine HPV infection and risk factors in the cervical cancer patients and in the controls. Odds ratios (ORs) at 95% confidence interval (CI) were calculated to compare risk for the HPV infection and evaluate the association of the variables in the questionnaire. A P-value less than 0.05 was considered as significant.

Results

Data for risk factors for HPV infection are presented with ORs in Table 1. Number of sexual partners and a smoking history increased the risk of high-risk HPV infection. Women who had more than one sexual partner demonstrated a statistically significant 3.94-fold higher risk of HPV infection (95% CI = 1.82-8.82, p-value<0.001) than those who had one or none. Smoking history of partner at present elevated the risk 3.03-fold (95%CI=1.42-6.58, *p-value* < 0.002). After adjustment for age and the *p53* genotype, significant differences were still observed with the number of sexual partners (*p-value* <0.0001) and the smoking history of the partner (*p-value*<0.005).

Age at the first sexual intercourse, history of reproduction, use of contraception, history of sexually transmitted diseases and smoking of the subjects, and circumcision of the partner were not associated with any significant increase in the risk of HPV infection (*p-value* > 0.05).

Discussion

A large series of molecular and epidemiological studies have confirmed that cervical infection with certain HPV types is a precursor event in the genesis of cervical neoplasia (zur Hausen, 1991; Schiffman and Castle, 2003). In Northeastern Thai women, oncogenic high-risk group of HPV infection was earlier identified among 86.7% of patients with SCCA and increased the risk for cervical cancer development as much as 43.5-fold (Settheetham-Ishida et

Table 1 Association between risk factors and HPV infection

Variables	HPV infection, n (%)		OR [95% CI]	
	Negative	Positive	Crude OR	Adjusted OR[a]
Total subjects	99 (100.0)	91(100.0)		
Age at menarche				
> 14 years old	67 (67.7)	69 (75.8)	1	1
≤14 years old	32 (32.3)	22 (24.2)	0.66[0.33-1.32]	0.73 [0.36-1.48]
Number of sexual partners				
< 1	86 (86.8)	57 (62.6)	1	1
≥ 1 (2-5)[b]	13 (13.1)	34 (37.4)	3.94 [1.82-8.82] **	3.89[1.87-8.48] **
Age at first sexual intercourse				
> 17 years old	83 (83.8)	67 (73.6)	1	1
≤ 17 years old[b]	16 (16.2)	24 (26.4)	1.85 [0.86-4.05]	1.47[0.69-3.14]
Age at first life birth				
> 20 years	91 (91.9)	86 (94.5)	1	1
≤ 20 years	8 (8.1)	5 (5.5)	0.66 [0.16-2.40]	0.51 [0.14-1.82]
Number of pregnancies				
< 3	61 (61.6)	45 (49.5)	1	1
≥ 3	38 (38.4)	46 (50.6)	1.64 [0.88-3.04]	1.05 [0.51-2.15]
Number of abortions				
0	62 (62.6)	60 (66.7)	1	1
1	27 (27.3)	19 (21.1)	0.79 [0.36-1.69]	0.71 [0.33-1.51]
>1	10 (10.1)	11 (12.1)	1.13 [0.40-3.22]	1.11 [0.17-6.94]
Number of parities				
< 3	80 (80.8)	57 (62.6)	1	1
≥ 3	19 (19.2)	34 (37.4)	2.51 [1.24-5.14]	2.50 [0.88-7.03]
Use of oral contraceptive pills				
Not used	50 (50.5)	50 (55.0)	1	1
1-4 years used	38 (38.4)	17 (18.7)	0.44 [0.20-0.94]	0.62 [0.28-1.35]
5-9 years used	5 (5.1)	12 (13.2)	2.40 [0.71-9.28]	2.74 [0.73-9.53]
≥ 10 years used	6 (6.1)	12 (13.2)	2.00 [0.63-6.98]	2.81 [0.87-9.04]

Table 1. Continued

Variables	HPV infection, n (%)		OR [95% CI]	
	Negative	Positive	Crude OR	Adjusted OR[a]
Use of contraceptive injection				
No	70 (70.7)	70 (76.9)	1	1
Yes	29 (29.3)	21 (23.1)	0.72 [0.35-1.45]	0.84 [0.41-1.73]
Use of IUD				
No	69 (69.7)	65 (71.4)	1	1
Yes	30 (30.3)	26 (28.6)	0.92 [0.46-1.80]	1.24 [0.63-2.42]
History of STD				
Subjects				
Yes	88 (88.9)	76 (83.5)	1	1
No	11 (11.1)	15 (16.5)	1.57 [0.63-4.04]	1.43 [0.57-3.54]
Partners				
Yes	89 (89.9)	76 (83.5)	1	1
No	10 (10.1)	15 (16.5)	1.75 [0.64-4.63]	1.57 [0.61-3.99]
History of smoking				
Subjects				
Non-smoker	89 (89.9)	84 (92.3)	1	1
Present smoker	9 (9.1)	7 (7.7)	0.74 [0.22-2.27]	0.76 [0.26-2.21]
Past smoker	1 (1.0)	0 (0.0)		
Partners				
Non-smoker	38 (38.4)	18 (18.7)	1	1
Present smoker[b]	39 (39.4)	53 (58.2)	3.03 [1.42-6.58] *	2.93 [1.39-6.14] *
Past smoker[b]	22 (22.2)	21 (23.1)	2.13 [0.86-5.30]	2.19 [0.85-5.66]
Circumcision of partner				
Yes	8 (8.1)	7 (7.7)	1	1
No	91 (91.9)	84 (92.3)	1.05 [0.31-3.55]	1.05 [0.33-3.35]

[a]Adjusted OR for *p53* genotypes and age * *p-value* < 0.01; ** *p-value* < 0.001 [b]significant for cervical cancer development (Settheetham-Ishida et al., 2004)

al., submitted). In the present study, multiple sexual partners and partner's smoking habit were nominated as the risks for HPV infection. Having multiple sexual partners increased the risk for high-risk type HPV infection 3.94-fold. This is comparable to the data obtained in Central, Northern and Southern Thailand (Thomas et al., 1996; Sukvirach et al., 2003). Women who have multiple sexual partners are easily to be transmitted HPV from their partners (Thomas et al., 2001a). Moreover, husband's behavior is also important; extramarital sexual contact of the husband causes HPV infection in women who are in a monogamous condition (Thomas et al., 2001b).

Any smoking experience of the partner was confirmed as a risk for cervical cancer in our previous study (Settheetham-Ishida et al., 2004). As for the HPV infection, an increased OR (3.03; 95%CI=1.42-6.58; *p-value* < 0.002) was observed when the subject had (a) a current smoking partner(s); we have thus confirmed passive or secondary smoking (Coker et al., 2002) to be a risk factor for high-risk type HPV infection. The association between sexual partner's smoking and HPV infection is explained by either inhalation of environmental smoke or exposure to smoke-related mutagens/carcinogens in semen (Tokudome, 1997) and also smoke-related agents have been detected in cervical mucus (Prokopczyk et al., 1997). Smoking, thus, might cause a local immunological depletion and the smoke components could favor HPV persistence (Poppe et al., 1995; Lazcano-Ponce et al., 2001). Moreover, smoking maintains cervical HPV infection longer and has a lower potential of clearing an oncogenic infection (Giulian et al., 2002). Since the women in this region rarely have a smoking habit, most of the exposure to smoke is passive but the cancer promotion is active in them.

Increased ORs for age at first sexual intercourse, number of parities, long-term use of oral contraceptive pills and sexual partner's smoking experience in the past were here observed, even though they did not statistically increase risk for HPV infection. Since these factors are associated with risk for cervical cancer (Settheetham-Ishida et al., 2004), together with multiple sexual partners and partner's smoking habit, they may share a role in development of cervical cancer. To decrease incidence of cervical cancer, prevention of HPV infection is indispensable and the present finding of multiple sexual partners and partner's smoking as risks for HPV infection, should be reflected in the public health planning in this region.

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